Haptoglobin Genotype

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MyGenetx Laboratory, LLC
4037 Rural Plains Cir., Suite 150, Franklin, TN 37064
CLIA ID: 44D2031868
Laboratory Director: Jack T. Pearson, M.D.

Patient Information		Ordering Provider	Sample Information	
Name:	SMITH, JANE	BD TEST	Specimen:	Dried Blood Spot
DOB:	01/01/1980	Imaware	Draw Date:	01/13/2020
Gender:	Female	3625 Willow Bend Blvd.	Accession Date:	01/13/2020
Patient ID:	2766D61E-1A3F-4756-BAF8-4	Suite 106	Report Date:	01/13/2020
Accession #:	20H000004	Houston, TX 7054		
Requistion #:	30044971			

Result

INTERMEDIATE RISK

Test Performed	Result
Haptoglobin	INTERMEDIATE RISK
Haptoglobin Genotype	Hp 1-2

Interpretation

The results of this Haptoglobin Genotype Test indicate that your patient isHp 1-2 and has intermediate additional risk for Cardiovascular Disease (CVD).

Comments

Significance: Haptoglobin genotype is a screening for diabetic patient at risk for cardiovascular disease (CVD). Haptoglobin (Hp) is an acute-phase protein that binds to freely circulating hemoglobin. Haptoglobin exists as two distinct forms, Hp1 and Hp2. The larger Hp2 form has been associated with cardiovascular events and mortality in individuals with type 2 diabetes. Haptoglobin allele frequency in European populations is 40% for Hp1 and 60% for Hp2. The expected genotype frequencies in the western world are 16% for Hp1-1, 48% for Hp1-2 and 36% for Hp2-2.

Risk: In patients with diabetes, the antioxidant capacity of Hp for glycosylated hemoglobin is reduced.

Consider: Haptoglobin genotype is a predictor of CVD in the diabetic population but not in the general population. Diabetic patients with the Hp2-2 genotype are 5 times more likely to have CVD than patients with Hp1 -1. Diabetic patients with Hp1-2 are 3 times more likely to have CVD than patients with Hp1-1.

The Haptoglobin genotype is performed by Real-Time PCR using a fluorescently labeled primerence assay. The clinical interpretation is a Laboratory Developed Test (LDT). The Haptoglobin Genotype test was developed and its performance characteristics determined by MyGenetx Laboratory (MGL), LLC. The laboratory is regulated under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) and is accredited to perform high-complexity clinical testing. The test has not been approved by the U.S. Food and Drug Administration. Such approval is not necessary. MGL is not liable for any outcomes arising from clinicians' treatment protocols and decisions.

*** Final Report ***

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Cardiology Genetic Plus Report for JANE SMITH

Patient:	SMITH, JANE	Accession #:	20H000004	Received Date:	1/13/2020
Gender:	Female	Report Date:	1/13/2020	Collection Date:	1/13/2020
DOB:	01/01/1980	Ordered By:	BD TEST	Specimen Type:	

Risk Management

Atrial Fibrillation

No increased risk of atrial fibrillation

The patient does not have a mutation in 4q25 variant rs2200733.

Unless other risk factors are present, noncarriers of 4q25 variant rs2200733 do not have an increased risk of atrial fibrillation.

No action is needed for this patient unless other cardiovascular risk factors are present.

Coronary Artery Disease

No increased risk for coronary artery disease

The patient does not carry the variants rs1333049 and rs1075278 within the 9p21 region.

Unless other risk factors are present, non-carriers of 9p21 rs1333049 and rs10757278 variants do not have an increased risk of coronary artery disease compared to the general population.

No action is needed for this patient unless other genetic and non-genetic risk factors (e.g., high blood pressure, smoking, diabetes, obesity, high blood cholesterol, excessive alcohol use) are present.

Type III Hyperlipoproteinemia

Not Associated with Type III Hyperlipoproteinemia

The patient is negative for both the APOE c.388 T>C (Cys130Arg) and c.526 C>T (Arg176Cys) mutations. The patient's genotype is wild-type, which is the most common genotype in the general population (frequency: >60%).

A patient with wild-type genotype does not have a defect in the apolipoprotein E (APOE), which is an integral structure of lipoprotein particles that have critical roles in blood lipid metabolism and transport. The APOE ε3/ε3 genotype is not associated with increased risk of cardiovascular disease.

No action is needed when a patient is normolipidemic.

GUIDANCE LEVELS		EVIDENCE LEVELS	
⊗	A medication has potentially reduced efficacy, increased toxicity or the patient has an increased risk for the indicated condition.	ACTIONABLE	Recommendations based upon publications by international pharmacogenetic expert groups, consortia or regulatory bodies (CPIC, DPWG, FDA, EMA). Recommendations are suitable for implementation in a clinical setting. Guidelines may change as knowledge arises.
⚠	Guidelines exist for adjusting dosage, increased vigilance or the patient has a moderate risk for the indicated condition.		
✓	The medication can be prescribed according to standard regimens or the patient's risk for the indicated condition is not increased.	INFORMATIVE	There are insufficient or contradictory findings documenting the impact of a given genetic polymorphism or drug interaction. Recommendations are informative and implementation in a clinical setting is optional.

Pharmacogenetic Test Results

Gene	Genotype	Phenotype	Clinical Consequences	Alleles Tested
4q25	rs2200733 C/C	Wild-type for rs2200733	The patient is non carrier of 4q25 variants and are not associated increased risk atrial fibrillation unless other cardiovascular risk factors are present.	rs2200733

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Patient:	SMITH, JANE	Accession #:	20H000004	Received Date:	1/13/2020
Gender:	Female	Report Date:	1/13/2020	Collection Date:	1/13/2020
DOB:	01/01/1980	Ordered By:	BD TEST	Specimen Type:	

9p21	rs10757278 A/A rs1333049 G/G	**No increased risk for coronary artery disease**	The patient does not carry the variants rs1333049 and rs10757278 within the 9p21 region. Unless other risk factors are present, non-carriers of 9p21 rs1333049 and rs10757278 variants do not have an increased risk of coronary artery disease compared to the general population.	rs10757278, rs1333049
Apolipoprotein E	ε3/ε3	**Normal APOE function**	Not associated with type III hyperlipoproteinemia - No increased risk of cardiovascular disease	ε2, ε4, (ε3 is reference)
KIF6	rs20455 A/A	**Homozygous for rs20455 A allele**	Preliminary studies suggests that this patient may have decreased but not absent risk of coronary artery disease.	rs20455

Disclaimer: These tests were developed and characterized by MyGENETX. It has not been cleared or approved by the U.S. Food and Drug Administration (FDA). The FDA has determined that such clearance or approval is not necessary.

All clinical decisions relative to test results should be directed by the patient's healthcare provider. MyGENETX makes no representations or recommendations in regards to results. Please consult your physician for all medical advice

Methodology: All SNP genotyping tests performed at MyGENETX. use the Applied Biosystems (ABI) TaqMan technology and the LifeTechnology Quant Studio 12K Flex platform. All PCR based methods are subject to rare interference such as inhibitors or quality or quantity of DNA. If present, the interference typically yields a no result requiring a repeat rather than an inaccurate one.

Lab CLIA #: 44D-2031868

Lab Director: Dr. Jack Pearson

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Translational Software Disclaimer: The information presented on this report is provided as general educational health information. The content is not intended to be a substitute for professional medical advice, diagnosis, or treatment. Only a physician, pharmacist or other healthcare professional should advise a patient on the use of the medications prescribed.

The pharmacogenetic assay involves use of reporting software and genotype-phenotype associations performed by Translational Software (www.translationalsoftware.com). The software has not been evaluated by the Food and Drug Administration. The software, and the report generated by the software, is not intended to diagnose, treat, cure, or prevent any disease. A qualified designee within the lab uses Translational Software to generate and subsequently review the report. The pharmacogenetic report is one of multiple pieces of information that clinicians should consider in guiding their therapeutic choice for each patient. It remains the responsibility of the health-care provider to determine the best course of treatment for a patient. Adherence to dose guidelines does not necessarily assure a successful medical outcome.

4q25 Monograph

Clinical Utility

Variants on 4q25 chromosomal region are associated with atrial fibrillation risk. This locus on 4q25 is also known as atrial fibrillation familial 5 (ATFB5). A genome wide association study replicated in several populations found a strong association between 4q25 variant rs2200733 and atrial fibrillation. No specific gene was identified in the 4q25 region to be associated with atrial fibrillation. However, the variant rs2200733 is located adjacent to gene PITX2.

Assay Interpretation

Variant rs2200733 at the 4q25 region is associated with increased risk of atrial fibrillation. The risk allele in rs2200733 variant is found in 30% of caucasian population and 70% of chinese population. The risk of atrial fibrillation increases by 1.7 times per copy of the risk allele in variant rs2200733 at 4q25 location. A critical point to be noted here is that even if a patient is carrying a risk allele in variant rs2200733 does not mean that the patient will suffer from atrial fibrillation.

Clinical Implications

Atrial fibrillation (AF) is the most common sustained cardiac rhythm disturbance, affecting more than 2 million Americans, with an overall prevalence of 0.89%. The most dreaded complication is thromboembolic stroke. A genomewide association scan found a strong association between sequence variants on chromosome 4q25, rs2200733 and atrial fibrillation. In chinese patients, there was a strong association between rs2200733 and lone atrial fibrillation than for atrial fibrillation associated with other cardiovascular diseases.

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9p21 Monograph

Clinical Utility

9p21 is an independent marker of cardiovascular risk. The 9p21 locus is also called as CHDS8 or coronary heart disease susceptibility 8. Genetic polymorphisms at 9p21 locus were amongst the first markers of increased cardiovascular disease and have been subsequently confirmed in different ethnic populations of European, Chinese, Japanese and Indian ancestry. However, the use of 9p21 has not been substantiated in African population.

Assay Interpretation

There are 2 most common polymorphisms at 9p21 locus rs1333049 (G>C) and rs10757278 (A>G). There are six different alleles resulting from combination of the two genetic polymorphisms. Population frequency for non-carriers is 27%, for heterozygous carriers is 50% and for homozygous carriers is 23%.

Clinical Implications

Non-carriers do not predict an increased risk of coronary artery disease. However, heterozygous mutant of 9p21 variant rs1333049 is associated with a 50% increased coronary artery disease risk and a twofold increased risk for homozygous carriers for early onset coronary artery disease. Also, the heterozygous mutations in rs10757278 are associated with a 40% increased risk, whereas the homozygous mutations are associated with 70% increased risk for abdominal aortic aneurysm. For coronary heart disease, the risk is increased by 30% and 60% in heterozygous and homozygous carriers. 9p21 locus does not predict the risk in African population.

References

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APOE Monograph

Clinical Utility

Apolipoproteins (APO) are structural constituents of lipoprotein particles that have critical roles in blood lipid metabolism and transport. Apolipoprotein E (APOE) is a major constituent of triglyceride-rich chylomicrons, very low-density lipoproteins (VLDL), and some subclasses of high-density lipoproteins (HDL). APOE acts as a lipid carrier and transports cholesterol from the cells in the blood vessel wall to the liver for excretion. It also binds to several cell surface receptors to support membrane homeostasis and injury repair in the brain. Defects in APOE can result in hyperlipidemia, which is an important risk factor in the genesis of atherosclerosis and subsequent development of cardiovascular disease (CVD).

Assay Interpretation

There are three common APOE alleles designated ε2, ε3, and ε4, resulting from combinations of the two common variants c.388T>C (rs429358, p.Cys130Arg) and c.526 C>T (rs7412, p.Arg176Cys). These alleles result in E2, E3, and E4 protein isoforms, respectively. The approximate allele frequencies for most populations are 8-12% for ε2, 74-78% for ε3, and 14-15% for ε4.

The reference ranges for both mutations of APOE are c.388T/T and c.526C/C. This is consistent with a ε3/ε3 genotype and a normal APOE function.

Clinical Implications

The apolipoprotein E3 is considered the normal isoform and is associated with normal lipid metabolism. The apolipoprotein E2 isoform shows defective binding of remnants to hepatic lipoprotein and delayed clearance from plasma. It is associated with a slower conversion of intermediate-density lipoproteins (IDL) to low-density lipoproteins (LDL), lower cholesterol, and higher triglycerides, compared to the normal apolipoprotein E3 isoform. The apolipoprotein E4 isoform results in the down regulation of the LDL receptor and is associated with increased total cholesterol, triglycerides, and LDL.

1 - Type III Hyperlipoproteinemia

Result Interpretation: APOE genotyping can be used to confirm the diagnosis of suspected type III hyperlipoproteinemia. Patients with symptoms (xanthomas) and with a lipid profile consistent with type III hyperlipidemia are candidates for APOE genotype analysis. Homozygosity for the APOE ε2 allele is strongly associated with type III hyperlipoproteinemia. Over 90% of individuals presenting the clinical type III hyperlipoproteinemia have the rare ε2/ε2 genotype. These individuals have an increased risk of premature vascular disease.

Only 1-5% of individuals with the APOE ε2/ε2 genotype develop type III hyperlipoproteinemia, suggesting that other genetic, hormonal, or environmental factors must contribute the expression of this disease. Despite the accumulation of remnants in the circulation, most (>95%) APOE ε2 homozygous subjects are normolipidemic or even hypolipidemic because of low LDL cholesterol levels. Other non-ε2/ε2 APOE genotypes (ε3/ε3, ε2/ε3 ε2/ε4 ε3/ε4 ε4/ε4) are not associated with type III hyperlipoproteinemia.

Summary: patients with a lipid profile (tendinous/tuberous xanthomas, elevated cholesterol, triglycerides, very low density lipoprotein (VLDL)) consistent with type III hyperlipoproteinemia are candidates for APOE genotyping. Most patients with type III hyperlipoproteinemia are homozygous for the APOE ε2 allele and homozygosity for ε2 allele is the only genotype associated with type III hyperlipoproteinemia. Factors in addition to the defective receptor binding activity of the apolipoprotein E2 isoform are necessary for manifestation of this disorder and only 1-5% of APOE ε2 homozygotes develop type III hyperlipoproteinemia.

2 - Atherosclerotic Cardiovascular Disease

Result Interpretation: genetic testing of APOE genotyping has been proposed for individual cardiovascular risk assessment and/or to predict the response to statin therapy. APOE genotyping can be informative in individuals with premature coronary heart disease or a family history of premature coronary heart disease. The APOE ε4 allele has been linked to pure elevations of low-density lipoproteins (LDL), and the ε4/ε4 and ε3/ε4 genotypes are associated with increased serum cholesterol levels.

Although the evidence is not fully consistent, it has been estimated that having the ε3/ε4 or ε4/ε4 genotype is associated with on average a 30-40% increased risk of cardiovascular disease relative to the common ε3/ε3 genotype.

There is some evidence that having an ε2/ε2 or ε2/ε3 genotype may be associated with a lower CVD risk in Caucasians normolipidemic patients. A proposed explanation of such observation is the association between APOE2 allele and lower Lp(a) concentrations.

Summary: the APOE ε4 allele results in the down regulation of the LDL receptor and is associated with increased total cholesterol, triglycerides, and LDL. Several studies indicate that the ε3/ε4, ε2/ε4 or ε4/ε4 genotypes are associated with increased plasma cholesterol levels. The presence of the ε3/ε4 or ε4/ε4 genotype has been suggested as a risk factor for atherosclerosis and coronary heart disease. Thus, the APOE genotype may be useful and informative in individuals with a family history of coronary heart disease as an additional tool for assessing their risk in conjunction with other clinical or laboratory findings. No clinical practice guidelines or position statements from U.S. professional associations were identified that recommended the use of APOE genotyping in cardiovascular risk assessment, including but not limited to the following: the 2013 American College of Cardiology/American Heart Association guidelines for the assessment of cardiovascular risk in asymptomatic patients; the 2009 U.S. Preventive Services Task Force (USPSTF) recommendations on the use of nontraditional risk factors for the assessment of coronary heart disease; the American Diabetes Association and the American College of Cardiology Foundation consensus conference publication.

References

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