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

Physician: Doctor, Example

Patient: Patient, Example

DOB	Unknown
Gender:	Unknown
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Beta Globin (HBB) Sequencing and Deletion/Duplication

ARUP test code 2010117

Beta Globin (HBB) Seq, Del/Dup Spcm	Whole Blood	
Beta Globin (HBB) Seq, DelDup Interp	**Positive**	*

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

TEST PERFORMED - 2010117
TEST DESCRIPTION - Beta Globin (HBB) Sequencing and Deletion/Duplication
INDICATION FOR TEST - Not Provided

RESULT
Two copies of a pathogenic variant were detected in the HBB gene.

DNA VARIANT
Classification: Pathogenic
Gene: HBB
Nucleic Acid Change: c.20A>T; Homozygous
Amino Acid Alteration: p.Glu7Val
Commonly known as: Hb S

INTERPRETATION
Two copies of the pathogenic Hb S variant were detected in the beta globin (HBB) gene by sequencing; thus this individual is predicted to be affected with sickle cell anemia. The clinical presentation may vary due to other genetic modifiers or co-existing conditions.

No large deletions involving the genes of the beta globin gene cluster (HBB, HBD, HBG1, HBG2 and HBE1) or its locus control region were detected.

Evidence for variant classification: The Hb S variant (HBB: c.20A>T; p.Glu7Val, also known as Glu6Val when numbered from the mature protein) is a common pathogenic beta globin variant. Heterozygosity for Hb S is consistent with sickle cell trait. Homozygosity for Hb S results in sickle cell anemia. Hb S in combination with a different pathogenic HBB variant on the opposite chromosome results in various forms of sickle cell disease (see HbVar link and references therein).

RECOMMENDATIONS
Hematologic and genetic consultations are recommended. Family members should be offered carrier testing for the identified pathogenic variant. This individual's reproductive partner should be offered carrier testing for hemoglobinopathies.

COMMENTS
Reference Sequences: GenBank # NM_000518.4 (HBB), # NG_000007.3 (Beta globin gene cluster)
Nucleotide numbering begins at the "A" of the ATG initiation codon.
Likely benign and benign variants are not included in this report.

REFERENCES
Link to HbVar database for Hb S:
http://globin.bx.psu.edu/cgi-bin/hbvar/query_vars3?mode=output&display_format=page&i=226

This result has been reviewed and approved by Rong Mao, M.D.

BACKGROUND INFORMATION: Beta Globin (HBB) Sequencing and 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. Structural hemoglobinopathies may result in sickling disorders, microcytic or hemolytic anemia, cyanosis, or erythrocytosis. 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: 99 percent for beta thalassemia and hemoglobinopathies associated with the HBB gene.
METHODOLOGY: Bidirectional sequencing of the HBB coding regions, intron-exon boundaries, 5proximal promoter and untranslated region, 3polyadenylation signal and intronic variants c. 93-21 (IVS-I-110), c.316-197 (IVS-II-654), c.316-146 (IVS-II-705), c.316-106 (IVS-II-745), and c.316-86_316-85 (IVS-II-765 L1). 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. Breakpoints of large deletions will not be determined; therefore, the precise clinical phenotype associated with a particular deletion (eg., 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 HBD, HBG1, HBG2 or HBE1. Apparent copy number changes detected by probes solely in the HBG1-HBG2 region will not be reported, as they can result from benign sequence variants or gene conversion events.

Test developed and characteristics determined by ARUP Laboratories. See Compliance Statement C: aruplab.com/CS

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Beta Globin (HBB) Seq, Del/Dup Spcm	20-036-104860	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Beta Globin (HBB) Seq, DelDup Interp	20-036-104860	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