ARUP LABORATORIES | www.aruplab.com
500 Chipeta Way, Salt Lake City, Utah 84108-1221
phone: (801) 583-2787, toll free: (800) 522-2787
Julio C. Delgado, MD, MS, Director of Laboratories

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

Physician: Doctor, Example

Patient: Patient, Example

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

Hemoglobin Evaluation Reflexive Cascade

ARUP test code 2005792

Hemoglobin A	**67.3 %**	**L**	**(Ref Interval: 95.0-97.9)**
Hemoglobin A2	2.9 %		(Ref Interval: 2.0-3.5)
Hemoglobin F	0.3 %		(Ref Interval: 0.0-2.1)
	REFERENCE INTERVAL: Hemoglobin F Access complete set of age- and/or gender-specific reference intervals for this test in the ARUP Laboratory Test Directory (aruplab.com).		
Hemoglobin S	**29.5 %**	**H**	**(Ref Interval: 0.0-0.0)**
Hemoglobin C	0.0 %		(Ref Interval: 0.0-0.0)
Hemoglobin E	0.0 %		(Ref Interval: 0.0-0.0)
Hemoglobin - Other	0.0 %		(Ref Interval: 0.0-0.0)
Sickle Cell Solubility	Positive		

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

Hemoglobin, Capillary Electrophoresis	Performed
Hemoglobin Evaluation	See Note
Beta Globin Full Gene Sequencing	Performed
Beta Globin (HBB) Del/Dup Result	Not Applicable
Alpha Thalassemia HBA1 and HBA2 Seq	Not Applicable
Hemoglobin Lepore (HBD/HBB) 3 Mutations	Not Applicable
Hemoglobin Cascade Interpretation	See Note

RESULT
One copy of the Hb S pathogenic variant was detected by beta globin (HBB) gene sequencing.
See comments.

COMMENTS
One copy of the Hb S pathogenic variant was detected in the beta globin (HBB) gene by sequencing. This individual is at least a carrier of sickle cell trait. The clinical presentation may vary due to other genetic modifiers or co-existing conditions.

No large deletions or duplications were detected in the alpha globin gene cluster.

DNA MUTATIONS/VARIANTS
Classification: Pathogenic
Gene: HBB
Nucleic Acid Change: c.20A>T; Heterozygous
Amino Acid Alteration: p.Glu7Val
Commonly Known As: Hb S

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
Medical management should rely on clinical findings and family history. Family members should be offered carrier testing for the identified variant. This individual's reproductive partner should be offered carrier testing for hemoglobinopathies. Genetic consultation is recommended.

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

NOTES
Reference Sequences: GenBank # NM_000518.4 (HBB)
Nucleotide numbering begins at the "A" of the ATG initiation codon.
Benign and likely benign variants are not reported.

Controls were run and performed as expected.
This result has been reviewed and approved by Archana Agarwal, M.D.

BACKGROUND INFORMATION: Beta Globin (HBB) Sequencing

CHARACTERISTICS: Structural hemoglobinopathies or thalassemias (insufficient or absent beta- chain production).
INCIDENCE: Varies with ethnicity.
INHERITANCE: Usually autosomal recessive, infrequently autosomal dominant.
CAUSE: Pathogenic mutations in the HBB gene.
MUTATIONS TESTED: The complete protein coding sequence with exon/intron boundaries, proximal promoter, 5' and 3' untranslated regions, and intronic mutations IVS-II-654, IVS-II-705 and IVS-II-745.
CLINICAL SENSITIVITY: Up to 97 percent, depending upon ethnicity.
METHODOLOGY: Bidirectional sequencing of the HBB coding regions, intron-exon boundaries, proximal promoter, 5' and 3' untranslated regions, and intronic mutations IVS-II-654 , IVS-II-705 and IVS-II-745.
ANALYTICAL SENSITIVITY: 99 percent.
LIMITATIONS: Diagnostic errors can occur due to rare sequence variations. Large deletions, and mutations in distal regulatory elements are not detected.

See Compliance Statement C: www.aruplab.com/CS

BACKGROUND INFORMATION: Alpha Globin (HBA1 and HBA2) Deletion/Duplication
CHARACTERISTICS: Alpha thalassemia is caused by decreased or absent synthesis of the hemoglobin alpha-chain resulting in variable clinical presentations. Alpha (+) thalassemia results from mutation of a single alpha2 globin gene (-a/aa) and is clinically asymptomatic (silent carrier). Alpha (0) thalassemia (trait) is caused by mutation of both alpha2 globin genes (-a/-a), or mutations in the alpha1 and alpha2 globin genes on the same chromosome, (--/aa) and results in mild microcytic anemia. Hemoglobin H disease occurs due to mutation of three alpha globin genes (--/-a) and results in hemolysis with Heinz bodies, moderate anemia, and splenomegaly. Hb Bart Hydrops Fetalis Syndrome results when mutations occur in all four alpha globin genes (--/--) and is lethal in the fetal or early neonatal period. Alpha globin gene triplications result in three active alpha globin genes on a single chromosome.
INCIDENCE: Carrier frequency in Mediterranean (1:30-50), Middle Eastern, Southeast Asian (1:20), African, African-American (1:3).
INHERITANCE: Autosomal recessive.
CAUSE: Pathogenic mutations in the alpha globin gene cluster.
CLINICAL SENSITIVITY: Varies by ethnicity, up to 95 percent.
METHODOLOGY: Multiplex ligation-dependent probe amplification (MLPA) of the alpha globin gene cluster (HBZ, HBM, HBA2, HBA1, HBQ1) and its HS-40 regulatory region.
ANALYTICAL SENSITIVITY AND SPECIFICITY: 99 percent.
LIMITATIONS: Diagnostic errors can occur due to rare sequence variations. Specific breakpoints of large deletions/duplications will not be determined; therefore, it may not be possible to distinguish mutations of similar size. This assay does not assess for non-deletional mutations within the coding or regulatory regions of the alpha globin cluster genes. Individuals carrying both a deletion and duplication within the

alpha globin gene cluster may appear to have a normal number of alpha globin gene copies. Rare syndromic or acquired forms of alpha thalassemia associated with ATRX mutations will not be detected.

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

Alpha Globin (HBA1 and HBA2) Del/Dup Rst	Performed

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Glucose-6-Phosphate Dehydrogenase	19-288-121696	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Hemoglobin A	19-288-121696	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Hemoglobin A2	19-288-121696	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Hemoglobin F	19-288-121696	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Hemoglobin S	19-288-121696	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Hemoglobin C	19-288-121696	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Hemoglobin E	19-288-121696	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Hemoglobin - Other	19-288-121696	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Sickle Cell Solubility	19-288-121696	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Hemoglobin, Capillary Electrophoresis	19-288-121696	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Hemoglobin Evaluation	19-288-121696	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Beta Globin Full Gene Sequencing	19-288-121696	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Beta Globin (HBB) Del/Dup Result	19-288-121696	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Alpha Thalassemia HBA1 and HBA2 Seq	19-288-121696	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Hemoglobin Lepore (HBD/HBB) 3 Mutations	19-288-121696	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Hemoglobin Cascade Interpretation	19-288-121696	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Alpha Globin (HBA1 and HBA2) Del/Dup Rst	19-288-121696	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