Client: Example Client ABC123
123 Test Drive
Salt Lake City, UT 84108
UNITED STATES

Physician: Doctor, Example

Patient: Patient, Example

DOB	7/31/2005
Gender:	Male
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Deletion/Duplication Analysis by MLPA

ARUP test code 3003144

Deletion/Duplication Interpretation	Positive

H=High, L=Low, *=Abnormal, C=Critical

Deletion/Duplication Analysis by MLPA

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

DNA VARIANT(S)
HPFH Variant
Nucleic Acid Change: Deletion of HBB, HBD, and HBBP1;
Heterozygous
Commonly Known As: HPFH-2 deletion; Ghanaian deletion
Variant Phenotype: Hereditary Persistence of Fetal Hemoglobin

INTERPRETATION
One copy of a deletion of the HBB and HBD genes as well as the nearby HBBP1 pseudogene was detected by deletion/duplication analysis of the beta globin gene cluster and its locus control region. 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 NC_000011.9:g.(5173030_5221268)_(5263263_5264714)del variant deletes the entire HBB gene as well as the nearby HBD gene and HBBP1 pseudogene. Although the breakpoints of this deletion cannot be determined by this assay, this variant most closely resembles the HPFH-2 deletion, which is also known as the Ghanaian deletion (HbVar ID: 1022) (1)(3)(4). This deletion is common in individuals of African descent and results in continued expression of fetal (gamma) globin. It has been reported as a heterozygous variant in individuals with no clinical symptoms and homozygous in individuals with mild erythrocytosis (2)(3).

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 3004547) 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)

REFERENCES
1: Collins FS, Cole JL, Lockwood WK et al, The deletion in both common types of hereditary persistence of fetal hemoglobin is approximately 105 kilobases. Blood 1987. PMID:2445400
2: Fritsch EF, Lawn RM, Maniatis T, Characterisation of deletions which affect the expression of fetal globin genes in man. Nature 1979. PMID:450109
3: Link to HbVar database:
https://globin.bx.psu.edu/hbvar/menu.html
4: Tuan D, Feingold E, Newman M et al, Different 3' end points of deletions causing delta beta-thalassemia and hereditary persistence of fetal hemoglobin: implications for the control of gamma-globin gene expression in man. Proc Natl Acad Sci U S A 1983. PMID:6196781

This result has been reviewed and approved by [redacted]

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Deletion/Duplication Gene

BG DD

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.

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.

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Deletion/Duplication Interpretation	24-230-400989	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Deletion/Duplication Gene	24-230-400989	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00

END OF CHART

H=High, L=Low, *=Abnormal, C=Critical