

Learn how to interpret CardiaX Panel markers to **detect heart disease and related conditions early and accurately**, so you can implement clinical strategies based on your patient’s unique genetics.

	Gene	Metabolic Consequence—What is it?	Risk Associations with Polymorphisms/Variations	Clinical Implications/ Recommendations
Hypertension	ADRB2	B2 Adrenergic Receptor A receptor protein that binds with epinephrine to control smooth muscle relaxation.	Associated with: <ul style="list-style-type: none"> • Obesity and type 2 diabetes • High blood pressure • Ischemic stroke • Idiopathic thromboembolism • Asthma 	*Therapeutic Lifestyle Changes (TLC) for cardio-metabolic disease risk reduction, including: <ul style="list-style-type: none"> • Reduced sodium/<u>DASH diet</u> • Weight loss • High-fiber diet • Avoiding unhealthy fats • Alcohol moderation • Aerobic exercise
	Corin	A key enzyme in the biosynthesis of atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) , which regulates salt and water balance, intravascular volume, and blood pressure.	<ul style="list-style-type: none"> • Increased risk of hypertension and preeclampsia in pregnant women • Increased risk for cardiovascular disease (CVD) and congestive heart failure (CHF) 	<ul style="list-style-type: none"> • *TLC • Optimize dietary sodium/potassium ratio • Pregnant women: consult with a medical professional before making changes • ACE inhibitors or Angiotensin blockers

(continued on next page)

	Gene	Metabolic Consequence—What is it?	Risk Associations with Polymorphisms/Variations	Clinical Implications/ Recommendations
Hypertension (cont)	CYP1A2	Gene responsible for 95% of caffeine metabolism in the liver.	<p>Genetic polymorphisms can result in increased or decreased caffeine metabolism.</p> <p>Dose and age-related response:</p> <ul style="list-style-type: none"> Homozygotes are slower metabolizers than heterozygotes <p>Fast metabolizers</p> <ul style="list-style-type: none"> Decreased risk for hypertension (HTN) and myocardial infarction (MI) <p>Slow metabolizers</p> <ul style="list-style-type: none"> Represents 50% of the population Risk of hypertension and heart attack is directly based on amount of caffeine consumption and age Moderate increased risk for: <ul style="list-style-type: none"> HTN MI Congenital heart defects (CHD) Tachycardia Stiff aorta Pulse wave velocity Aortic insufficiency Vascular inflammation Increased catecholamines 	<p>Slow metabolizers should consume no more than 200 mg of caffeine per day, if any.</p> <p>Possible caffeine sources include:</p> <ul style="list-style-type: none"> Coffee, tea, soda, and other caffeinated beverages Chocolate Medications
	CYP11B2	Aldosterone Synthase The gene responsible for aldosterone synthesis in the adrenal glands.	<ul style="list-style-type: none"> Polymorphisms associated with increased aldosterone. Higher aldosterone levels increase blood pressure (BP) Increased risk for HTN and aldosterone enzyme disorder 	<ul style="list-style-type: none"> Spironolactone treatment for resistant hypertension. *TLC to reduce HTN
	ACE I/D	Angiotensin Converting Enzyme Enzyme found in the lungs that is a major player in the speed and regulation of renin-angiotensin-aldosterone system (RAAS).	<ul style="list-style-type: none"> Insertion/deletion genomics Mutation stimulates the RAAS Higher risk for CVD and MI Higher salt sensitivity Higher risk of HTN with sodium intake 	<ul style="list-style-type: none"> *TLC to reduce HTN and cardiometabolic disease risk Low sodium/DASH diet

(continued on next page)

	Gene	Metabolic Consequence—What is it?	Risk Associations with Polymorphisms/Variations	Clinical Implications/ Recommendations
Hypertension (cont)	CYP4A11	Gene that codes for an enzyme that produces a metabolite 20-HETE , an eicosanoid metabolite of arachidonic acid	<p>20-HETE is a potent vasoconstrictor and contributes to elevations in:</p> <ul style="list-style-type: none"> • Oxidative stress • Endothelial dysfunction <p>20-HETE also increases peripheral vascular resistance associated with some forms of hypertension—particularly salt-sensitive hypertension</p>	<ul style="list-style-type: none"> • Amiloride use in conjunction with other diuretics to control HTN • *TLC to reduce HTN
	CYP4F2	Codes for an enzyme that starts the process of inactivating and degrading Leukotriene B4 , a potent mediator of inflammation.	<p>Polymorphisms associated with:</p> <ul style="list-style-type: none"> • Decreased degradation of Leukotriene B4 • Higher levels of Leukotriene B4 • Increased inflammation • Increased risk of HTN and MI 	<ul style="list-style-type: none"> • *TLC • DASH diet
	AGTR1	Angiotensin II Receptor Type 1 Involved in the regulation of blood pressure and renal function.	Variations directly affect the RAAS system, which controls blood pressure, depending on potassium intake.	<ul style="list-style-type: none"> • Use ACE inhibitors and angiotensin blockers to control HTN • *TLC to control HTN • Optimize sodium: potassium ratio in diet

	Gene	Metabolic Consequence—What is it?	Risk Associations with Polymorphisms/Variations	Clinical Implications/Recommendations
Dyslipidemia and Metabolic Disease	ADRB2	<p>Beta-2 Adrenergic Receptor Interacts with epinephrine and adrenaline to indirectly control smooth muscle relaxation and bronchodilation.</p>	<p>Associated with:</p> <ul style="list-style-type: none"> • Obesity and type 2 diabetes • High blood pressure • Ischemic stroke • Idiopathic thromboembolism • Asthma 	<ul style="list-style-type: none"> • *TLC • Lots of plant-based foods
	ApoE	<p>ApoE is a gene that codes for Apolipoprotein E, produced primarily by the liver and brain.</p> <p>ApoE-containing lipoproteins transport lipids (fats) from the diet to other tissues for storage and transport cholesterol from those tissues to the liver for excretion.</p> <p>The genetic variation influences susceptibility to dietary fat and other lifestyle factors.</p> <p>There are three variations (alleles) of Apo E2, E3, and E4, and individuals carry two alleles for a variety of genetic combinations:</p> <ul style="list-style-type: none"> • E2/2 • E2/3 • E2/4 • E3/3 • E3/4 • E4/4 <p>E4 allele is found in 25% of the population and predisposes an individual to:</p> <ul style="list-style-type: none"> • Elevated levels of LDL cholesterol and triglycerides • Increased risk of atherosclerosis 	<ul style="list-style-type: none"> • ApoE e4 genotype (E3/4, E 4/4, or E3/e4) is associated with increased cholesterol, absorption rates, higher serum LDL, and delayed clearance • Increased CVD risk with smoking and alcohol intake • Reduced ability to repair vascular endothelium due to inability to activate Apo E2 receptor to produce nitric oxide (NO) • Lowered response to statin • Increased risk of CHD, CVD, MI, Alzheimer’s, and dementia 	<ul style="list-style-type: none"> • Individualized omega-3 treatment/supplementation • Diet low in trans fats, refined oils, and conventional saturated fats • Avoid refined, high glycemic foods • Diet high in plant-based foods and fiber • Apo E4’s: Avoid smoking and alcohol intake • Daily physical activity is particularly important for Apo E4’s • Simvastatin may be a better choice than statin therapy, as Apo E4’s are less responsive to statin therapy • May need to combine statins with other lipid-lowering agents

(continued on next page)

	Gene	Metabolic Consequence—What is it?	Risk Associations with Polymorphisms/Variations	Clinical Implications/ Recommendations
Dyslipidemia and Metabolic Disease (cont)	SCARB1	A liver protein receptor involved in HDL clearance .	<ul style="list-style-type: none"> HDL cannot attach to receptor for breakdown, leading to decreased HDL clearance and elevated levels of <i>dysfunctional</i> (nonprotective) HDL 	<ul style="list-style-type: none"> *TLC Exercise Moderate alcohol Healthy fats and oils
	1q25	Variation on chromosome position 1q25 . Important in: <ul style="list-style-type: none"> Cell proliferation and signaling Inhibition of apoptosis Insulin and glucose metabolism Incretin Enterocyte health Endothelial cell metabolism 	<ul style="list-style-type: none"> Reduced expression of glutamine synthase, which converts glutamic acid to glutamine Higher risk for diabetes and insulin resistance 	Optimize diet for glycemic control with: <ul style="list-style-type: none"> Exercise Low sugar/high fiber Low glycemic index Consider glutathione supplement
	ApoA1	Gene that provides instructions for making Apo A1 Lipoprotein Found on HDL lipoprotein and is involved with a reaction called cholesterol esterification that converts cholesterol to a form that can be fully integrated into HDL and transported through the bloodstream.	<ul style="list-style-type: none"> Results in impaired reverse cholesterol transport Dyslipidemia risk 	<ul style="list-style-type: none"> *TLC Increase in omega-3's Moderate alcohol consumption
	ApoA2	Gene that provides instructions for making Apo A2 lipoprotein , the second most abundant high-density lipoprotein particle.	Increased risk for obesity, dyslipidemia, and diabetes	*TLC
	ApoC3	ApoC3 protein is a component of VLDL . It inhibits lipoprotein lipase and hepatic lipase and is thought to delay catabolism of triglyceride-rich particles.	Results in increased levels of ApoC3, which can result in: <ul style="list-style-type: none"> Hypertriglyceridemia Dyslipidemia CHD NAFLD 	Aggressive management and treatment of lipids

	Gene	Metabolic Consequence—What is it?	Risk Associations with Polymorphisms/Variations	Clinical Implications/ Recommendations
Advanced Predictive Markers	9p21	<p>A chromosomal region for which there are 4 SNPs.</p> <p>Discovered in 2007 and said to be “a genetic revolution for cardiovascular disease”.</p> <p>Involved in regulation of inflammatory pathways and significantly correlated with adverse events independent of other lifestyle factors.</p>	<p>Associated with:</p> <ul style="list-style-type: none"> • Increased risk for inflammation • Plaque rupture • Thrombosis • Abdominal aortic aneurysm • Atherosclerotic cardiovascular disease • CHD • MI • Diabetes mellitus • Insulin resistance 	<ul style="list-style-type: none"> • Aggressive early detection, prevention, and risk factor control • Aggressive dietary management (anti-inflammatory) and emphasis on plant-based foods
	4q25	<p>Chromosomal regions with 2 SNPs.</p>	<ul style="list-style-type: none"> • Increased risk for atrial fibrillation and ischemic stroke 	<ul style="list-style-type: none"> • *TLC • Emphasis on sodium restriction (<1500 mg per day)
	6p24.1	<p>A gene that codes for a peptide that is a potent vasoconstrictor.</p>	<p>Increased risk for venous thrombosis and CHD</p>	<ul style="list-style-type: none"> • Early detection and preventative treatment • *TLC • Emphasize lower fat and high plant-based foods/fiber

	Gene	Metabolic Consequence—What is it?	Risk Associations with Polymorphisms/Variations	Clinical Implications/ Recommendations
Detoxification and Methylation	MTHFR	<p>Methylene Tetrahydrofolate Reductase Enzyme that catalyzes the methylation (activation) of folic acid to L methyl folate, which is involved in:</p> <ul style="list-style-type: none"> • Homocysteine clearance • And the formation of tetrahydrobiopterin (BH4), an important cofactor in the production of neurotransmitters, synthesis of nitric oxide, and detoxification of ammonia 	<p>2 SNPs possible: 677 and 1298</p> <p>Increased risk for:</p> <ul style="list-style-type: none"> • Endothelial dysfunction • Hypertension • Thrombosis • CVD • CHD • MI • Hyper-homocysteinemia • Neurological diseases such as depression and anxiety 	<ul style="list-style-type: none"> • Methylation treatment as appropriate • Emphasize foods high in dietary folate, vitamins B12, B6 and B2, zinc • TMG (trimethylglycine) or betaine supplement can be considered
	GSHPx	<p>Glutathione Peroxidase enzyme</p> <p>“Master detoxifier”</p> <p>Increased levels help lower BP and decrease risk for MI, LVH, and CHF</p>	<p>Low levels associated with:</p> <ul style="list-style-type: none"> • Decreased enzyme activity • Less detoxification • Increased risk for CVD 	<ul style="list-style-type: none"> • Supplementation with selenium and glutathione • *TLC • High antioxidant diet
	NOS3	<p>Nitric Oxide Synthase 3 Nitric oxide, an important molecule to quench free radicals, is synthesized by NOS from L-arginine</p>	<p>3 polymorphisms possible</p> <p>Leads to a decreased production of NOS and less nitric oxide availability, resulting in higher free radical accumulation</p>	<ul style="list-style-type: none"> • Nitric oxide precursor supplements • Upregulate nitric oxide with exercise (very important) • Diet high in dietary nitrates that act as precursors to nitric oxide (leafy greens, beets)

(continued on next page)

	Gene	Metabolic Consequence—What is it?	Risk Associations with Polymorphisms/Variations	Clinical Implications/ Recommendations
Detoxification and Methylation (cont)	COMT	<p>Catechol-o-Methyltransferase An enzyme that breaks down neurotransmitters</p> <p>Particularly prominent in the region of the brain that processes:</p> <ul style="list-style-type: none"> • Personality • Abstract thinking • Emotion • Aggressive behavior • Short-term memory 	<p>Variations result in reduced enzyme activity, leading to elevated norepinephrine and prolonged stimulation of sympathetic nervous system.</p> <p>May be at the root cause of aggression, anger, and hostility, and increased risk for HTN</p>	<ul style="list-style-type: none"> • Evaluate use of Vitamin E and aspirin based on COMT mutation. • Give aspirin or Vitamin E to met/met (A/A-homozygous mutant) but neither to val/met(G/A) nor val/val (G/G-homozygous wild)

*TLC: Therapeutic Lifestyle Changes

Diet Recommendations

- Limit refined carbohydrates from dietary sugar and processed grains
- Maximize plant-based fiber with a wide range of vegetables and fruits in a range of colors
- Optimize dietary sodium and potassium ratio
- Incorporate healthy dietary oils and fats as appropriate for energy requirements
 - Non-refined/expeller pressed oils such as olive and avocado oil
 - Foods that supply unsaturated fats, including olives, avocado, raw nuts and seeds, natural nut butters, and nut milks
 - Omega-3 fats from oily fish and plant-based sources
 - Saturated fats in moderation from high-quality sources such as grass-fed butter, game meats, eggs, grass-fed beef, organic dark meat chicken, cheese, coconut oil, and coconut milk
- NO hydrogenated or partially hydrogenated oils (trans fats)
- Consume high-quality protein as appropriate for energy requirements
- Consider prebiotic and probiotic food sources
- Choose organic foods recommended by the [Environmental Working Group](#)

Lifestyle Modifiers

- Tobacco cessation
- Exercise according to [ACSM \(American College of Sports Medicine\) guidelines](#)
- Adequate hydration with clean water
- Stress management
- Sleep hygiene

Abbreviations:

HTN = Hypertension

CVD = Cardiovascular Disease

RAAS = Renin Angiotensin-Aldosterone System

SNS = Sympathetic Nervous System

Published 2/22/2023