GENOVA DIAGNOSTICS

63 Zillicoa Street
Asheville, NC 28801

CV Health plus genomics

Patient: **SAMPLE PATIENT**
DOB:
Sex:
MRN:

3701 CV Health Plus Genomics- Plasma, Serum & Buccal Swab

Methodology: Chemiluminescent, Enzymatic, Immunoturbidimetric, NMR and PCR

Lipid Markers

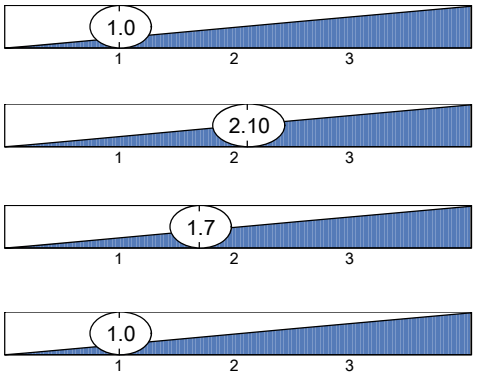
Cholesterol	Result	Reference Range
LDL- Cholesterol	90	< 100 mg/dL
HDL- Cholesterol	48	> 39 mg/dL
Triglycerides	147	< 150 mg/dL
Total Cholesterol	158	< 200 mg/dL

Particle Concentration & Size by NMR	Result		Reference Range
LDL-Particle # (LDL-P)	1,050	H	< 1,000 nmol/L
HDL-Particle # (HDL-P)	2.5	L	> 34.9 µmol/L *
LDL-Size	Large (Pattern A):		Small (Pattern B):
	23.0-20.6 *		20.5-19.0 *
	20.0		
Lp(a)	11		< 30 mg/dL

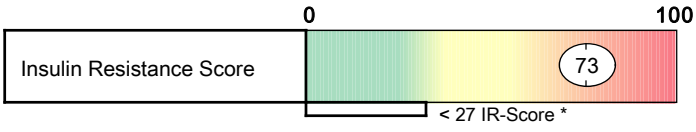
Independent Risk Factors

	Result		Reference Range
hs-CRP	0.89		< 1.00 mg/L
Lp-PLA 2 (PLAC)	245	H	< 225 nmol/min/mL
Fibrinogen	343		198-437 mg/dL
Homocysteine	8.8		3.7 - 10.4 µmol/L

Relative Risk for Cardiovascular Disease



Insulin Resistance Score by Lipid Fractionation



The Insulin Resistance Score combines Small LDL-Particle #, LDL Size, Large VLDL-Particle #, VLDL Size, Large HDL-Particle # and HDL Size to assess insulin resistance and diabetes risk.

HDL L	LDL S	VLDL L	HDL Size	LDL Size	VLDL Size
2.5	255	4.5	8.4	20.0	47.6
>7.3 µmol/L *	<117 nmol/L *	<0.9 nmol/L *	>9.6 nm *	>21.2 nm *	<42.4 nm *

Optimal | Borderline | Abnormal

Percentiles Apply to Biomarkers indicated with * and are performed using NMR technology.

Optimal: Either 0-25th or 75-100th percentile based on reference population.

Borderline: 25-75th Percentile

Abnormal: Inverse of Optimal (0-25th or 75-100th percentile distribution)

Apo E

Apolipoprotein E : CHOLESTEROL REGULATION

Location:
Chromosome 19
APOE
APO E2: cys / cys
APO E3: cys / arg
APO E4: arg / arg
Your Genotype:

3 4

The two SNPs lead to 3 possible variants for each chromosome, known as ApoE2, E3, & E4.

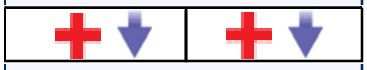
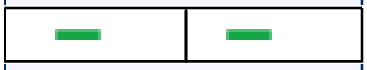
Apolipoprotein E (Apo E) plays a key role in lipid metabolism by helping to remove dietary cholesterol (chylomicrons and VLDL) from the bloodstream.

Health Implications

- The E3/E4 genotype is the second most prevalent after E3/E3, accounting for >25% in most populations.
- ApoE4 confers a tendency toward higher total- and LDL cholesterol, lower HDL-C.
- Increased risk of stroke (esp. among Asians), hypertension, and MI; also increased risk of cognitive impairment after stroke; generally lower CRP levels with E4 allele despite higher CV risk.
- ApoE4 allele may be an independent predictor of CAD and type 2 diabetes, especially in obese individuals and smokers.
- Increased risk of low BMD, oxidative stress, also easier toxicity by heavy metals such as lead and mercury
- ApoE4 may increase risk and disease severity of multiple sclerosis

Clinical Management Considerations

- Stress management: ApoE4 is associated with poor response to life stressors; prolonged stress contributes to memory decline.
- Restriction of saturated fat and cholesterol lowers total- and LDL cholesterol and CAD risk the most effectively in E4 individuals, also reduces risk of MI.
- Avoid smoking and minimize high-glycemic index foods, both of which augment E4-associated risk of CHD.
- Alcohol may raise LDL-C in men (neutral effect in women), increase IL-6 levels, and fail to raise HDL-C.
- Reduce excess weight, which synergizes with effects of E4 on insulin and lipids.
- Fish oils may lower triglycerides but increase LDL-C in E4 carriers; mixed studies.
- Antioxidants may help to counteract low antioxidant tissue levels; anti-inflammatory agents help preserve cognitive function.
- Lipid response to statins, and triglyceride response to fibrates, are usually the most positive in E2 > E3 > E4; studies are mixed.
- Estrogen therapy is particularly efficacious for both cholesterol and bone in postmenopausal E4 carriers.

MTHFR	5,10-methyltetrahydrofolate reductase : METHYLATION
Location: Chromosome 1 **C677T** **Your Genotype:**  **A1298C** **Your Genotype:** 	5,10-methylenetetrahydrofolate reductase (MTHFR) is a key enzyme in folate metabolism, facilitating the formation of methyltetrahydrofolate, 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, which can limit methylation reactions in the body · Increased risk of high homocysteine, esp. when low levels of B vitamins, mainly folate; several studies also indicate a tendency for lower folate levels · Most studies suggest increased risk of venous thrombosis, heart disease, hypertension, stroke and diabetic nephropathy; population differences may reflect the influence of B vitamin fortification, which lowers Hcy · Several studies show moderately increased risks of depression and schizophrenia · Most studies suggest increased risk of birth defects in the offspring, e.g., neural tube or congenital heart defects, cleft lip and/or palate, and Down syndrome; possible increased risk of recurrent pregnancy loss and male infertility in Asians · Possible slight increased risk of fracture and/or low bone density; in some studies these associations depend on B vitamin status, while others show no associations · Increased risk of gastric and esophageal cancer, which may be reversed with adequate folate intake; some studies show higher risk of breast, lung, and cervical cancer in Asians · Decreased risk of colorectal cancer, but only when high folate status; decreased risk of acute lymphoblastic leukemia in children and Caucasians; and decreased risk of cervical cancer in Caucasians **Clinical Management Considerations** · Ensure adequate intake of dark-green leafy vegetables and other B vitamin-rich foods · Consider supplementation with folic acid (or 5-methyltetrahydrofolate, which bypasses the MTHFR step), B2, B6 (pyridoxal 5-phosphate), B12 (or methylcobalamin), and betaine (trimethylglycine) · Most studies suggest easier toxicity from chemotherapy

FACTOR II

Location:
Chromosome 11
G20210A
Your Genotype:

Factor II (Prothrombin) : COAGULATION

Factor II is also known as prothrombin, which is converted to its active form, thrombin, and forms the essential part of a blood clot.

Health Implications

· Elevated levels of prothrombin, with 3.8-fold increased risk of venous thrombosis; risk increases 20-fold if coexisting Factor V Leiden SNP

· Increased chance of atherosclerosis, atrial fibrillation, and heart attack

· Slightly increased risk of pre-eclampsia during pregnancy

Clinical Management Considerations

· Avoid oral contraceptives, HRT, and smoking

· Platelet activation inhibitors include: fish oils, garlic, onions, ginger, ginkgo biloba, thyme, rosemary, genistein, and aspirin

· Glycyrrhizin (licorice) inhibits conversion of prothrombin to thrombin

FACTOR V

Location:
Chromosome 1
R506Q
Your Genotype:

Factor V (Leiden) : COAGULATION

Factor V combines with Factor X to convert prothrombin to thrombin, the essential part of a blood clot. Factor Va is held in check by Protein C.

Health Implications

· Elevated levels of thrombin; 7-fold increased risk of clot formation

· Increased chance of heart attack and atherosclerosis

· Increased risk of miscarriage, pre-eclampsia, and placental abruption

Clinical Management Considerations

· Avoid oral contraceptives; risk of DVT increases 35-fold

· Avoid oral HRT, smoking, high homocysteine

· Platelet activation inhibitors include: fish oils, garlic, onions, ginger, ginkgo biloba, thyme, rosemary, genistein, and aspirin

· Glycyrrhizin (licorice) inhibits conversion of prothrombin to thrombin

· Exercise caution with hypertension

Key

- - Neither chromosome carries the genetic variation.
+ - One chromosome (of two) carries the genetic variation.
+ + Both chromosomes carry the genetic variation.

(You inherit one chromosome from each parent)

+ ▲ Gene activity increased
+ ▼ Gene activity decreased

This test has been developed and its performance characteristics determined by Genova Diagnostics, Inc. It has not been cleared or approved by the U.S. Food and Drug Administration.

Commentary is provided to the practitioner for educational purposes, and should not be interpreted as diagnostic or treatment recommendations. Diagnosis and treatment decisions are the responsibility of the practitioner.

The accuracy of genetic testing is not 100%. Results of genetic tests should be taken in the context of clinical representation and familial risk. The prevalence and significance of some allelic variations may be population specific.

Any positive findings in your patient's test indicate genetic predisposition that could affect physiologic function and risk of disease. We do not measure every possible genetic variation. Your patient may have additional risk that is not measured by this test. Negative findings do not imply that your patient is risk-free.

DNA sequencing is used to detect polymorphisms in the patient's DNA sample. The sensitivity and specificity of this assay is <100%.

The LP(a), Lp-PLA$_2$ (PLAC), hs-CRP, Homocysteine and Fibrinogen analytes have been cleared by the U.S. Food and Drug Administration, and are performed by Genova Diagnostics, Inc. All other assays are performed by LabCorp, 1447 York Court, Burlington, NC 27215, CLIA#34D0655059.

The reference range for homocysteine is based on the sex-specific 5th to 95th percentile values for men and women (20 to 39 years of age) in the NHANES nutritionally replete cohort. Annals of Internal Medicince 1999; 131 (331-338).

The methodology for Lp-PLA$_2$ (PLAC) has been changed to measure activity. Please note the reference range and relative risk for cardiovascular disease have been updated.