Lifetime SCIENCES

Lifetime Sciences

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Cardiology Genetic Report for CARDIO RISK TEST

Patient:	**Cardio Risk TEST**	Accession #:	**Z001633**	Received Date:	**10/12/2018**
Gender:	**Unknown**	Report Date:	**10/15/2018**	Collection Date:	**10/12/2018**
DOB:	**1/1/2000**	Ordered By:	**J. Terry Pearson**	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

Slightly increased risk for coronary artery disease

The patient carries one mutation in each of the two variants of 9p21. There is a heterozygous mutation in 9p21 variant rs1333049 and a heterozygous mutation in 9p21 variant rs10757278.

The patient's genotype is associated with a 25 - 50% increased risk of coronary artery disease as compared to the general population.

Patient needs to be monitored for cardiovascular health and for other genetic and non-genetic cardiovascular risk factors such as diabetes, hypertension, high cholesterol and alcohol use.

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
9p21	rs10757278 G/A rs1333049 C/G	**Slightly increased risk for coronary artery disease**	The patient carries one mutation in each of the two variants of 9p21. There is a heterozygous mutation in 9p21 variant rs1333049 and a heterozygous mutation in 9p21 variant rs10757278. The patient's genotype is associated with a 25 - 50% increased risk of coronary artery disease as compared to non-carriers of the 9p21 variants.	rs10757278, rs1333049
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 Lifetime Sciences. 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. Kifetime Sciences makes no representations or recommendations in regards to results. Please consult your physician for all medical advice

Methodology: All SNP genotyping tests performed at Lifetime Sciences. 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.

References

1: Benjamin Shoemaker M, Muhammad R, Parvez B et al. Common atrial fibrillation risk alleles at 4q25 predict recurrence after catheter-based atrial fibrillation ablation. Heart Rhythm. 2013 Mar;10(3):394-400.2: Shi L, Li C, Wang C, et al. Assessment of association of rs2200733 on chromosome 4q25 with atrial fibrillation and ischemic stroke in a Chinese Han population. Hum Genet. 2009 Dec;126(6):843-9.3: Gretarsdottir S, Thorleifsson G, Manolescu A, et al. Risk variants for atrial fibrillation on chromosome 4q25 associate with ischemic stroke. Ann Neurol. 2008 Oct;64(4):402-9. 4: Gudbjartsson DF, Arnar DO, Helgadottir A, et al.Variants conferring risk of atrial fibrillation on chromosome 4q25. Nature. 2007 Jul 19; 448(7151):353-7.

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

1: Slavin TP, Feng T, Schnell A et al. Two-marker association tests yield new disease associations for coronary artery disease and hypertension. Hum Genet. 2011 Dec;130(6):725-33. 2: Wellcome Trust Case Control Consortium. Genome-wide association study of 14,000 cases of seven common diseases and 3,000 shared controls. Nature. 2007 Jun 7;447(7145):661-78. 3:Schunkert H, Götz A, Braund P et al. Repeated replication and a prospective meta-analysis of the association between chromosome 9p21.3 and coronary artery disease. Circulation. 2008 Apr 1;117(13):1675-84. 4: Helgadottir A, Thorleifsson G, Magnusson KP et al. The same sequence variant on 9p21 associates with myocardial infarction, abdominal aortic aneurysm and intracranial aneurysm. Nat Genet. 2008 Feb;40(2):217-24. 5: Roberts R, Stewart AF. 9p21 and the genetic revolution for coronary artery disease. Clin Chem. 2012 Jan;58(1):104-12.