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Patient: JANE
DOE
DOB: December 16, 1965
Sex: F
MRN:

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<i>Apo E</i>	<i>Apolipoprotein E : CHOLESTEROL REGULATION</i>
<p>Location: Chromosome 19 APOE APO E2: cys / cys APO E3: cys / arg APO E4: arg / arg Your Genotype:</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 APO E2/3 genotype is common, accounting for 10-15% of most populations · APO E2 is associated with lower LDL cholesterol and higher HDL-C, but higher triglycerides (as found in Metabolic Syndrome) compared to the other genotypes · APO E2 also confers a lower risk of atherosclerosis, myocardial infarction, stroke, and osteoporosis, and higher antioxidant activity
<p>2 3</p>	<p>Treatment Options</p>
<p>The two SNPs lead to 3 possible variants for each chromosome, known as ApoE2, E3, & E4.</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 high-glycemic index foods, which produce the largest triglyceride (TG) response in E2 carriers · Dietary fiber, fish oils, and exercise generally improve the lipid profile in this genotype; fish oils reduce TGs most effectively in E2 individuals · Alcohol may reduce LDL-C in men (neutral in women) · E2 individuals generally respond the most favorably to statins and would therefore likely respond to statin mimetics such as inositol hexaniacinate, red rice yeast, and policosanol · Gemfibrozil may be particularly effective at lowering TGs and total cholesterol · HRT improves the lipid profile in this genotype, although oral estrogen may significantly increase TGs




Key


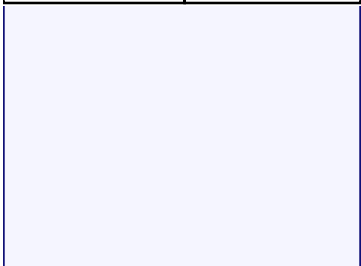
- - Neither chromosome carries the genetic variation.
- + - One chromosome (of two) carries the genetic variation.
- + + Both chromosomes carry the genetic variation.





(You inherit one chromosome from each parent)



- + ↑ Gene activity increased
- + ↓ Gene activity decreased





<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 Treatment Options <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
RSA I405V Your 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 Treatment Options <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 · Increased risk of elevated homocysteine, esp. if low levels of B vitamins · Possible methylation impairment, including disrupted neurotransmitter metabolism and synthesis of DNA, carnitine and coenzyme Q10 · Increased risk of autism, depression, schizophrenia, neural tube defects, cardiovascular disease, essential hypertension, diabetic retinopathy, osteoporosis, and cancers of the stomach · Low levels of vitamins B2, B6, B12, and/or folate often determines the risk of these associated disorders 	
A1298C Your Genotype:		Treatment Options <ul style="list-style-type: none"> · Ensure adequate intake of folate-rich green vegetables · Consider supplementation with folic acid (or folinic acid or 5-methyltetrahydrofolate), vitamins B2, B3, B6 (pyridoxal 5-phosphate), B12 (or methylcobalamin), and betaine (trimethylglycine) 	
 			



<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 	
		Treatment Options <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>AGTR1</i>		<i>Angiotensin II Receptor-1- HYPERTENSION</i>
Location: Chromosome 3 A1166C Your Genotype:		AGTR1 mediates the effects of angiotensin II including: contractility, vasoconstriction, vascular hypertrophy, inflammation & oxidative stress.
		Health Implications: <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
		Treatment Options: <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>
Location: Chromosome 17 PL(A1)/ PL(A2) Your Genotype:		GP3A is a protein component of the platelet fibrinogen receptor IIb/IIIa, playing a pivotal role in platelet aggregation and thrombus formation.
		Health Implications <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
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).		Treatment Options <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%;">  4G </td> <td style="text-align: center; width: 50%;">  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>Treatment Options</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%;">  </td> <td style="text-align: center; width: 50%;">  </td> </tr> </table>				<p>Health Implications</p> <ul style="list-style-type: none"> · Normal levels of prothrombin · No increased risk of venous thromboembolism 	
					
		<p>Treatment Options</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.	
		<p>Health Implications</p> <ul style="list-style-type: none"> · Normal inactivation of Factor V by activated Protein C · No increased risk of venous thromboembolism 	
		<p>Treatment Options</p> <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 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%.