



PATIENT:
Vpcaj Rxjgf
DOB: 09/27/46

ORDERING PROVIDER:
Dr. Ronald Hunninghake
Jtx-Ljpydn Hmp

LABORATORY INFORMATION:
Lab ID Number: 170126039HLA
Sample Collection Date: 01/24/17
Sample Test Date: 01/26/17
Report Date: 02/02/17

GENE MARKER	NORMAL/WILD TYPE	TEST RESULT	RISK ALLELE	ASSOCIATION	COMMENT
9p21	GG	GC	●	Plaque development in coronary arteries	Up to 25% increased risk of coronary heart disease or atherosclerosis
AGT	CC	TT	●	Blood Pressure	Often found to have increased risk of coronary heart disease
ENOS/ NOS3	GG	TT	●	Nitric Oxide Synthesis	May have reduced enzyme function and increased susceptibility to ischemic heart disease, ischemic stroke, hypertension, and myocardial infarction
MTHFR C677T / A1298C	CC/AA	CT/AC	⊙	Conversion of homocysteine to methionine	One copy of the C677T allele and one copy of the A1298C allele were detected which indicates 48% enzymatic activity. This genotype is unlikely to exhibit higher levels of homocysteine and likely no increased risk for thrombosis
Factor II	GG	AA	●	Clotting	Often found to have increased risk for thrombophilia, venous thromboembolism, and stroke
Factor V	GG	AA	●	Clotting	Often found to have increased risk for thrombophilia, venous thromboembolism, and stroke
APOE	E2/E2 E2/E3 E3/E3	E2/E3	○	Lipid transportation and Cholesterol levels	Decreased risk for cardiovascular disease. Although two copies of E2 can put someone at risk for the rare genetic condition hyperlipoproteinemia, one copy does not confer any risk
SLCO1B1*5	T/T	C/C	●	Statin metabolization	Decrease in ability to metabolize statins. Less likely to respond to statin therapy. Consider routine creatine kinase monitoring. High dose statin therapy may not be advisable

RISK ALLELE KEY: ○ No Risk ● Risk Allele Heterozygous ● Risk Allele Homozygous ⊙ Double Heterozygous ⊕ Double Homozygous



SCIENTIFIC DETAILS OF GENETIC MARKERS

❖ **9p21**

9p21 is one of the first identified and most researched risk factors associated with coronary artery disease. 9p21 is thought to reduce plaque formation in coronary arteries¹. Plaque build-up can lead to a condition called atherosclerosis in which the artery walls harden and the arteries vessels narrow. Both changes are dangerous for the cardiovascular system. Studies have shown that one copy of the risk allele increases the risk for development of coronary artery disease (CAD), and two copies of the risk allele double the risk for development of CAD¹.

❖ **AGT**

The AGT gene produces the precursor to angiotensin II, a protein that causes blood vessels to tighten and blood pressure to increase. Higher angiotensin II levels frequently result in higher blood pressure². The risk allele for this gene is associated with higher amounts of angiotensin and therefore an increased risk for poor cardiovascular health mainly in Caucasians³.

❖ **ENOS/NOS3**

This gene produces an important enzyme responsible for keeping the levels of nitric oxide in balance. Nitric oxide (NO) helps the blood vessels to relax and decrease blood pressure⁴. This enzyme also helps lower the amount of blood clots that form in blood vessels. The risk allele is associated with a form of the enzyme that does not work properly, resulting in lower levels of NO⁵. This risk allele may increase the risk of ischemic heart disease, ischemic stroke, and myocardial infarction in young patients⁶.

❖ **MTHFR C677T and A1298C**

This gene makes an enzyme called MTHFR that turns folic acid into folate, the chemical the body uses for many processes such as amino acid breakdown. MTHFR is also important because it keeps homocysteine amounts in a normal range. When homocysteine is high there is increased risk of ischemic stroke, thrombotic and cardiovascular disease⁷. People with the C677T or A1298C risk alleles can have low levels of folate and high levels of homocysteine⁸⁻¹⁰. Because diet and environment can also affect levels of folate, this condition does not always lead to high levels of homocysteine. People with the C677T risk allele have more trouble maintaining normal amounts of folate and homocysteine.

❖ **Factor II Prothrombin**

This gene helps to make an enzyme called thrombin that causes the blood to clot¹¹⁻¹³. The risk allele for this gene can increase the risk of forming blood clots in someone age 55 or older. Blood clots can cause strokes, which can lead to severe vascular injury and sometimes death.

❖ **Factor V**

The Factor V gene makes a protein called Human factor V¹⁴ which helps in forming blood clots. Having the risk allele for this gene means that factor V is always working therefore increasing the likelihood of more blood clots¹³⁻¹⁵. Blood clots can cause strokes which can lead to severe vascular injury and sometimes death.

❖ **ApoE**

The APOE gene makes a protein called apolipoprotein E (ApoE). There are three different types of this protein, called ApoE2, ApoE3, and ApoE4. The job of these proteins in the body is to help cholesterol and fat get into cells¹⁶. Some of the ApoE proteins are better at this transport process than others. Of the three types of proteins, ApoE4 has the hardest time transporting fat and cholesterol from the blood into the cell, thus leaving more fat and cholesterol circulating in the blood. The ApoE4 risk allele increases the risk of heart disease¹⁷. Two copies of the risk allele ApoE2 may increase the risk of developing type III hyperlipidemia, however this happens in less than 10% of cases¹⁶.

❖ **SLCO1B1*5**

This gene encodes for a protein called organic anion transporting polypeptide B1 (OATPB1), which helps the liver absorb certain chemicals¹⁸. One type of chemical that needs the help of the OATPB1 protein to be absorbed is a type of drug called statins¹⁸. The risk allele for OATPB1 reduces the liver's ability to absorb statins. This means less of the drug enters into the blood stream and therefore it has less clinical effect. In people who have this risk allele high dose statin drugs may be harmful and should be avoided¹⁸.



TREATMENT CONSIDERATIONS

1. **9p21**

Due to the association with increased plaque formation, treatment should focus on decreasing any factors that cause injury to blood vessels. Blood vessels are most frequently damaged as a result of inflammation. Consuming fish rich in n-3 polyunsaturated fatty acids (PUFA) at least twice a week is beneficial for decreasing vascular damage¹⁹. Fish containing high levels of these fatty acids, such as omega 3 and omega 6, are herring, salmon, mackerel and tuna. Fish oil supplements are also a source of the omega 3 and 6 fatty acids which make up PUFA. Resveratrol has also been shown in some studies to have protective effects on blood vessels²⁰.

2. **MTHFR**

Supplementation with methylated B vitamins is a consideration, including B-6 (in the form of P-5-P), methylated folate, and B-12. Increase foods in the diet that are high in folate; for instance green leafy vegetables such as kale, chard, spinach, lettuce, broccoli, asparagus, and also some beans such as lentils.

3. **Factor V Leiden and Factor 2 Prothrombin**

Omega 3 fatty acids help make blood platelets less likely to stick together; and fish oils are a good source of omega 3 fatty acids²¹. Fish oils should never be taken with blood thinners without a doctor's supervision.

4. **ApoE and SLCO1B1*5**

Fiber binds bile in the small intestines causing the body to use cholesterol to make more bile, and thus lowering cholesterol levels²². The daily recommended amount of fiber is 25-38 grams; the average American consumes about 15 grams a day through food²³. Supplementation should depend on diet, and fiber should always be taken with lots of water in order to avoid constipation. For ApoE - to lower triglycerides, the best recommendation is to decrease simple carbs in the diet²⁴.

CARDIAC HEALTH GLOSSARY

- ❖ **Genotype** – The entire set of genes in a cell
- ❖ **Allele** – Any of the alternative forms of a gene that may occur
- ❖ **Risk Allele** – A significant gene variant that can have an influence on health
- ❖ **Phenotype** – The observable properties of an organism that are produced by the interaction of the genotype and the environment
- ❖ **Receptor** – A structure on the surface of a cell (or inside a cell) that selectively receives and binds a specific substance
- ❖ **Mutation** – A permanent change in the nucleotide sequence of a gene
- ❖ **Wild Type** – The common or “normal” version of a gene



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