



63 Zillicoa Street
Asheville, NC 28801
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Patient: **SAMPLE
PATIENT**

DOB:




Sex:


MRN:



Apo E	Apolipoprotein E : CHOLESTEROL REGULATION
<p>Location: Chromosome 19 APOE APO E2: cys / cys APO E3: cys / arg APO E4: arg / arg Your Genotype:</p> <div style="display: flex; justify-content: center; gap: 10px;"> <div style="background-color: #90EE90; padding: 5px; border: 1px solid black; font-weight: bold; font-size: 1.2em;">2</div> <div style="background-color: #FFD700; padding: 5px; border: 1px solid black; font-weight: bold; font-size: 1.2em;">3</div> </div> <p>The two SNPs lead to 3 possible variants for each chromosome, known as ApoE2, E3, & E4.</p>	<p>Apolipoprotein E (Apo E) plays a key role in lipid metabolism by helping to remove dietary cholesterol (chylomicrons and VLDL) from the bloodstream.</p> <p>Health Implications</p> <ul style="list-style-type: none"> · The E2/E3 genotype is common, accounting for 10-15% of most populations. · ApoE2 is associated with lower LDL-C and higher HDL-C, but also higher triglycerides (TGs). · Slightly increased risk of type 2 diabetes and diabetic nephropathy · ApoE2 is generally associated with lowest risk of atherosclerosis, MI and stroke; however, CAD and MI risk may increased with elevated TGs. · Tendency toward higher plasma C-reactive protein despite lower CV risk. · ApoE2 associated with reduced risk of osteoporosis and higher antioxidant activity. · The APOE-ε2ε3 genotype and the APOE-ε2 allele are associated with serum uric acid levels in Chinese subjects, indicating that individuals carrying the APOE-ε2 allele have a higher risk of hyperuricemia than non-carriers. <p>Clinical Management Considerations</p> <ul style="list-style-type: none"> · The cholesterol-lowering effect of a low saturated fat and low cholesterol diet is least effective with E2 individuals. · Minimize sugar and high-glycemic index foods, which produce the largest TG response in E2 carriers. · Fish oils may reduce TGs the most effectively in E2 carriers. · Alcohol may reduce LDL-C in men (neutral in women), but may increase risk of hemorrhagic stroke in men (at least in Asians). · Lipid response to statins, and triglyceride response to fibrates, are usually the best in E2 > E3 > E4; studies are mixed. · Gemfibrozil may help lower TGs and total cholesterol. · HT appears to improve the lipid profile in this genotype, although oral estrogen may significantly increase TGs.


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	
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<i>CETP</i>		<i>Cholesterol Ester Transfer Protein : CHOLESTEROL REGULATION</i>	
Location: Chromosome 16 TAQ1B Your Genotype:		CETP is a plasma glycoprotein that plays a major role in regulating levels of LDL- and HDL-cholesterol. Higher CETP activity tends to increase LDL-C, while decreasing HDL-C.	
		Health Implications <ul style="list-style-type: none"> · Highest CETP activity, increased LDL-C, small dense LDL particles and triglycerides (TGs); lower HDL and Apo-A1 in Taq1B (+) individuals · HDL-C is significantly reduced in these individuals who are smokers (> 20 cigarettes/day), have elevated triglycerides, or are overweight · Increased risk of coronary artery disease, hypertension, and cardiac events, including early MI in smokers 	
RSA I405V Your Genotype:		Clinical Management Considerations <ul style="list-style-type: none"> · A low-cholesterol, low saturated fat diet helps decrease LDL and VLDL · Bile sequestrants (e.g. cholestyramine), fiber, plant sterols, garlic, weight reduction, and exercise training help lower plasma CETP and cholesterol levels, LDL, and TGs; gemfibrozil lowers TGs · Alcohol may have less positive effect on HDL-C in Taq1B carriers; avoid smoking · Statins may be the most effective among individuals with this Taq1B genotype 	
			
D442G Your Genotype:			
			







<i>SELE</i>		<i>E-Selectin : CHOLESTEROL METABOLISM</i>	
Location: Chromosome 1q23 S128R Your Genotype:		E-selectin facilitates adhesion and infiltration of neutrophils through the endothelium into the arterial intima after NFκB-mediated inflammation, a critical and early event in the development of atherosclerosis.	
		Health Implications <ul style="list-style-type: none"> · Normal adhesion activity of E-selectin · Low risk of atherosclerosis and coronary artery disease 	
		Clinical Management Considerations <ul style="list-style-type: none"> · Ensure healthy anti-oxidant status to preventive up-regulation of E-selectin activity from oxidative stress 	







<i>MTHFR</i>		<i>5,10-methyltetrahydrofolate reductase : METHYLATION</i>	
Location: Chromosome 1 C677T Your Genotype:		5,10-methylenetetrahydrofolate reductase (MTHFR) is a key enzyme in folate metabolism, facilitating the formation of methyltetrahydrofolate, a required cofactor in the remethylation of homocysteine (Hcy) to methionine.	
		Health Implications <ul style="list-style-type: none"> · 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 	
A1298C Your Genotype:		Clinical Management Considerations <ul style="list-style-type: none"> · 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) 	
			



<i>GNB3</i>		<i>Guanine Nucleotide-binding Protein 2-3 : HYPERTENSION</i>	
Location: Chromosome 12 C825T Your Genotype:		G-proteins regulate cell-to-cell signal transduction in ~80% of cellular receptors. GNB3 influences cellular signal transduction and ion transport.	
		Health Implications <ul style="list-style-type: none"> · Lowest activity of G-proteins and "normal" signal transduction · Decreased risk of hypertension, atherosclerosis, obesity, and depression 	
		Clinical Management Considerations <ul style="list-style-type: none"> · Sibutramine (SNRI) produces greater satiety and weight loss · Less favorable response to anti-depressant medications · Decreased immune response to Hepatitis B vaccination, Hepatitis C response to interferon(a)/ribavirin, and anti-retroviral therapy in HIV 	

<i>AGTRI</i>		<i>Angiotensin II Receptor-1- HYPERTENSION</i>	
<p>Location: Chromosome 3 A1166C Your Genotype:</p>		<p>AGTR1 mediates the effects of angiotensin II including: contractility, vasoconstriction, vascular hypertrophy, inflammation & oxidative stress.</p>	
<p>  </p>		<p>Health Implications</p> <ul style="list-style-type: none"> · Increased sensitivity to AGT II, with increased risk/ severity of HTN · Increased risk of pre-eclampsia, especially if AGT (+/+) · Increased severity of coronary artery disease and kidney disease HTN, faster disease progression in chronic renal disease 	
		<p>Clinical Management Considerations</p> <ul style="list-style-type: none"> · Favorable BP response to resistance training and exercise · Reduction in arterial stiffness with ACE inhibitors; less favorable response to Ca channel blockers · Low-Sodium diet may improve BP response to losartan · Nutrients that minimize the effects of AGT II include: fish oils, borage seed oil, magnesium, potassium, L-arginine and taurine 	

<i>GP3A PL(A)</i>		<i>Platelet Glycoprotein IIIa : COAGULATION</i>	
<p>Location: Chromosome 17 PL(A1)/ PL(A2) Your Genotype:</p>		<p>GP3A is a protein component of the platelet fibrinogen receptor IIbIIIa, playing a pivotal role in platelet aggregation and thrombus formation.</p>	
<p>  A1 A1</p>		<p>Health Implications</p> <ul style="list-style-type: none"> · Decreased platelet aggregability and decreased risk of clot formation · Greater risk of perioperative bleeding due to longer bleeding time 	
<p>The GP3A polymorphism is a L33P change that results from the substitution of cytosine for thymidine at position 1565. Clinical studies commonly refer to this change as PL(A1) -> PL(A2).</p>		<p>Clinical Management Considerations</p> <ul style="list-style-type: none"> · Aspirin and oral platelet antagonists are most effective in this genotype · This genotype may be less sensitive to platelet - inhibiting effects of estrogen 	

<i>PAI-1</i>		<i>Plasminogen Activation Inhibitor-1 : COAGULATION</i>			
<p>Location: Chromosome 7 Del/Ins (4G/5G) Your Genotype:</p>		<p>PAI-1, present in platelets and vascular endothelium, decreases activation of plasminogen, inhibiting fibrinolytic activity and increasing clots.</p>			
<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="text-align: center; width: 50%; padding: 5px;">  4G </td> <td style="text-align: center; width: 50%; padding: 5px;">  5G </td> </tr> </table>		 4G	 5G	<p>Health Implications</p> <ul style="list-style-type: none"> · Higher PAI-1 levels and moderately increased risk of thrombosis · Possible increased risk of periodontitis, asthma and allergic disease, and PCOS · Slightly increased risk of obesity, especially in post-menopausal women 	
 4G	 5G				
<p>The PAI-1 polymorphism represents a single base-pair guanine (hence 5G->4G) in the promoter region. 5G is the norm and 4G is the variant or polymorphism.</p>		<p>Clinical Management Considerations</p> <ul style="list-style-type: none"> · Evaluate insulin resistance; thiazolidinediones and metformin tend to reduce PAI-1 · PAI-1 is reduced by weight reduction and regular exercise · Avoid smoking, which increases PAI-1 and risk of restenosis · Minimize stressors, high intake of saturated fat, and alcohol · ARBs reduce PAI-1 levels and ACE inhibitors are particularly effective in hypertensive patients with genotype · Hormone therapy and DHEA supplementation reduces PAI-1, decreasing clots post-menopausally · Nattokinase dissolves fibrin and inactivates PAI-1 			

<i>FACTOR II</i>		<i>Factor II (Prothrombin) : COAGULATION</i>			
<p>Location: Chromosome 11 G20210A Your Genotype:</p>		<p>Factor II is also known as prothrombin, which is converted to its active form, thrombin, and forms the essential part of a blood clot.</p>			
<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="text-align: center; width: 50%; padding: 5px;">  </td> <td style="text-align: center; width: 50%; padding: 5px;">  </td> </tr> </table>				<p>Health Implications</p> <ul style="list-style-type: none"> · Normal levels of prothrombin · No increased risk of venous thromboembolism 	
					
		<p>Clinical Management Considerations</p> <ul style="list-style-type: none"> · None indicated 			

<i>FACTOR V</i>		<i>Factor V (Leiden) : COAGULATION</i>	
Location: Chromosome 1 R506Q Your Genotype:		Factor V combines with Factor X to convert prothrombin to thrombin, the essential part of a blood clot. Factor Va is held in check by Protein C.	
		Health Implications <ul style="list-style-type: none"> · Normal inactivation of Factor V by activated Protein C · No increased risk of venous thromboembolism 	
		Clinical Management Considerations <ul style="list-style-type: none"> · None indicated 	

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

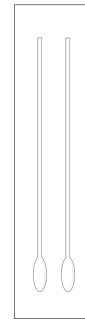
3. Test Requisition Form with Payment

- Test Requisition Form is complete - Test is marked, Patient's first and last name, date of birth, gender, date of collection
- Test requisition is placed in the collection kit envelope.
- Payment is included

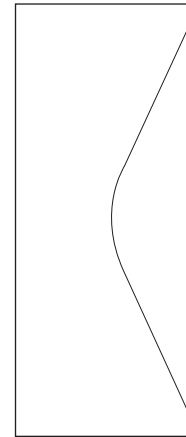
This specimen collection kit can be used for the following tests:

- 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



Collection Kit Package

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

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.



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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.

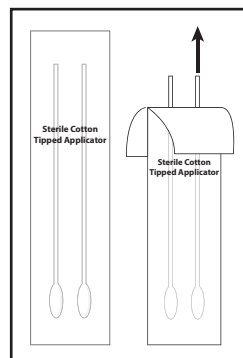


figure 1



figure 2

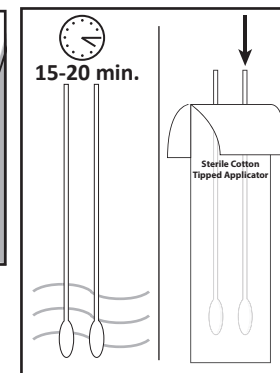


figure 3A

figure 3B

(REPEAT FIGURES 1 - 3)

