The AYUMETRIX Cardiac Health Panel gives insight into how a patient’s genetic predisposition to cardiac problems can help healthcare providers optimize diagnosis and treatment.

Cardiovascular disease is a leading contributor to morbidity and mortality, with 17.3 million deaths annually worldwide. Risk increases in adults over age 60, and in part is attributable to our inherited genetic makeup. Cardiovascular disease – which includes coronary heart disease, cerebrovascular disease, peripheral artery disease, and atherosclerosis – is heavily influenced by factors such as insulin resistance, hypertension, dyslipidemia, inflammation, and coagulation properties. Many of these factors can be mitigated by lifestyle changes including smoking cessation, increasing aerobic exercise, and eating a well-balanced diet, which can reduce the risk of catastrophic events such as myocardial infarction, or ischemic and hemorrhagic stroke. However, in some cases, particularly where family history of cardiovascular disease is prevalent, medications are needed to better manage health outcomes. In some patients, lifestyle and medication are still not enough, and greater intervention is necessary.

Clinical Utility
The AYUMETRIX Cardiac Health Panel is designed to highlight confounding factors barring appropriate cardiovascular risk reduction in patients. The panel focuses on eight genetic markers affecting hypertension, total cholesterol, LDL (low-density lipoproteins) and HDL (high-density lipoproteins) cholesterol, triglycerides, thrombotic risk, homocysteinemia, insulin resistance, and statin-induced myopathy risk.

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Questions?
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OR
Email at info@ayumetrix.com
Genetic Markers Included:

1. **9p21** – The genetic marker 9p21 is located between two key cell-cycle inhibitor genes (cyclin-dependent kinase inhibitors) and is strongly associated with coronary artery disease. Researchers believe that mutations in this region may affect uncontrolled cell proliferation leading to atherosclerosis, and eventually coronary artery disease. Carrying one variant allele increases the risk of coronary artery disease by 25 percent, with the risk doubling in a person with two of these variant alleles.

2. **AGT** – Angiotensinogen (AGT) is a protein produced by the liver, which plays a role in the renin-angiotensin-aldosterone system (RAAS). This system is crucial for maintaining blood pressure and cardiovascular homeostasis, and is a target of many antihypertensive drugs. A mutation in the gene that codes for AGT may be associated with altered function of the AGT protein. A hyperactive RAAS resulting from genetic variants, in addition to environmental factors, can lead to coronary artery disease.

3. **APOE** – Apolipoprotein E (APOE) is a lipid/protein complex associated with chylomicron formation and the transport of dietary lipids via binding of the LDL (low-density lipoprotein) receptor. APOE is synthesized mainly in the liver, with a small amount of synthesis occurring in other organs such as the brain. There are three alleles of the APOE gene: E2, E3, and E4. E2 is a protective allele, and individuals with this variant have a reduced risk of coronary disease. E4 is the risk allele and is associated with increased cholesterol levels, as well as coronary disease, myocardial infarction, stroke, and Alzheimer’s disease.

4. **eNOS/NOS3** – Nitric oxide synthase (NOS) exists in three forms: neuronal, inducible, and endothelial. The form predominantly associated with cardiovascular health is the endothelial form, known as eNOS or NOS3. The eNOS/NOS3 gene regulates vascular nitric oxide production, which helps to regulate vasodilation, vascular repair, platelet aggregation and adhesion, reduction of vascular smooth muscle proliferation, and oxidation of low-density lipoprotein (LDL) particles leading to atherosclerotic plaques. The homozygous variant of eNOS/NOS3 is associated with decreased nitric oxide production and a higher rate of endothelial dysfunction, leading to an increased risk of hypertension, myocardial infarction, and stroke.

5. **Factor II (Prothrombin)** – Single nucleotide polymorphisms (SNPs) affecting the coagulation cascade have been implicated in many cardiovascular ailments, such as venous thrombosis, ischemic stroke, pulmonary embolisms, coronary artery disease, and myocardial infarction. Prothrombin G20210A is an inherited mutation that increases the likelihood of blood clot formation. The mutation is located in the untranslated region of the prothrombin gene, increasing the levels of circulating prothrombin, which is activated to thrombin in the bloodstream. Thrombin is a key protease enzyme in the coagulation cascade that converts fibrinogen into fibrin, a protein that polymerizes to form blood clots. The variant 20210A allele of the prothrombin gene significantly elevates thrombin generation, and increases risk for coronary disease, as well as embolisms.
6. Factor V Leiden – Factor V is part of the coagulation cascade, a multi-tiered interaction of proteins and co-factors responsible for proper blood clotting.\textsuperscript{18} Factor V is degraded by activated protein C in the absence of hemostasis. A mutation at position 1691 in the gene encoding factor V increases the protein’s resistance to degradation, thereby increasing the risk of venous thrombosis and thromboembolisms. Factor V Leiden Thrombophilia is the common and inherited blood clotting disorder associated with this genetic mutation that predisposes patients to thrombosis.\textsuperscript{16-18}

7. MTHFR – Methylene tetrahydrofolate reductase (MTHFR) is an enzyme that helps convert folate into the specific form of 5-methyltetrahydrofolate. The key metabolic role of this form of folate is to aid homocysteine conversion to methionine.\textsuperscript{19} Two common mutations in the MTHFR gene (C677T and A1298C) can result in reduced enzyme functionality,\textsuperscript{20} and may contribute to increased levels of homocysteine, a known risk factor for heart disease,\textsuperscript{21} atherosclerosis and venous thrombosis.\textsuperscript{22}

8. SLC01B1*5 – The SLC01B1 gene encodes a transporter that brings statin medications to the main tissues of the liver.\textsuperscript{23} The variant allele SLC01B1*5 affects the body’s ability to metabolize statins, impairing transport to the liver cells, and leading to higher systemic levels of the statin medication. Individuals who carry one or two copies of the variant allele have a reduced response to treatment for low-density lipoprotein (LDL) cholesterol (a risk factor for cardiac health), and with too much statin medication in the liver, an increased risk of statin-induced myopathy.\textsuperscript{23, 24} Knowing if the patient is a carrier for this variant allele allows for a modification of dosage level or selection of a different cholesterol-lowering medication to reduce the risk of adverse drug reactions.

Method
AYUMETRIX utilizes a variety of molecular biology techniques including Luminex, RT-PCR, Sanger Sequencing, and Next Generation Sequencing.

Tying it all Together
The genetic markers included in the AYUMETRIX Cardiac Health Panel have been rigorously analyzed by our experienced researchers. It is our mission to provide healthcare providers with a deeper understanding of the genetic basis of their patients’ cardiac health, to provide more timely and effective care.
References:


