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Patient Report

Patient Age/Sex: Female

Specimen Collected: 08-Jun-22 15:50

Deletion/Duplication Analysis by MLPA | **Received: 08-Jun-22 15:50** | **Report/Verified: 15-Jun-22 17:09**

Procedure	Result	Units	Reference Interval
Deletion/Duplication Interpretation	Positive [f1]		
Deletion/Duplication Gene	BG DD [f2] [i1]		

Result Footnote

f1: Deletion/Duplication Interpretation

Section 79-1 of New York State Civil Rights Law requires informed consent be obtained from patients (or their legal guardians) prior to pursuing genetic testing. These forms must be kept on file by the ordering physician. Consent forms for genetic testing are available at www.aruplab.com. Incidental findings are not reported unless clinically significant but are available upon request.
Deletion/Duplication Analysis by MLPA

TEST PERFORMED - 3003144
TEST DESCRIPTION - Beta Globin (HBB) Deletion/Duplication
INDICATION FOR TESTING - Confirm Diagnosis

RESULT
One HPFH deletion was detected in the beta globin gene cluster.

HPFH Variant
Nucleic Acid Change: Deletion of HBD exons 1-3 and HBB exons 1-3; Heterozygous
Commonly Known As: HPFH-1 (Black) or HPFH-4 (Italian)
Variant Phenotype: Hereditary Persistence of Fetal Hemoglobin

INTERPRETATION
One copy of a hereditary persistence of fetal hemoglobin deletion, HPFH-1 or HPFH-4, was detected by deletion/duplication analysis of the beta globin gene cluster and its locus control region. Because the specific breakpoints cannot be determined using this assay, this HPFH deletion could represent either HPFH-1 (Black) or HPFH-4 (Italian). This large deletion is associated with hereditary persistence of fetal hemoglobin (HPFH). Individuals heterozygous for this deletion typically have normal red blood cell indices but elevated levels of Hb F. The clinical presentation may vary due to other genetic modifiers or co-existing conditions. A more severe disorder is possible if a second HBB pathogenic variant is present on the opposite chromosome that is not detected by this assay.

Evidence for variant classification: The HPFH-1 (Black) and HPFH-4 (Italian) deletions remove delta globin (HBD) exons 1-3 and beta globin (HBB) exons 1-3. Heterozygous carriers of HPFH-1 or HPFH-4 are relatively clinically asymptomatic but homozygous carriers of HPFH-1 can have mild erythrocytosis (see HbVar links and references therein; HbVar IDs:1021, 1024; (1)).

RECOMMENDATIONS
Medical management should rely on clinical findings and family history. If suspicion for a clinically significant form of beta thalassemia remains, consideration should be given to beta globin gene sequencing (ARUP test code 0050578) which detects up to 97 percent of all beta globin gene variants. A hemoglobin evaluation should be offered to this individual's reproductive partner and family members to assess carrier status for hemoglobin variants. Genetic consultation is recommended.

COMMENTS
Reference Sequences: GenBank # NG_000007.3 (Beta globin gene cluster)

Result Footnote

f1: Deletion/Duplication Interpretation

REFERENCES
1: Link to HbVar database: https://globin.bx.psu.edu/hbvar/menu.html

This result has been reviewed and approved by [redacted]

f2: Deletion/Duplication Gene

BACKGROUND INFORMATION: Beta Globin (HBB)
Deletion/Duplication
CHARACTERISTICS: Beta thalassemia is caused by decreased or absent synthesis of the hemoglobin beta-chain resulting in variable clinical presentations ranging from mild anemia to transfusion dependence. Hereditary persistence of fetal hemoglobin (HPFH) is a clinically benign condition caused by variants within the beta globin gene cluster that alter normal hemoglobin switching and result in persistent fetal hemoglobin (Hb F) production.
INCIDENCE: Varies by ethnicity.
INHERITANCE: Usually autosomal recessive, infrequently autosomal dominant.
CAUSE: Pathogenic variants within the HBB gene or variants involving the beta globin gene cluster and its regulatory elements.
CLINICAL SENSITIVITY: Varies by ethnicity.
METHODOLOGY: Multiplex ligation-dependent probe amplification (MLPA) of the beta globin gene cluster (HBB, HBD, HBG1, HBG2, HBE1) and its locus control region.
ANALYTICAL SENSITIVITY AND SPECIFICITY: 99 percent.
LIMITATIONS: Diagnostic errors can occur due to rare sequence variations. HBB single base pair substitutions, small deletions/duplications, deep intronic and promoter variants will not be detected. Breakpoints of large deletions/duplications will not be determined; therefore, the precise clinical phenotype associated with a particular deletion (e.g., HPFH vs. delta-beta thalassemia) may not be known. Intragenic deletions in the beta globin cluster genes, other than HBB, may not be detected. This assay does not assess for sequence variants within the coding or regulatory regions of HBB, HBD, HBG1, HBG2 or HBE1. Apparent copy number changes detected solely in the HBG1-HBG2 region will not be reported as they can result from benign sequence variants or gene conversion events.

Test Information

i1: Deletion/Duplication Gene

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.

*=Abnormal, #=Corrected, C=Critical, f=Result Footnote, H-High, i-Test Information, L-Low, t-Interpretive Text, @=Performing lab