

Cardiovascular Disease

CVD StripAssays

Cardiovascular disease (CVD), the all-encompassing term for disorders of the heart and blood vessels, is a complex medical condition and the leading cause of death and disability in industrialized countries. The two major manifestations, atherosclerosis and venous thrombosis, are known to be caused by a complex interaction of multiple environmental and genetic parameters. Although separate pathophysiological entities, the two disorders are interrelated and share common risk factors, including advanced age, obesity, dislipidemia and diabetes.

The pathological process leading to atherosclerosis is characterized by endothelial dysfunction, hyperlipidemia, inflammation and hypertension. Polymorphisms in genes involved in these processes in combination with an unhealthy lifestyle (e.g. smoking, high-fat diet, physical inactivity) support thromboembolic events on disrupted atherosclerotic lesions in the vessel wall, the basic mechanism underlying myocardial infarction (MI) and ischemic stroke.

In the etiology of venous thromboembolism (VTE) additional transient or long-term adverse influences, such as immobilization, surgery, cancer or female hormone intake, as well as genetic variations in factors of the coagulation system play an important role.

A single genetic defect rarely exerts a dramatic effect in the development of CVD. Most gene variations contribute with minor effects, and the individual cardiovascular risk is related to a critical accumulation of detrimental polymorphisms acting in synergy with unfavourable environmental factors.



CVD StripAssays:

ViennaLab offers a range of reliable and convenient reverse-hybridization assays for the detection of 17 mutations and polymorphisms in 13 genes predisposing to atherosclerosis and venous thromboembolism.

Each StripAssay provides ready-to-use reagents for 20 tests. The entire assay can be accomplished in less than 6 hours, and may be carried out manually or largely automated.

Principle of the assay:

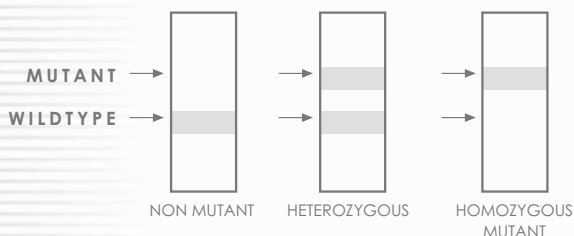
The CVD-related StripAssays are based on reverse-hybridization of biotinylated PCR products to a parallel array of allele-specific oligonucleotides immobilized on membrane teststrips. The StripAssays provide ready-to-use reagents for completion in four easy steps:

- Rapid and convenient isolation of genomic DNA from anticoagulated blood.
- Single multiplex PCR for the amplification of relevant sequences in the respective genes.
- Hybridization of biotinylated amplification products to oligonucleotide probes on the teststrip.
- Detection of specifically bound mutant and wild-type alleles by visible enzymatic color reaction.

Interpretation of results:

For each polymorphic position, one of three possible staining patterns may be obtained^{*)}:

1. wild-type probe positive: normal genotype
2. wild-type and mutant probe positive: heterozygous genotype
3. mutant probe positive: homozygous mutant genotype



^{*)} A special pattern applies for Apo E variants (see kit insert).



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Polymorphisms covered by ViennaLab CVD-related StripAssays:

Factor V (FV):

FV Leiden (G1691A; R506Q): leads to activated protein C resistance; occurs in 20-50% of patients with VTE; represents one of the most important genetic risk factors for inherited thrombophilia.

FV R2 haplotype (H1299R): mild risk factor for thrombosis; increases CVD risk for carriers of FV Leiden.

Prothrombin (PTH; Factor II) G20210A: the A allele is associated with increased prothrombin levels; carriers have about 3-fold elevated risk for cerebral and deep vein thrombosis; risk significantly increases in combination with FV Leiden.

5,10-Methylenetetrahydrofolate Reductase (MTHFR):

MTHFR C677T: the thermolabile variant (T allele) is associated with reduced enzyme activity and elevated plasma homocysteine levels in conjunction with folate deficiency; homozygosity predisposes to arterial and venous thrombosis in the presence of additional risk factors.

MTHFR A1298C: compound heterozygosity with C677T is also associated with reduced MTHFR enzyme activity.

Factor XIII (FXIII) V34L: the L variant has generally been assigned a protective effect against VTE.

Plasminogen Activator Inhibitor 1 (PAI-1, Serpin E1) 4G/5G:

the 4G allele is associated with higher PAI-1 transcription rates and considered to be a mild risk factor for VTE and MI.

Endothelial Protein C Receptor (EPCR):

EPCR 4600 A>G (A3 haplotype): carriers of A3 show higher soluble EPCR plasma levels and are predisposed to VTE and fetal loss.

EPCR 4678 G>C (A1 haplotype): homozygous A1 exerts a protective effect in carriers of FV Leiden.

Apolipoprotein B (Apo B) R3500Q: dominant but rare genetic defect causing severe hypercholesterolemia and elevated risk for atherosclerosis.

Apolipoprotein E (Apo E) E2/E3/E4: important predictors of the plasma lipid profile with E2 showing lowest and E4 showing highest LDL and total cholesterol levels; E4 allele is associated with increased susceptibility to early-onset MI, particularly in smokers.

Beta-Fibrinogen (FGB) -455 G>A: confers elevated β -fibrinogen plasma levels and increases risk for premature MI and ischemic stroke.

Human Platelet Antigen 1 (HPA1; Gp IIIa; integrin β 3) L33P (1a/b): HPA1b is a risk factor for early-onset MI and stroke, particularly in smokers.

Angiotensin-Converting Enzyme (ACE) 287 bp insertion/deletion (I/D):

D allele is associated with the elevated ACE activity and plasma levels; represents a risk factor for MI in elder patients and in smokers.

Endothelial Nitric Oxide Synthase (eNOS; NOS3):

eNOS -786 T>C: the C allele causes a higher susceptibility to coronary heart disease.

eNOS 894 G>T (Glu298Asp): the T allele confers an increased risk for premature MI.

Lymphotoxin Alpha (LTA) 804 C>A (Thr26Asn): is in almost complete linkage with 252A>G; both variants act strongly proinflammatory and are associated with coronary artery disease.

| Gene | Polymorphism | 4-330 | 4-340 | 4-350 | 4-290 | 4-260 | 4-360 | 4-370 | 4-280 |
|-------|-----------------|-------|-------|-------|-------|-------|-------|-------|-------|
| FV | G1691A (Leiden) | X | | | X | X | X | | |
| | H1299R (R2) | | | | | | X | | |
| PTH | G20210A | | X | | X | X | X | | |
| MTHFR | C677T | | | X | | X | X | | |
| | A1298C | | | | | | X | | |
| FXIII | V34L | | | | | | X | | |
| PAI-1 | 4G / 5G | | | | | | X | | |
| EPCR | A4600G (A3) | | | | | | X | | |
| | G4678C (A1) | | | | | | X | | |
| Apo B | R3500Q | | | | | | | X | |
| Apo E | E2 / E3 / E4 | | | | | | | X | X |
| FGB | -455 G>A | | | | | | X | | |
| HPA1 | a / b | | | | | | X | | |
| ACE | I / D | | | | | | X | | |
| | -786 T>C | | | | | | X | | |
| eNOS | G894T | | | | | | X | | |
| | -786 T>C | | | | | | X | | |
| LTA | C804A | | | | | | | X | |

FV StripAssay

Cat.no.: 4-330

PTH StripAssay

Cat.no.: 4-340

MTHFR StripAssay

Cat.no.: 4-350

FV-PTH Strip Assay

Cat.no.: 4-290

FV-PTH-MTHFR StripAssay

Cat.no.: 4-260

CVD StripAssay T

Cat.no.: 4-360

CVD StripAssay A

Cat.no.: 4-370

Apo E StripAssay

Cat.no.: 4-280

Further StripAssays are available or under development for:

Thalassemia (α -Globin, β -Globin), Familial Mediterranean Fever (FMF), Gaucher Disease, Haemochromatosis, Sugar Intolerance (lactose, fructose), Pharmacogenetics, Cancer.