



# CardioGenomic® Profile



sample type: **BUCCAL or BLOOD**

**CardioGenomic® Profile** evaluates genetic variations, called single nucleotide polymorphisms (SNPs), in genes that modulate blood pressure regulation, lipid balance, nutrient metabolism, inflammation, and oxidative stress.

### The test uncovers potential genetic susceptibility to:

- Hypercholesteremia
- Atherosclerosis
- Obesity
- Hypertension
- Coronary Artery Disease
- Myocardial Infarction
- Thromboses
- Endothelial Dysfunction
- Stroke

### Cholesterol Regulation and Atherosclerosis

**ApoE** (apolipoprotein E)

**CETP** (cholesteryl ester transfer protein)

**SELE** (selectin E)

These genes affect how the body breaks down and clears fats and how cholesterol is processed. They also affect lipid balance, plaque formation, and blood vessel integrity and function.

### Methylation

**MTHFR** (methylenetetrahydrofolate reductase)

Polymorphisms of this enzyme can disrupt the metabolism of homocysteine, resulting in its accumulation as well as impaired methylation. The presence of these SNPs can increase risk of cardiovascular disease, blood vessel damage, thromboses (blood clots), stroke, and degenerative aging.

### Hypertension

**GNB3** (guanine nucleotide-binding protein)

**AGT** (angiotensin)

**AGTR1** (angiotensin II receptor-1)

Polymorphisms of these genes are associated with blood vessel constriction, sodium and water retention, obesity, and increased susceptibility to hypertension.

### Coagulation

**Factor 2** (prothrombin)

**Factor 5** (Leiden)

These genetic variants can over-activate blood clotting processes, increasing the risk of sudden cardiac events such as thromboses, heart attacks, and strokes.

### Reduction-Oxidation Balance

**CYBA\*8** (cytochrome b-245-alpha)

This genetic variant mediates the balance between oxidative stress and antioxidant defense in smooth muscle cells lining blood vessels.

#### • Specimen Requirements:

- **Buccal**—Two morning collections of mouthwash rinse (20 ml)  
or
- **Blood**—One 9 ml blood sample in EDTA tube

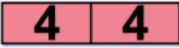
#### • Before Taking this Test:

- See instructions inside test kit for more details

## Cholesterol Regulation & Atherosclerosis

### APOE

Chromosome 19



CGTG [T? C] GCGG

GAAG [T? C] GCCT

[www.genovations.com/gcapo](http://www.genovations.com/gcapo)

**HEALTH IMPLICATIONS:** Apolipoprotein E (Apo E) plays a key role in lipid metabolism by helping to mediate the clearance of chylomicrons and VLDL remnants from dietary fat. APOE genotype has a significant influence on serum cholesterol and triglyceride concentrations. The APO E4/4 genotype is rare, usually accounting for less than 3% of a given population. An E4 allele is associated with a greater tendency toward elevated total- and LDL cholesterol and lower HDL-C. Risk is also significantly increased for atherosclerosis, myocardial infarction, stroke, and osteoporosis, as well as easier toxicity by heavy metals such as lead and mercury.

**MINIMIZING RISKS:** The effects of dietary fat and cholesterol on serum cholesterol levels is least with the E2 allele and greatest with the E4 allele. Restriction of saturated fat and cholesterol lowers total- and LDL cholesterol most effectively in E4 allele carriers. Avoid smoking and minimize high-glycemic index foods, both of which augment the E4-associated risk of coronary heart disease. Reduce excess weight, which synergizes with effects of the E4 allele on insulin and lipids. Fish oils and vigorous exercise should improve the lipid profile, dietary fiber only moderately so. Alcohol may raise LDL-C in men (neutral effect in women).

Statins are generally least effective at lowering total- and LDL cholesterol in E4 carriers (especially men). However, lipid profiles have been found to respond to probucol (now unavailable in the U. S. ). Since the E4 allele is associated with the lowest antioxidant activity, and probucol inhibits the oxidation and deposition of LDL-C, higher doses of mixed natural antioxidants may be helpful. Estrogen replacement appears to be particularly efficacious for both lipids and bone in postmenopausal E4 allele carriers. Consider vitamin K supplementation for bone protection.

**FURTHER EVALUATION:** EVALUATION: Since APO E polymorphisms affect cholesterol and triglyceride values, a comprehensive cardiovascular assessment is recommended, including TGs, cholesterol fractions, and independent risk factors. Bone density tests and regular bone resorption assessments are also warranted for detection of possible bone loss.

## Cholesterol Regulation & Atherosclerosis

### CETP

Chromosome 16



Multiple Loci

Taq1B [ + + ]

Rsa I [ + - ]

D442G [ - - ]

[www.genovations.com/gccetp](http://www.genovations.com/gccetp)

**HEALTH IMPLICATIONS:** Cholesteryl ester transfer protein helps regulate levels of LDL- and HDL-cholesterol by transferring cholesteryl esters from HDL to lipoproteins of lesser density such as LDL, IDL, and VLDL, and returning them from peripheral tissues to the liver. This Taq1B genotype is associated with higher CETP activity, LDL and small dense LDL particles, and lower levels of protective HDL and Apo-A1. HDL is especially suppressed in Taq1B homozygotes who smoke or who have elevated triglycerides (TGs), high body mass index, and/or central adiposity. Risk is also increased for coronary artery disease, cardiac events, hypertension and renal macroangiopathy. The Rsa1 polymorphism has been linked to lower CETP activity and higher HDL, yet increased risk of atherosclerosis. This risk may be limited to women and/or to individuals with high TGs (>165 mg/dL) or high intake of alcohol when (+/+).

**MINIMIZING RISKS:** A low-cholesterol, high polyunsaturated/saturated fat diet is most efficacious at reducing LDL and VLDL. Reducing excess weight and/or insulin resistance will help raise HDL and reduce small dense LDL. Avoid smoking, which raises CETP activity and suppresses HDL the most in Taq1B carriers. Although alcohol generally reduces CETP activity, it has negligible effects in these genotypes and may even be harmful to male Rsa1 homozygotes. Exercise training reduces CETP levels, in general, and may reduce lipids the most in Taq1B (+/+) individuals.

A recent meta-analysis suggests no significant impact of CETP genotype on response to statins. Gemfibrozil lowers TGs the most in Taq1B (+/+) men. CETP can be reduced by CETP inhibitors (e. g. , torcetrapib), garlic, and bile sequestrants (e. g. , cholestyramine or dietary fiber). Plant sterols (e. g. , beta sitosterol) reduce lipid levels by competing with cholesterol for intestinal absorption, and may be most effective in individuals with higher CETP activity.

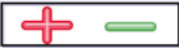
**FURTHER EVALUATION:** A comprehensive baseline cardiovascular assessment is recommended, as well as ruling out metabolic dysglycemia in overweight individuals.

## Cholesterol Regulation & Atherosclerosis

### SELE

Chromosome 1

S128R



CTGC [A? C] GTGG

[www.genovations.com/gcsele](http://www.genovations.com/gcsele)

**HEALTH IMPLICATIONS:** E-selectin is a glycoprotein expressed on the surface of endothelial cells following stimulation by inflammatory mediators (NF $\kappa$ B-mediated). E-selectin plays an important role in the adhesion and infiltration of white blood cells through the endothelium into the arterial intima, a critical and early event in the development of atherosclerosis. Polymorphisms in SELE increase the adhesion activity of E-selectin, resulting in increased risk of early severe atherosclerosis and coronary artery disease (CAD). Thrombin production during inflammation is also increased (thus increasing risk of coagulation), as well as risk of restenosis following angioplasty in individuals with CAD. Risk may be reduced for disease progression in "relapsing-remitting" multiple sclerosis patients.

**MINIMIZING RISKS:** The primary therapeutic aim is to decrease NF $\kappa$ B stimulation, which in turn will decrease SELE expression. NF $\kappa$ B inhibitors include vitamins E and C, zinc, N-acetyl cysteine, alpha lipoic acid and other antioxidants, curcumin, resveratrol, green tea, stinging nettle, milk thistle, glucocorticoids, aspirin and other NSAIDs. Fish oils are inversely related to E-selectin levels. Avoid trans fats, which can increase levels by as much as 20%. Diets high in fruits, vegetables, legumes, fish, poultry, and whole grains are inversely related to E-selectin, whereas diets high in red- and processed meats, sugar, French fries, and refined grains show a positive correlation. Avoid smoking, which upregulates E-selectin expression in blood vessels. Weight loss reduces E-selectin in obese individuals. Both oral and transdermal estrogens reduce E-selectin in post-menopausal women.

**FURTHER EVALUATION:** A comprehensive oxidative stress analysis is indicated for assessing reduction-oxidation balance in the body.

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## Customized commentary includes:

### Health Implications

Outlines disease risks associated with specific SNP results

### Minimizing Risk

Suggests possible dietary, environmental, lifestyle, supplement, and pharmaceutical interventions to optimize genomic potential of patient

### Further Evaluation

Alerts to the potential for related physiological imbalances and the clinical need for follow-up assessment

## Related Phenotype Assessments

### Baseline:

To assess baseline expression of genetic tendency

### Follow-up:

To regularly monitor therapeutic interventions that modify genetic expression

- **Comprehensive Cardiovascular Profile 2.0**
- **Amino Acids Analysis (plasma or urine)**
- **Elemental Analysis (hair, urine, or packed erythrocytes)**

For test kits, clinical support, or more information contact:

Client Services

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More detailed publications with references are also available: [www.GDX.net](http://www.GDX.net)