CV Health Plus Genomics analyzes blood for state-of-the-art lipid markers and independent risk factors that illuminate the clinical complexity of cardiovascular disease (CVD) as well as a patient’s genomic predisposition to cardiovascular diseases. Together, these markers provide a thorough assessment of cardiovascular health status, revealing the biochemical environment and cardiogenomic risk associated with inflammation, lipid deposits, endothelial dysfunction, and clotting factors underlying cardiovascular disease.

The CV Health Plus Genomics is a comprehensive evaluation featuring an advanced lipid profile that utilizes NMR fractionation technology, inflammatory markers and a novel Insulin Resistance Score. It also includes an assessment of single nucleotide polymorphisms (SNPs) in 4 cardiovascular genes. These markers provide insight to clinically modify the expression of these genes.

Nearly 50% of all heart attack victims have normal levels of typical risk markers for CVD, including total cholesterol. This unique combination of advanced markers for cardiovascular disease helps physicians to identify up to 85% of individuals at risk for cardiovascular disease. In addition, the markers for cardiogenomic risk provide an understanding of genetic concerns related to cholesterol metabolism, methylation and clotting activity.

The CV Health Plus Genomics includes:

**Markers for Cardiogenomic Risk**
- Apolipoprotein E (APO-E) plays a key role in the metabolism of cholesterol and triglycerides.
- Methylenetetrahydrofolate reductase (MTHFR) is a key enzyme in folate metabolism. Two variants of the MTHFR polymorphisms result in reduced enzyme activity, impaired methylation, and increased risk of cardiovascular disease, stroke, abdominal aortic aneurysm, hypertension, and venous thrombosis.
- Factor II is also known as prothrombin. Polymorphisms of Factor II result in increased coagulability - and increased risk of venous thrombosis. Factor II SNP is also associated with increased risk of CVD, carotid atherosclerosis, atrial fibrillation, and MI (when other cardiovascular risk factors are present).
- Factor V (Leiden) is the name given to the variation of the gene that affects the conversion of prothrombin to thrombin. Individuals with this polymorphism have increased risk for coagulation and coronary artery disease, worsened by coexisting SNPs in Factor II or MTHFR.

**Advanced Markers for Cardiovascular Disease**
- LDL-Particle Number (LDL-P) is independent of the LDL cholesterol concentration. A person with normal LDL-C concentration and high LDL-P is still at high-risk for plaque build-up.
- Parathyroid hormone (Pth), Associated with hypercalcaemia, increased risk of CVD, and increased risk of cardiovascular disease, stroke, abdominal aortic aneurysm, hypertension, and venous thrombosis.
- Insulin Resistance Score is determined by lipid sub-fractionation.
Apolipoprotein E (Apo E) plays a key role in lipid metabolism by helping to remove dietary cholesterol (and triglycerides) from the bloodstream.

**Health Implications**
- The APO E4/4 genotype is the second most prevalent after E3/3 and accounts for >25% in most populations
- APO E4 confers a tendency toward higher total- and LDL-cholesterol and lower HDL-C
- Risk is also increased for atherosclerosis, myocardial infarction, stroke, and osteoporosis, as well as toxicity by heavy metals such as lead and mercury

**Treatment Options**
- Restriction of saturated fat and cholesterol lowers total- and LDL cholesterol the most effectively in E4 individuals
- Avoid smoking and minimize high-glycemic index foods, both of which augment E4-associated risk of coronary heart disease
- Reduce excess weight, which synergizes with effects of E4 on insulin and lipids
- Fish oils and exercise should improve the lipid profile, dietary fiber only moderately so
- Alcohol may raise LDL-C in men (neutral effect in women)
- Cholesterol responds only slightly to statin drugs in E4 carriers (especially in men)
- Estrogen therapy is particularly efficacious for both cholesterol and bone in postmenopausal E4 carriers
- Consider vitamin K supplementation for bone protection

---

**MTHFR**

5,10-methylene tetrahydrofolate reductase (MTHFR) is a key enzyme in folate metabolism, facilitating the formation of methylenetetrahydrofolate, a required cofactor in the remethylation of homocysteine (Hcy) to methionine.

**Health Implications**
- Homozygosity for 677 (+/+) results in 60-70% reduction in MTHFR enzyme activity
- Increased risk of high homocysteine, esp. if low levels of B2, B6, B12, or folate
- Possible methylation impairment, including disrupted neurotransmitter metabolism and synthesis of DNA, carnitine and coenzyme Q10
- Increased risk of autism, depression, bipolar disorder, schizophrenia, neural tube defects, cardiovascular disease, essential hypertension, atherosclerosis, diabetic retinopathy, osteoporosis
- Increased risk of cancers of the breast (esp. if prolonged estrogen exposure and/or low folic acid intake), stomach, pancreas (esp. if smoke or drink)
- Possibly decreased risk of colorectal cancer and lung cancer only when high folate status; otherwise increased risk
- Low levels of vitamins B2, B6, and B12, and/or folate often determines the risk of these associated disorders

**Treatment Options**
- Ensure adequate intake of folate-rich green vegetables; folate levels tend to be lower
- Consider supplementation with folic acid (or folic acid or 5-methyltetrahydrofolate), riboflavin, B6 (pyridoxal 5-phosphate), B12 (or methylcobalamin), and betaine (trimethylglycine); individuals with this genotype show the best homocysteine response to B-vitamin supplementation
- Easier toxicity and less clinical efficacy with methotrexate chemotherapy

---

**Key on following page**

© Genova Diagnostics - CLIA Lic. #34D0655517 - Medicare Lic. #34-8475

---

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

Client Services
Genova Diagnostics
63 Zillicoa St.
Asheville, NC 28801-1074
800-522-4762 • Fax: 828-252-9303

More detailed publications with references are also available: www.GDX.net