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Patient Report

Patient Age/Gender: Male

Specimen Collected: 19-Aug-21 15:38

Hemophilia A (F8) Comp Reflex **|Received: 22-Aug-21 09:32** **Report/Verified: 24-Aug-21 12:13**

Procedure	Result	Units	Reference Interval
Hemophilia A (F8) Interpretation	Negative [f1] [i1]		

Result Footnote

f1: Hemophilia A (F8) Interpretation

This result has been reviewed and approved by [redacted]

Test Information

i1: Hemophilia A (F8) Interpretation

BACKGROUND INFORMATION: Hemophilia A (F8) 2 Inversions with Reflex to Sequencing and Reflex to Deletion/Duplication

CHARACTERISTICS: Hemophilia A is characterized by deficiency of factor VIII clotting activity. Less than 1 percent factor VIII activity results in severe deficiency associated with spontaneous joint or deep muscle bleeding. Moderate deficiency (1-5 percent activity) and mild deficiency (6-40 percent activity) are associated with prolonged bleeding after tooth extractions, surgery, or injuries, and recurrent or delayed wound healing. Female carriers of hemophilia A may have increased bleeding tendencies.

EPIDEMIOLOGY: 1 in 5,000 live male births worldwide

CAUSE: Pathogenic F8 germline variants

INHERITANCE: X-linked recessive. In the estimated 30 percent of cases that appear to be de novo, the mother is found to be a carrier at least 80 percent of the time.

PENETRANCE: 100 percent in males. Approximately 30 percent of female carriers have factor VIII activity levels of less than 40 percent and are at risk for bleeding symptoms typically consistent with mild hemophilia A.

CLINICAL SENSITIVITY: 98 percent

GENE TESTED: F8 (NM_000132.4)

METHODOLOGY: F8 intron 22-A and intron 1 inversions detected by inverse PCR and electrophoresis. Capture of all coding exons and exon-intron junctions of the F8 gene, followed by massively parallel sequencing. Sanger sequencing performed as necessary to fill in regions of low coverage and confirm reported variants. Multiplex ligation-dependent probe amplification (MLPA) of the F8 gene.

ANALYTICAL SENSITIVITY/SPECIFICITY: The analytical sensitivity and specificity for inversion analysis and MLPA is 99 percent. The analytical sensitivity of sequencing is approximately 99 percent for single nucleotide variants (SNVs) and greater than 93 percent for insertions/duplications/deletions from 1-10 base pairs in size. Variants greater than 10 base pairs may be detected, but the analytical sensitivity may be reduced.

LIMITATIONS: A negative result does not exclude a diagnosis of or carrier status for hemophilia A. This test only detects variants within the coding regions and intron-exon boundaries of the F8 gene. Variants in regions that are not included in the preferred transcript are not detected. Regulatory region variants and deep

Test Information

i1: Hemophilia A (F8) Interpretation

intronic variants, other than the type 1 or type 2 intron 22-A and intron 1 inversions, will not be identified. Rare F8 intron 22-A and intron 1 inversions with different breakpoints may not be detected by this assay. Breakpoints for large deletions/duplications will not be determined. Single exon deletion/duplications may not be detected based on the breakpoints of the rearrangement. Deletions/duplications/insertions of any size may not be detected by massively parallel sequencing. Diagnostic errors can occur due to rare sequence variations. In some cases, variants may not be identified due to technical limitations in the presence of pseudogenes, repetitive, or homologous regions. This assay may not detect low-level mosaic or somatic variants associated with disease. Interpretation of this test result may be impacted if this patient has had an allogeneic stem cell transplantation. Noncoding transcripts were not analyzed.

This test was developed and its performance characteristics determined by ARUP Laboratories. It has not been cleared or approved by the US Food and Drug Administration. This test was performed in a CLIA-certified laboratory and is intended for clinical purposes.

Counseling and informed consent are recommended for genetic testing. Consent forms are available online.