Product Specification

Factor VIII (F8, Hemophilia A)

• F8 Genemer™ for F8 Exon Specific Amplification and Mutation Scanning by SSCP or Sequence Analysis

• GLF8 GeneProber™ for F8, Hemophilia A Intron 22 Inversion Genotyping by Southern Blot Analysis

For research use only. Not for use in diagnostic procedures for clinical purposes.

Background

Inherited factor VIII deficiency, commonly known as Hemophilia A, is an X-linked bleeding disorder affecting 1:5,000 men and results from a deficiency or abnormality in the activity of factor VIII (FVIII). Factor VIII deficiency is the result of heterogeneous mutations within the factor VIII gene (F8) located at Xq28. The molecular genetic analysis of hemophilia A has been complicated by the large size of the gene, its complex genomic organization, and the mutational heterogeneity exhibited by this disease. The F8 gene is 186-kb long, has 26 exons, and encodes a 9-kb mRNA. Due to the large size of the gene a high mutation frequency is observed resulting in approximately 20 to 30% of the sporadic cases (1-4).

Molecular Analysis

F8 gene inversions occur through recombination between a sequence located within intron 22 with one of usually two additional copies of homologous sequences that are located far from the *F8* gene near the telomere of the long arm of the X chromosome. *Gene inversions account for about 45% of the F8 mutations in severe hemophilia A*(1-3). The remaining mutations span the entire spectrum of mutations, including complete or partial gene deletions, large insertions, sequence duplications, frameshifts, splice junction alterations, non-sense mutations, and mis-sense mutations.

Non-gene inversion mutations can be screened by amplification of all the 26 exons and the promoter region followed by SSCP analysis by direct staining or silver staining and by direct sequencing (4).

Southern Based Intron 22 Inversion Analysis

Gene Link's GLF8-1 GeneProber™ detects F8 Intron 22 inversions.

F8 Mutation Scanning

Non-gene inversion mutations can be screened by amplification of all the 26 exons and the promoter region followed by SSCP analysis by direct staining or silver staining and by direct sequencing. Gene Link's F8 Genemer™ series primers can be used for mutation scanning.

Molecular Analysis Used in Hemophilia A

Severe Hemophilia A	Mild to Moderately Severe Hemophilia A	Genetic Mechanism	Test Type
45%		*F8* gene intron 22 inversion	Southern Analysis
Up to 45%		Gene deletions or rearrangements, frameshift, splice junction, nonsense or missense mutations	Mutation scanning or DNA sequencing of all amplified exons and promoter sequence.
	80-95%	Missense or occasionally splicing or in-frame deletion mutations	PCR amplification and mutation scanning or DNA sequencing
80-90% of families		Linkage analysis for F8	RFLP or PCR based linkage analysis

References

1. Antonarakis, S.E; Rossiter, J.P; Young, M; Horst, J; et al (1995) Factor VIII gene inversions in severe hemophilia A: results of an international consortium study. *Blood* 86:2206-12.
2. Windsor, S.; Taylor, S.M; and David Lillicrap, D. (1994) Direct Detection of a Common Inversion Mutation in the Genetic Diagnosis of Severe Hemophilia A. *Blood* 84:*2202-2205.*
3. Lakich, D.; Kazazian, H.H, Antonarakis, S.E, and Gitschier, J. (1993) Inversions disrupting the factor VIII gene are a common cause of severe haemophilia A. Nat Genet.;5:236-241.
4. Arruda, V.R; Pieneman, W.C; Reitsma, P.H; Deutz-Terlouw, P.P; Annichino-Bizzacchi, J.M; Briet, E. and Costa, F.F. (1995) Eleven Novel Mutations in the Factor VI11 Gene From Brazilian Hemophilia A Patients. *Blood* 86:3015-3020.

Gene Link™

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Factor VIII, Hemophilia A, F8 Product Ordering Information

GeneProber™ Probe

Product	Size	Catalog No.	Price, $
F8 GLF8-1 GeneProber™ Factor VIII, Probe unlabeled Factor VIII, Hemophilia A Intron 22 Inversion Genotyping by Southern Blot Analysis. Unlabeled probe for radioactive labeling and Southern blot detection. Suitable for random primer labeling.	500 ng	40-2036-40	350.00
F8 GLF8-Dig1 GeneProber™ Factor VIII, Probe Digoxigenin labeled Factor VIII, Hemophilia A Intron 22 Inversion Genotyping by Southern Blot Analysis. Digoxigenin labeled probe for non-radioactive labeling and Southern blot detection.	110 µl	40-2036-41	400.00

Genemer™ Primer pair for gene or mutation specific amplification. Special optimized conditions may be required for certain amplifications.

Product	Size	Catalog No.	Price, $
F8-Exon 01 Genemer™	10 nmols	40-2036-51	100.00
F8-Exon 02 Genemer™	10 nmols	40-2036-52	100.00
F8-Exon 03 Genemer™	10 nmols	40-2036-53	100.00
F8-Exon 04 Genemer™	10 nmols	40-2036-54	100.00
F8-Exon 05 Genemer™	10 nmols	40-2036-55	100.00
F8-Exon 06 Genemer™	10 nmols	40-2036-56	100.00
F8-Exon 07 Genemer™	10 nmols	40-2036-57	100.00
F8-Exon 08 Genemer™	10 nmols	40-2036-58	100.00
F8-Exon 09 Genemer™	10 nmols	40-2036-59	100.00
F8-Exon 10 Genemer™	10 nmols	40-2036-60	100.00
F8-Exon 11 Genemer™	10 nmols	40-2036-61	100.00
F8-Exon 12 Genemer™	10 nmols	40-2036-62	100.00
F8-Exon 13 Genemer™	10 nmols	40-2036-63	100.00
F8-Exon 14A Genemer™	10 nmols	40-2036-64A	100.00
F8-Exon 14B Genemer™	10 nmols	40-2036-64B	100.00
F8-Exon 14C Genemer™	10 nmols	40-2036-64C	100.00
F8-Exon 15 Genemer™	10 nmols	40-2036-65	100.00
F8-Exon 16 Genemer™	10 nmols	40-2036-66	100.00
F8-Exon 17-18 Genemer™	10 nmols	40-2036-67	100.00
F8-Exon 19 Genemer™	10 nmols	40-2036-68	100.00
F8-Exon 20 Genemer™	10 nmols	40-2036-69	100.00
F8-Exon 21 Genemer™	10 nmols	40-2036-70	100.00
F8-Exon 22 Genemer™	10 nmols	40-2036-71	100.00
F8-Exon 23 Genemer™	10 nmols	40-2036-72	100.00
F8-Exon 24 Genemer™	10 nmols	40-2036-73	100.00
F8-Exon 25 Genemer™	10 nmols	40-2036-74	100.00
F8-Exon 26 Genemer™	10 nmols	40-2036-75	100.00
F8-Exon Genemer™ Pack, Contains 10 nmols each of all F8 Genemer™	10 nmols	40-2036-10	$650.00

***Please visit www.genelink.com for other Genemer™ not listed here**

Genemer™ (Selected List) Primer pair for gene or mutation specific amplification. Special optimized conditions may be required for certain amplifications

Product	Size	Catalog No.	Price, $
Fragile X (spanning CGG triple repeat region)	10 nmols	40-2004-10	100.00
Huntington Disease (spanning CAG triple repeat region)	10 nmols	40-2025-10	100.00
Myotonic Dystrophy (spanning CTG triple repeat region)	10 nmols	40-2026-10	100.00
Friedreich's Ataxia (spanning GAA triple repeat region)	10 nmols	40-2027-10	100.00
Factor V	10 nmols	40-2035-10	100.00
Factor VIII (Hemophilia) Genemer™ Pack	10 nmols	40-2036-10	650.00
STS (Steroid Sulfatase)	10 nmols	40-2023-10	100.00
HGH (Human Growth Hormone)	10 nmols	40-2024-10	100.00
Sickle Cell	10 nmols	40-2001-10	100.00
RhD (Rh D gene exon 10 specific)	10 nmols	40-2002-10	100.00
Rh EeCc (Rh Ee and Cc exon 7 specific)	10 nmols	40-2003-10	100.00
Gaucher (various mutations)	10 nmols	40-2047-XX	100.00
Cystic Fibrosis (various mutations)	10 nmols	40-2029-XX	100.00
SRY (sex determining region on Y)	10 nmols	40-2020-10	100.00
X alphoid repeat	10 nmols	40-2021-10	100.00
Y alphoid repeat	10 nmols	40-2022-10	100.00

***Please visit www.genelink.com for other Genemer™ not listed here**

**The polymerase chain reaction (PCR) process is covered by patents owned by Hoffmann-La Roche. A license to perform is automatically granted by the use of authorized reagents.

Prices subject to change without notice **All Gene Link products are for research use only**

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