

New Xpert™ HemosIL® FII & FV

*The First Fully Integrated, Real-Time PCR for
FII G20210A and FV Leiden Genotyping*

Hemostasis



**HemosIL: The Most Complete
Thrombophilia Panel**
Now with Molecular Technology

Thrombophilia Testing

Thrombophilia is defined as an increased risk or tendency to develop thrombosis as a consequence of pre-disposing factors that may be congenital (genetically derived) or acquired. A thrombus may form in either the venous or arterial vascular system. Venous thrombophilia is usually related to an abnormality of the coagulation system and may result in deep venous thrombosis (DVT) or pulmonary embolism (PE).

Historically, laboratory analysis for thrombophilia has consisted primarily of detecting deficiencies of Antithrombin, Protein C and Protein S, and testing for dysfibrinogenemia and antiphospholipid antibodies/lupus anticoagulants. However, in the last decade, discoveries have led to the testing of activated Protein C resistance with or without the Factor V (FV) Leiden mutation, hyperprothrombinemia attributable to the presence of the prothrombin gene mutation, G20210A, and hyperhomocysteinemia.

Risk Factors for Venous Thrombosis

Congenital	Acquired	Mixed/Unknown*
Antithrombin defect	Lupus Anticoagulants-APL syndrome	Hyperhomocysteinemia
Protein C defect	Pregnancy, oral contraceptive therapy, hormone replacement therapy	Elevated Levels of FVIII
Protein S defect	Immobilization	APC resistance in the absence of FV Leiden
FV Leiden	Previous thrombosis	
Prothrombin G20210A	Age	
Dysfibrinogenemia	Surgery, malignancy	

* Elevated levels of FIX, FXI, Prothrombin and TAFI are also reported as risk factors for venous thrombosis

Frequency and Relative Risk for Venous Thrombosis

Thrombophilic Trait	Frequency in Caucasian General Population* (%)	Frequency in Patients with VTE** (%)	Relative Risk of VTE (Case-controlled Studies)
FVL - Heterozygous - Homozygous	2.5 - 5 -	20 - 60 -	5 - 10 40 - 80
Prothrombin G20210A - Heterozygous - Homozygous	1 - 4 -	6 - 7 -	2 - 3 -
Protein C defect	0.2 - 0.4	3 - 5	5 - 10
Protein S defect	-	2 - 5	5 - 10
Antithrombin defect	0.02 - 0.05	1 - 2	10 - 20
Hyperhomocysteinemia	5 - 6	13 - 25	2 - 3

* The frequencies reported may vary according to the geographical distribution

** The frequencies reported may vary according to the patient selection

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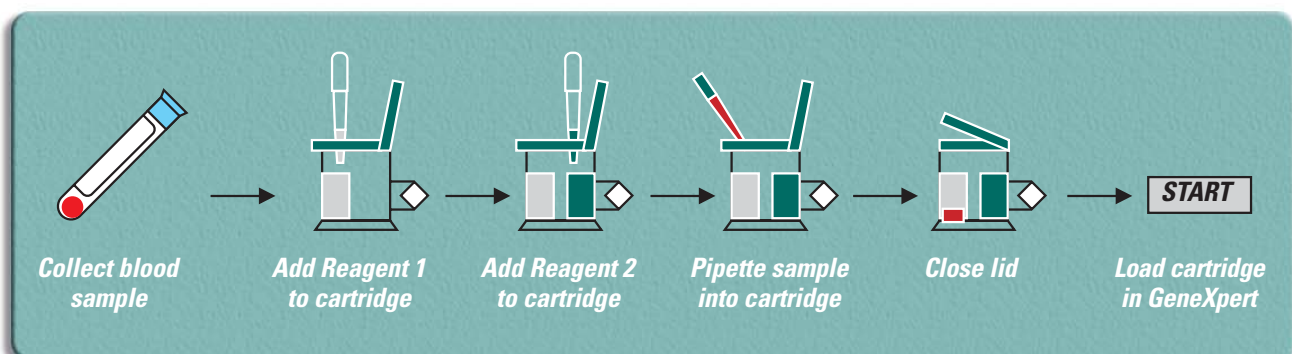
GeneXpert® Dx System

- Self-contained, fully integrated, real-time, automated PCR system
- From DNA extraction to result, in a single cartridge
- Up to 16 random-access, independent modules

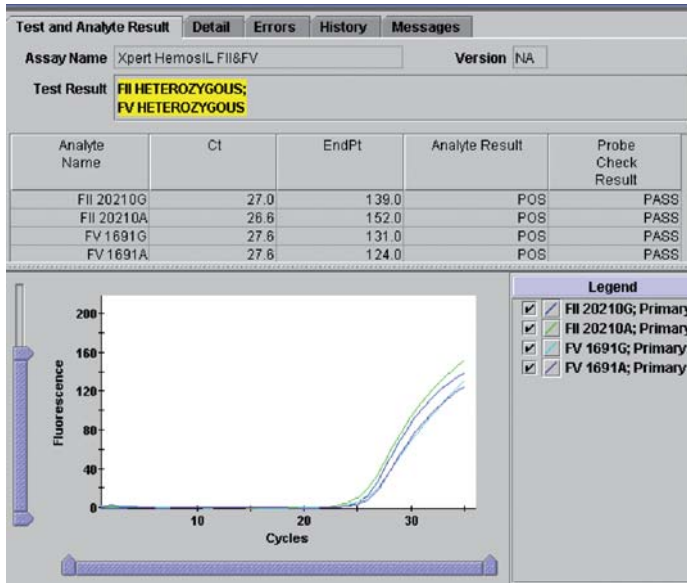
Xpert HemosIL FII & FV

- One cartridge = One sample
- Uses citrated or EDTA whole blood; fully integrated sample prep
- FII and FV testing, combined in a single cartridge
- Time to result ~ 30 minutes
- Self-controlled

Fast and Easy Prep



The Xpert HemosIL FII & FV kit is a qualitative *in vitro* diagnostic genotyping test for the rapid detection of Factor II (G20210A) and FV Leiden (G1691A) single-point mutations from sodium citrate or EDTA anticoagulated whole blood.



Technology

- Each cartridge contains freeze-dried beads with all the necessary components for PCR: DNA polymerase, nucleotides, primers and scorpions
- Scorpions include probes and primers specific for FII and FV normal and mutated DNA
- Each scorpion sequence is labeled with a specific fluorophore
- Through the PCR cycles, the specific binding of the scorpion sequence to the target mutation is detected by the system in real-time

GeneXpert software interprets amplification curves and delivers genotyping results.

Performance of Xpert HemosIL FII & FV Assay

The Xpert HemosIL FII & FV assay was compared with LightCycler® molecular tests on 348 patient samples in four different hospitals. The Xpert HemosIL FII & FV demonstrated 100% agreement with the reference method for both FII and FV mutations.

FII

		Reference Assay			
		Normal	Heterozygous	Homozygous	Total
Xpert HemosIL Assay	Normal	328	0	0	328
	Heterozygous	0	20	0	20
	Homozygous	0	0	0	0
	Total	328	20	0	348

FV

		Reference Assay			
		Normal	Heterozygous	Homozygous	Total
Xpert HemosIL Assay	Normal	296	0	0	296
	Heterozygous	0	48	0	48
	Homozygous	0	0	4	4
	Total	296	48	4	348



Self-contained, Fully Integrated, Real-time PCR Offers Efficiency for the Lab and Enhances Service to Physicians and Patients

- **Simple:**
 - DNA extraction, amplification and detection in one cartridge
 - No specialized personnel or lab facilities required
 - Run daily or weekly, with complete thrombophilia panel
- **Fast:**
 - FII and FV genotyping in approximately 30 minutes
 - No wait-time to obtain complete thrombophilia work-up
- **Cost-efficient:**
 - Avoids expensive "send-outs" to reference labs

Combine Xpert HemosIL FII & FV on the GeneXpert with HemosIL Assays on ACL TOP® Analyzers for a Complete Thrombophilia Work-up on the Same Citrated Sample

GeneXpert

- FII G20210A
- FV Leiden

ACL TOP Family

- Antithrombin
- Protein C (clotting)
- Protein C (chromogenic)
- Protein S (clotting)
- Protein S (antigen)
- Homocysteine
- Lupus Anticoagulants



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Xpert HemosIL FII & FV

Part Number	Kit Composition	Tests/Kit
460GXFIIFV-10	Ten FII & FV Combined Test Cartridges	Ten (FII and FV genotyping)

GeneXpert Dx System

Description (*)	Cartridges On-board
GeneXpert IV – one site with desktop computer	one
GeneXpert IV – one site with laptop computer	one
GeneXpert IV – two sites with desktop computer	two
GeneXpert IV – two sites with laptop computer	two
GeneXpert IV – four sites with desktop computer	four
GeneXpert IV – four sites with laptop computer	four

(*) For ordering information on GeneXpert systems, please contact your local Cepheid representative

References

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- Tripodi et al. Laboratory Investigation of Thrombophilia. *Clin Chem* 2001; 47:1597-1606.
- De Stefano et al. Screening for inherited thrombophilia: indications and therapeutic use. *Haematologica* 2002; 87:1095-1108.
- Caprini et al. Laboratory markers in the diagnosis of venous thromboembolism. *Circulation* 2004; 109(suppl I):I-4-I-8.
- ACMG Standards and Guidelines. Technical standards and guidelines: venous thromboembolism (Factor V Leiden and prothrombin 20210G>A testing): a disease-specific supplement to the standards and guidelines for clinical genetics laboratories. July/August 2005.
- Kubista et al. The real-time polymerase chain reaction. *Mol Aspects of Med* 2006; 27: 95-125.
- Cooper et al. An overview of methods for detection of Factor V Leiden and the prothrombin G20210A mutations. *Int J Lab Hematology* 2007; 29: 153-162.

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