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

Physician: Doctor, Example

Patient: Patient, Example

DOB	10/15/2012
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

Deletion/Duplication Analysis by MLPA

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

RESULT
One pathogenic variant was detected in the beta globin gene cluster.

DNA VARIANT
Classification: Pathogenic
Gene: HBB
Nucleic Acid Change: Deletion of exon 3; Heterozygous
Commonly Known As: 619 bp deletion
Variant Phenotype: Beta(0) Thalassemia (absence of beta chain synthesis)

INTERPRETATION
One copy of a pathogenic variant, deletion of exon 3 of the beta globin (HBB) gene, was detected by deletion/duplication analysis of the beta globin gene cluster and its locus control region. This result is consistent with beta thalassemia trait. 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: This deletion removes sequences at the 3' end of the HBB gene, including the conserved polyadenylation signal sequence and likely coding exon 3. Although the exact breakpoints of this deletion cannot be determined, it is consistent with a common exon 3 deletion, also known as the 619 bp deletion (HbVar ID: 979) (1,2,4). The 619 bp deletion is reported in the literature in numerous individuals with beta-thalassemia or beta-thalassemia trait and is commonly found in populations of the Indian subcontinent (1,3,5). Based on available information, this deletion is considered to be pathogenic.

RECOMMENDATIONS
Medical management should rely on clinical findings and family history. This result should be correlated with the result of beta globin gene sequencing, which was requested previously and reported under separate cover (ARUP accession 22-124-117542). Family members should be offered testing for the identified pathogenic variant (Deletion/Duplication Analysis by MLPA, ARUP test code 3003144). This individual's future reproductive partner should be offered carrier testing for hemoglobinopathies. Genetic consultation is recommended.

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

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

REFERENCES
1: Link to HbVar database: https://globin.bx.psu.edu/hbvar/menu.html
2: Pritchard CC, Tait JF, Buller-Burckle AM et al, Annotation error of a common beta-thalassemia mutation (619 bp-deletion) has implications for molecular diagnosis. Am J Hematol 2010. PMID:20960433
3: Saleh-Gohari N, Mashizi AK, A family with the 619 bp deletion on the beta-globin gene found in Kerman Province, Iran. Hemoglobin 2009. PMID:19958199
4: Spritz RA, Orkin SH, Duplication followed by deletion accounts for the structure of an Indian deletion beta (0)-thalassemia gene. Nucleic Acids Res 1982. PMID:7162987
5: Varawalla NY, Old JM, Sarkar R et al, The spectrum of beta-thalassaemia mutations on the Indian subcontinent: the basis for prenatal diagnosis. Br J Haematol 1991. PMID:2064964

This result has been reviewed and approved by [redacted]

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.

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

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	22-133-400855	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Deletion/Duplication Gene	22-133-400855	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