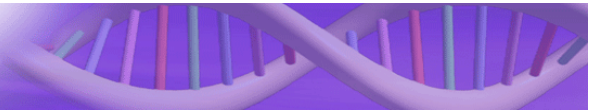


Detoxi Genomic Profile



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.

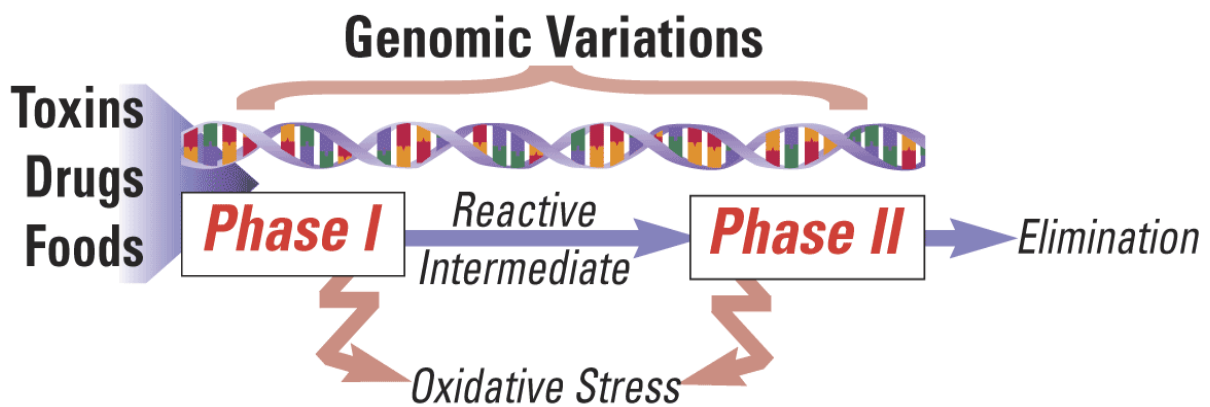
Toxic substances come from the environment, from the foods and medicines we consume, and from the body itself (natural waste products of metabolism). Examples include:

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

**Detoxi Genomic Profile
Personalized for**

BOB TEST

TEST TEST, MD



Your Detoxi Genomic 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.



GENOVATIONS™

Patient: **BOB**
TEST
Age: 37
Sex: M
MRN: TESTROBERT

Order Number: 34170491
Completed: October 17, 2002
Received: October 17, 2002
Collected: October 17, 2002

Security Code: 9752320

TEST WARD
TEST TEST MD
TEST
TEST, TE 11111

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.

<i>Cytochrome P-450</i>		
Result	Gene	internet information
✓	CYP1A1 *	www.genovations.com/gen01
●	CYP1B1 *	www.genovations.com/gen02
●	CYP2A6	www.genovations.com/gen10
✓	CYP2C9 *	www.genovations.com/gen05
✓	CYP2C19 *	www.genovations.com/gen06
●	CYP2D6	www.genovations.com/gen03
✓	CYP2E1	www.genovations.com/gen04
●	CYP3A4 *	www.genovations.com/gen07

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.

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.



GENOVATIONS™

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	Internet Information	Affects
+ -	COMT	V158M	www.genovations.com/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-acetyl transferase)				
SLOW METABOLIZER POLYMORPHISM				
Result	Gene	SNP Location	Internet Information	Affects
- -	NAT1	R64W	www.genovations.com/r64w	All Cells
- -	NAT1	R187Q	www.genovations.com/r187q	Liver/Gut
++	NAT2	I114T	www.genovations.com/i114t	Liver/Gut
- -	NAT2	A197Q	www.genovations.com/a197q	Liver/Gut
- -	NAT2	G286E	www.genovations.com/g286e	Liver/Gut
++	NAT2	R64Q	www.genovations.com/r64q	Liver/Gut
FAST METABOLIZER POLYMORPHISM				
+ -	NAT2	K268R	www.genovations.com/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	SNP Location	Internet Information	Affects
++	GSTM1	NULL	www.genovations.com/gstm1	Liver/Kidney
- -	GSTP1	I104V	www.genovations.com/gstp1	Brain/Skin
- -	GSTP1	A113V	www.genovations.com/a113v	Brain/Skin
++	GSTT1	NULL	www.genovations.com/gstt1	Liver

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	Internet Information	Affects
+ -	SOD1	G93A	www.genovations.com/g93a	Cytosol
+ -	SOD1	A4V	www.genovations.com/a4v	Cytosol
++	SOD2	A16V	www.genovations.com/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.
	NR	See commentary if applicable. (You inherit one chromosome from each parent)



This test has been developed and its performance characteristics determined by GSDL, 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.

Phase I Detoxification commentary is provided only for polymorphisms for which impaired activity is indicated by a red dot, ●

● **CYP1B1** www.genovations.com/cyp1b1

Health Implications: Cytochrome P450 1B1 converts estrogen into 4-hydroxy estrogen that may contribute to estrogen-sensitive carcinogenicity. CYP1B1 is also partially responsible for detoxifying polycyclic aromatic hydrocarbons (PAHs) products from the burning of organic materials, like car exhaust, cigarette smoke and charbroiled foods.

Minimizing Risk: Regular aerobic exercise is important. You should make soy foods (tofu, tempeh and soy beans) and cold water fish (salmon, mackerel, etc.) a regular part of your diet. Moderate consumption of red wine (i.e., 1-2 glasses per day) may be beneficial. Do not smoke. Avoid charbroiled and well-done meats. Minimize exposure to car and diesel exhaust. Avoid contact with industrial solvents.

Physician Recommendations:

● **CYP2A6** www.genovations.com/cyp2a6

Health Implications: Cytochrome P450 2A6 is responsible for detoxifying metabolism of nicotine, nitrosamines (from smoked meats), aflatoxin B1 (a mold found on peanuts) and numerous pharmaceuticals. Having this polymorphism may be mildly protective against developing lung cancer since nicotine is poorly metabolized and consequently people who smoke tend to smoke less.

Minimizing Risks: Even though this polymorphism is mildly protective, you still should not smoke as this increases your risk of lung cancer, emphysema and other diseases.

Physician Recommendations:

● **CYP2D6**

www.genovations.com/cyp2d6

Health Implications : Cytochrome P450 2D6 metabolizes ~25% of all prescription drugs including codeine, cholesterol-lowering drugs, many anti-depressants, beta-blockers and anti-psychotics. Slow metabolizers may experience side-effects at normal dosages. Therapeutic effectiveness is often achieved at significantly lower doses.

Minimizing Risks: Your health care provider has a list of drugs cleared through CYP2D6. Consult your physician. You may still need these drugs, but your physician may opt to prescribe a smaller therapeutic dose.

Physician Recommendations:

● **CYP3A4**

www.genovations.com/cyp3a4

Health Implications: Cytochrome P450 3A4 is used in the metabolism of 50-60% of all prescription medications, most of our steroid hormones (cortisol, estrogen, testosterone, etc.) and organophosphate insecticides (e.g., parathion). Activity of this enzyme can vary 10-fold between individuals due largely to genetic polymorphisms. Your test indicates that your CYP3A4 activity may be impaired, which may make you more susceptible to adverse drug reactions. Alterations in hormone metabolism may also make you more susceptible for developing prostate cancer.

Minimizing Risks: Avoid regular consumption of grapefruit juice. Consult with your health care provider before taking milk thistle. Your health care provider has a list of drugs cleared through CYP3A4. Consult your physician. You may still need these drugs, but your physician may opt to prescribe a smaller therapeutic dose.

Physician Recommendations:

Phase II Detoxification commentary is provided only for polymorphisms with known health implications.**+ - COMT** V158Mwww.genovations.com/v158m

Health Implications: Catechol-O-methyltransferase inactivates catecholamines and catechol drugs such as L-DOPA, epinephrine and norepinephrine. Reduced activity of COMT may play a role in some neuropsychiatric disorders. There is a moderate association with this polymorphism and late-onset alcoholism.

Minimizing Risks: Moderate alcohol consumption and seek help if alcohol consumption is a health issue.

Physician Recommendations:

++ NAT2 I114Twww.genovations.com/i114t**++ NAT2** R64Qwww.genovations.com/r64q

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 consistently reproducible 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:

+ - NAT2 K268Rwww.genovations.com/k268r

Health Implications: N-acetyltransferase 1 is found in extra-hepatic tissues, while N-acetyltransferase 2 is found predominantly in the liver and the gut. NAT2 is the enzyme that controls Phase II acetylation of numerous environmental toxins, including heterocyclic aromatic amines. Rapid acetylators increase O-acetylation of toxins that can actually make the toxins more reactive. These transformed toxins may increase risk of developing lung, colon, breast, bladder, head and neck cancer, though results have not been consistent in all studies. Colon cancer appears to have the most consistently reproducible association with fast acetylation.

Minimizing Risk: If you smoke, stop. Your risk of lung and breast cancer is substantially higher than someone with normal NAT activity. Do not eat fried foods and minimize red meat as these substantially increase your risk of colorectal cancer. Avoid well-done meats as these may substantially increase your risk of breast cancer. 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:

++ GSTM1 GSTM1www.genovations.com/gstm1**++ GSTT1** GSTT1www.genovations.com/gstt1

Health Implications: Glutathione-S-transferase affords protection against oxidative stress (especially by reducing hydrogen peroxide and by regenerating oxidized vitamins C and E). GST also detoxifies electrophilic compounds including solvents, herbicides, fungicides, polycyclic aromatic hydrocarbons and heavy metals (Hg, Pb, Cd). Decreased glutathione conjugation capacity may increase toxic burden and increase oxidative stress resulting in a greater risk for various cancers and fatigue syndromes, especially if exposed to toxic compounds.

Minimizing Risk: Liberally consume brassica vegetables (broccoli, cauliflower, kale, cabbage, bok choy, etc.) and allium vegetables (onions, garlic, shallots, etc.). Regardless of genotype, increasing the body's production of glutathione will reduce oxidative stress and afford greater protection against a wide array of toxins. Numerous supplements can help raise glutathione levels including liberal consumption of colorful vegetables and fruits, vitamin C, n-acetylcysteine and milk thistle. Vitamin E supplementation may also be helpful. Consult your health care provider to find the supplement regimen that best fits your overall health needs. If you smoke, stop. Avoid exposure to herbicides, fungicides, insect sprays and industrial solvents.

Physician Recommendations:

+ - SOD1	G93A	www.genovations.com/g93a
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+ - SOD1	A4V	www.genovations.com/a4v
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Health Implications: Superoxide dismutase is an anti-oxidant enzyme found inside cells. SOD1 converts reactive oxygen species into less reactive hydrogen peroxide. While rare, SOD1 polymorphisms are associated with increased risk of familial amyotrophic lateral sclerosis (ALS). These polymorphisms are associated with increased oxidative stress.

Minimizing Risk: Liberal consumption of dietary antioxidants in colorful vegetables and fruits. Therapies that raise glutathione levels may also be helpful since glutathione works with SOD1 to prevent oxidative damage. Numerous supplements can help raise glutathione levels including vitamin C, n-acetyl cysteine and milk thistle. Vitamin E supplementation may also be helpful. Consult your health care provider to find the supplement regimen that best fits your overall health anti-oxidant needs.

Physician Recommendations:

++ SOD2	A16V	www.genovations.com/a16v
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Health Implications: Superoxide dismutase is an anti-oxidant enzyme found inside 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 protective and are associated with a decreased risk of Parkinson's disease, breast cancer and motor neuron disease, including sporadic amyotrophic lateral sclerosis (ALS). These polymorphisms are associated with decreased oxidative stress.

Minimizing Risk: Even so, liberal consumption of dietary antioxidants in colorful vegetables and fruits is recommended. Therapies that raise glutathione levels may also be helpful since glutathione works with SOD2 to prevent oxidative damage. Numerous supplements can help raise glutathione levels including vitamin C, n-acetylcysteine and milk thistle. Vitamin E supplementation may also be helpful. Consult your health care provider to find the supplement regimen that best fits your overall health anti-oxidant needs.

Physician Recommendations:

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

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.

Dr. Shashi Pawar
Technical Director

A handwritten signature in black ink that reads "Shashi Pawar". The signature is written in a cursive, flowing style.

GENOVATIONS™

Patient: **BOB TEST**
Age: 37
Sex: M
MRN: TESTROBERT

Order Number: 34170491
Completed: October 17, 2002
Received: October 17, 2002
Collected: October 17, 2002

Security Code: 9752320

TEST WARD
TEST TEST MD
TEST
TEST, TE 11111

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 coumarin and sulfonureas.
- (CYP2C19) detoxifies H2 blockers (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.
- (CYP2E1) detoxifies nitrosamines and ethanol (acetaldehyde).
- (CYP3A4) detoxifies over 50% of all prescription medications and most steroid hormones.

Cytochrome P-450		
Result	Gene	internet information
✓	CYP1A1 *	www.genovations.com/gen01
●	CYP1B1 *	www.genovations.com/gen02
●	CYP2A6	www.genovations.com/gen10
✓	CYP2C9 *	www.genovations.com/gen05
✓	CYP2C19 *	www.genovations.com/gen06
●	CYP2D6	www.genovations.com/gen03
✓	CYP2E1	www.genovations.com/gen04
●	CYP3A4 *	www.genovations.com/gen07

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.



GENOVATIONS™

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	Internet Information	Affects
+ -	COMT	V158M	www.genovations.com/v158m	Liver/Gut

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

Acetylation (N-acetyl transferase)				
SLOW METABOLIZER POLYMORPHISM				
Result	Gene	SNP Location	Internet Information	Affects
- -	NAT1	R64W	www.genovations.com/r64w	All Cells
- -	NAT1	R187Q	www.genovations.com/r187q	Liver/Gut
++	NAT2	I114T	www.genovations.com/i114t	Liver/Gut
- -	NAT2	A197Q	www.genovations.com/a197q	Liver/Gut
- -	NAT2	G286E	www.genovations.com/g286e	Liver/Gut
++	NAT2	R64Q	www.genovations.com/r64q	Liver/Gut
FAST METABOLIZER POLYMORPHISM				
+ -	NAT2	K268R	www.genovations.com/k268r	Liver/Gut

(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	SNP Location	Internet Information	Affects
++	GSTM1	NULL	www.genovations.com/gstm1	Liver/Kidney
- -	GSTP1	I104V	www.genovations.com/gstp1	Brain/Skin
- -	GSTP1	A113V	www.genovations.com/a113v	Brain/Skin
++	GSTT1	NULL	www.genovations.com/gstt1	Liver

(SOD SNP) SOD1 is present in the cytosol; SOD2 is present in the mitochondria. While polymorphisms are fairly rare, they have been associated with neurodegenerative disorders like ALS.

Oxidative Protection				
Result	Gene	SNP Location	Internet Information	Affects
+ -	SOD1	G93A	www.genovations.com/g93a	Cytosol
+ -	SOD1	A4V	www.genovations.com/a4v	Cytosol
++	SOD2	A16V	www.genovations.com/a16v	Mitochondria

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

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.

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.

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
	NR	See commentary if applicable.	
		(You inherit one chromosome from each parent)	

This test has been developed and its performance characteristics determined by GSDL, 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.

Phase I Detoxification commentary is provided only for polymorphisms for which impaired activity is indicated with a red dot, ●

● CYP1B1www.genovations.com/gen02

Health Implications: Cytochrome P450 1B1 converts estrogen into 4-hydroxy estrogen that may contribute to estrogen-sensitive carcinogenicity. CYP1B1 is also partially responsible for detoxifying polycyclic aromatic hydrocarbons (PAHs), products of the burning of organic materials, like car exhaust, cigarette smoke and charbroiled foods.

Minimizing Risk: Regular aerobic exercise is important. You should make soy foods (tofu, tempeh and soy beans) and cold water fish (salmon, mackerel, etc.) a regular part of your diet. Moderate consumption of red wine (i.e., 1-2 glasses per day) may be beneficial. Do not smoke. Avoid charbroiled and well-done meats. Minimize exposure to car and diesel exhaust. Avoid contact with industrial solvents.

Increase the 2-hydroxylation of estrogens:

- Indol-3-carbinol (I3C) or diindolylmethane (DIM)
- Fish oil (EPA/DHA)

Down-regulate CYP1B1 induction and expression:

- DHEA
- Hesperetin (a flavonoid)
- A daily glass of red wine may be beneficial

Physician Recommendations:

● CYP2A6

www.genovations.com/gen10

Health Implications: Cytochrome P450 2A6 is responsible for detoxifying metabolism of nicotine, nitrosamines (from smoked meats), aflatoxin B1 (a mold found on peanuts) and numerous pharmaceuticals. Having this polymorphism may be mildly protective against developing lung cancer since nicotine is poorly metabolized and consequently people who smoke tend to smoke less.

Minimizing Risks: Even though this polymorphism is mildly protective, you still should not smoke as this increases your risk of lung cancer, emphysema and other diseases.

Substrate	Inhibitor	Inducers
Nicotine Nitrosamines Halothane - anesthesia Methoxyflurane Valproic Acid Disulfram (Antabuse) Aflatoxin B1	Grapefruit juice Hepatitis A	Not Applicable

Physician Recommendations:

CYP2D6

www.genovations.com/gen03

Health Implications : cytochrome P450 2D6 metabolizes ~25% of all prescription drugs including codeine, cholesterol-lowering drugs, many anti-depressants, beta-blockers and anti-psychotics. Slow metabolizers may experience side-effects at normal dosages. Therapeutic effectiveness is often achieved at significantly lower doses.

The clinical significance of the CYP2D6 polymorphism includes adverse drug reactions to substrate medications, especially the statin medicines. Slow metabolizers have a mildly increased risk of acute leukemia.

Minimizing Risks: Your health care provider has a list of drugs cleared through CYP2D6. Consult your physician. You may still need these drugs, but your physician may opt to prescribe a smaller therapeutic dose.

Substrate	Inhibitor	Inducers
<p>Cimetidine (Tagamet) Codeine and Hydrocodone Fexofenadine (Allegra) Loratidine (Claritin) Tamoxifen</p> <p>Statins: simvastatin</p> <p>Antidepressants: SSRIs & Tricyclics Amitriptyline (Elavil) Clomipramine (Anafranil) Doxepin (Sinequan) Fluoxetine (Prozac) Imipramine (Tofranil)* Nortriptyline (Pamelor) Paroxetine (Paxil) Venlafaxine</p>	<p>Antipsychotics: Haloperidol (Haldol) Perphenazine (Etrafon, Trilafon) Risperidone (Risperdal) Thioridazine (Mellaril)</p> <p>Beta-Blockers: Metoprolol (Lopressor) Penbutolol (Levatol) Propranolol (Inderal)* Timolol (Blocadren)</p>	<p>Paroxetine (Paxil) Fluoxetine (Prozac) Sertraline (Zoloft) Fluvoxamine (Luvox) Nefazodone (Serzone) Venlafaxine (Effexor) Clomipramine (Anafranil) Cimetidine (Tagamet) Prolixin Haloperidol (Haldol) Perphenazine (Etrafon, Trilafon) Risperidone (Risperdal) Thioridazine (Mellaril) Quinidine Ritonavir (Norvir)</p> <p>Not Applicable</p>

An asterisk (*) indicates multiple pathways used for detoxification

Physician Recommendations:

● CYP3A4

www.genovations.com/gen07

Health Implications: Cytochrome P450 3A4 is used in the metabolism of 50-60% of all prescription medications, most of our steroid hormones (cortisol, estrogen, testosterone, etc.) and organophosphate insecticides (e.g., parathion). Activity of this enzyme can vary 10-fold between individuals due largely to genetic polymorphisms. Your test indicates that your CYP3A4 activity may be impaired, which may make you more susceptible to adverse drug reactions. Alterations in hormone metabolism may also make you more susceptible for developing prostate cancer.

Minimizing Risks: Avoid regular consumption of grapefruit juice. Consult with your health care provider before taking milk thistle. Your health care provider has a list of drugs cleared through CYP3A4. Consult your physician. You may still need these drugs, but your physician may opt to prescribe a smaller therapeutic dose.

Milk thistle has been shown in vitro to inhibit CYP3A4 activity. Caution should be exercised in prescribing it, especially if the patient is taking pharmaceuticals cleared through CYP3A4.

Slow metabolizers have a significantly increased risk (up to 6-fold) of developing prostate cancer. Polymorphisms are associated with higher clinical stage and grade of these cancers. Black men have the highest prevalence of both prostate cancer and of CYP3A4 polymorphisms.

Substrate		Inhibitor	Inducers
<p>Steroids: Corticosteroids Testosterone, Estraderm, Estrace</p> <p>Benzodiazepines Alprazolam (Xanax) Triazolam (Halcion)</p> <p>Ca⁺⁺ Channel Blockers: Carbamazepine (Tegritol) Cisapride (Propulsid)</p> <p>Macrolide Antibiotics: Clarithromycin Erythromycin (NOT Azithromycin)</p> <p>HMG CoA Reductase Inhibitors: Atorvastatin, Cerivastatin Lovestatin (Mevacor)</p>	<p>Protease Inhibitors: Ritonavir (Norvir) Saquinavir (Invirase) Indinavir (Crixivan) Nelfinavir (Viracept)</p> <p>Miscellaneous: Amitriptyline (Elavil)* Dexamethasone (Decadron) Diazepam (Valium)* Glyburide (Micronase) Ketoconazole (Nizoral) Terfenadine (Seldane) Verapamil (Calan, Isoptin) Sertraline (Zoloft) Venlafaxine (Effexor)</p>	<p>Azole Antifungals: Itraconazole (Sporonox) Ketoconazole (Nizoral) Fluconazol (Diflucan) Metronidazole (Flagyl)</p> <p>Antibiotics: Clarithromycin Erythromycin Cyclosporine Ritonavir Verapamil Grapefruit Juice Milk Thistle</p>	<p>Carbamazepine Dexamethasone Phenobarbital Phenytoin (Dilantin) Rifampin St John's Wort</p>

An asterisk (*) indicates multiple pathways used for detoxification.

Physician Recommendations:

Phase II Detoxification commentary is provided only for polymorphisms with known health implications.**+ - COMT** V158Mwww.genovations.com/v158m

Clinical Implications: Catechol-O-methyltransferase inactivates catecholamines and catechol drugs such as L-DOPA, epinephrine and norepinephrine. Reduced activity of COMT may play a role in some neuropsychiatric disorders. There is a moderate association with this polymorphism and late-onset alcoholism.

Individuals carrying M alleles have a decreased ability to clear catecholamines from neural synapses, that is believed to result in a decreased number of post-synaptic catecholamine receptors. While early research postulated a connection with developing schizophrenia, bipolar disorder and ADHD, further studies have not confirmed these associations. The M allele is associated with ultra rapid cycling bipolar disorder and anti-social behavior, violence, and suicide in schizophrenics.

Minimizing Risks : Moderate alcohol consumption and seek help if alcohol consumption is a health issue.

Caution should be exercised in prescribing catechol drugs - homozygote positives have a 4-fold reduction in COMT activity.

Physician Recommendations:

++ NAT2 I114Twww.genovations.com/i114t**++ NAT2** R64Qwww.genovations.com/r64q

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 consistently reproducible 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:

+ - NAT2 K268Rwww.genovations.com/k268r

Health Implications: N-acetyltransferase 1 is found in extra-hepatic tissues, while N-acetyltransferase 2 is found predominantly in the liver and the gut. NAT2 is the enzyme that controls Phase II acetylation of numerous environmental toxins, including heterocyclic aromatic amines. Rapid acetylators increase O-acetylation of toxins that can actually make the toxins more reactive. These transformed toxins may increase risk of developing lung, colon, breast, bladder, head and neck cancer, though results have not been consistent in all studies. Colon cancer appears to have the most consistently reproducible association with fast acetylation.

Minimizing Risk: If you smoke, stop. Your risk of lung and breast cancer is substantially higher than someone with normal NAT activity. Do not eat fried foods and minimize red meat as these substantially increase your risk of colorectal cancer. Avoid well-done meats as these may substantially increase your risk of breast cancer. 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:

++ GSTM1	GSTM1	www.genovations.com/gstm1
++ GSTT1	GSTT1	www.genovations.com/gstt1

Health Implications: Glutathione-S-transferase affords protection against oxidative stress (especially by reducing hydrogen peroxide and by regenerating oxidized vitamins C and E). GST also detoxifies electrophilic compounds including solvents, herbicides, fungicides, polycyclic aromatic hydrocarbons and heavy metals (Hg, Pb, Cd). Decreased glutathione conjugation capacity may increase toxic burden and increase oxidative stress resulting in a greater risk for various cancers and fatigue syndromes, especially if exposed to toxic compounds.

GST is critical for removing the cellular debris from free radical attacks: lipid peroxides, damaged DNA, proteins, etc. All GST isozymes act similarly but predominate in various tissues of the body.

GST polymorphisms should be seen as disease-modifying rather than disease-causing, likely via their role in cellular protection against cellular oxidative stress - a risk that appears to be additive with increasing numbers of polymorphisms to various isozymes. Thus, cancer susceptibility will be dependent not only on GST polymorphisms, but also on carcinogen exposure and on polymorphisms in other detoxification enzymes.

GST polymorphisms increase risk of lung, prostate, head and neck and melanoma cancers, as well as Hodgkin's and non-Hodgkin's lymphomas. Smokers with breast cancer and GST polymorphisms had higher levels of DNA adducts than either non-smokers or those without GST polymorphisms.

GST polymorphisms generally indicate a poorer prognosis in cancer and chronic diseases. Ovarian cancer and malignant melanoma have decreased response to chemotherapy; while multiple sclerosis and cystic fibrosis also have poorer prognoses with GST polymorphisms.

Minimizing Risks: Liberally consume brassica vegetables (broccoli, cauliflower, kale, cabbage, bok choy, etc.) and allium vegetables (onions, garlic, shallots, etc.). Regardless of genotype, increasing the body's production of glutathione will reduce oxidative stress and afford greater protection against a wide array of toxins. Numerous supplements can help raise glutathione levels including liberal consumption of colorful vegetables and fruits, vitamin C, n-acetylcysteine and milk thistle. Vitamin E supplementation may also be helpful. Consult your health care provider to find the supplement regimen that best fits your overall health needs. If you smoke, stop. Avoid exposure to herbicides, fungicides, insect sprays and industrial solvents.

Rule out heavy metal burden using hair, blood, or urine elemental analysis. Whole blood glutathione levels may be monitored.

Physician Recommendations:

+ - SOD1 G93A

www.genovations.com/g93a

+ - SOD1 A4V

www.genovations.com/a4v

Health Implications: Superoxide dismutase is an anti-oxidant enzyme found inside cells. SOD1 converts reactive oxygen species into less reactive hydrogen peroxide. While rare, SOD1 polymorphisms are associated with increased risk of familial amyotrophic lateral sclerosis (ALS). These polymorphisms are associated with increased oxidative stress.

Minimizing Risk: Liberal consumption of dietary antioxidants in colorful vegetables and fruits. Therapies that raise glutathione levels may also be helpful since glutathione works with SOD1 to prevent oxidative damage. Numerous supplements can help raise glutathione levels including vitamin C, n-acetyl cysteine and milk thistle. Vitamin E supplementation may also be helpful. Consult your health care provider to find the supplement regimen that best fits your overall health anti-oxidant needs.

Physician Recommendations:

++ SOD2 A16V

www.genovations.com/a16v

Health Implications: Superoxide dismutase is an anti-oxidant enzyme found inside 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 protective and are associated with a decreased risk of Parkinson's disease, breast cancer and motor neuron disease, including sporadic amyotrophic lateral sclerosis (ALS). These polymorphisms are associated with decreased oxidative stress.

Minimizing Risk: Even so, liberal consumption of dietary antioxidants in colorful vegetables and fruits is recommended. Therapies that raise glutathione levels may also be helpful since glutathione works with SOD2 to prevent oxidative damage. Numerous supplements can help raise glutathione levels including vitamin C, n-acetylcysteine and milk thistle. Vitamin E supplementation may also be helpful. Consult your health care provider to find the supplement regimen that best fits your overall health anti-oxidant needs.

Physician Recommendations:

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 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.

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