

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

Physician: Doctor, Example

**Patient: Patient, Example**

**DOB:** 8/7/1986  
**Gender:** Female  
**Patient Identifiers:** 01234567890ABCD, 012345  
**Visit Number (FIN):** 01234567890ABCD  
**Collection Date:** 00/00/0000 00:00

**Alpha Thalassemia (HBA1 and HBA2) Deletion/Duplication with reflex to Hb Constant Spring, Fetal**

ARUP test code 3003656

Maternal Contamination Study Fetal Spec	Fetal Cells  Single fetal genotype present; no maternal cells present. Fetal and maternal samples were tested using STR markers to rule out maternal cell contamination.
Maternal Contam Study, Maternal Spec	whole Blood
Specimen HBA DDSCFE	Cultured Amnio
HBA DDSCFE Interpretation	See Note

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

Indication for testing: Prenatal testing for alpha thalassemia.

**RESULT**

One copy of the familial alpha globin gene deletion was detected.

**DNA VARIANT**

Pathogenic Deletion: --SEA; Heterozygous

Predicted Fetal Genotype: --/aa

**INTERPRETATION**

According to information provided to ARUP, both parents of this fetus carry the Southeast Asian (--SEA) alpha globin gene deletion. One copy of the familial --SEA deletion was detected in this fetal sample by deletion/duplication analysis of the alpha globin gene cluster. Hemoglobin Constant Spring (HbCS) was not detected. The identified deletion removes the HBM, HBA2, HBA1, and HBQ1 globin genes on a single chromosome. Thus, this fetus is predicted to be an unaffected carrier of alpha thalassemia trait. Heterozygosity for this deletion is often associated with mild anemia and microcytosis. The clinical presentation may vary due to other genetic modifiers or coexisting conditions.

Evidence for variant classification: The pathogenic --SEA deletion is a common large deletion observed in East Asian populations (HbVar database and references therein). This deletion removes approximately 20kb including both HBA1 and HBA2 on the same chromosome, and therefore no functional mRNA is produced. Heterozygosity for this deletion is often associated with mild anemia and microcytosis, whereas homozygosity for this deletion results in Hb Bart hydrops fetalis syndrome.

**RECOMMENDATIONS**

Genetic consultation is recommended.

**COMMENTS**

Reference Sequences: GenBank # NM\_000517.4 (HBA2), NG\_000006.1 (alpha globin gene cluster) Nucleotide numbering begins at the "A" of the ATG initiation codon.

**REFERENCES**

HbVar --(SEA) link:

[http://globin.bx.psu.edu/cgi-bin/hbvar/query\\_vars3?mode=output&display\\_format=page&i=1086](http://globin.bx.psu.edu/cgi-bin/hbvar/query_vars3?mode=output&display_format=page&i=1086)

This result has been reviewed and approved by [REDACTED]

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**INTERPRETIVE INFORMATION: AlphaThal (HBA1/2) De1Dup w/rflx HbCS FE**

Characteristics of Alpha Thalassemia: Decreased or absent synthesis of the hemoglobin (Hb) alpha-chain resulting in clinical presentations ranging from asymptomatic silent carriers to severe anemia and fetal lethality. Alpha thalassemia silent carrier commonly results from deletion of a single alpha globin gene (-a/aa) and is clinically asymptomatic. Alpha thalassemia trait may be caused by deletion of a single alpha globin gene from both chromosomes (-a/-a), or deletion of the HBA1 and HBA2 globin genes from the same chromosome (--/aa). Heterozygosity for Hb Constant Spring (HbCS) is usually asymptomatic but may be associated with mild microcytic anemia. Homozygous HbCS is characterized by overt hemolytic anemia, jaundice and splenomegaly. Hemoglobin H disease occurs due to inactivation of three alpha globin genes and results in hemolysis with Heinz bodies, moderate anemia, and splenomegaly. Hb Bart hydrops fetalis syndrome results from deletion of all four alpha globin genes (--/--) and is lethal in the fetal or early neonatal period. Alpha globin gene duplication results in three or more active alpha globin genes on a single chromosome.

Epidemiology: Carrier frequency of alpha thalassemia in African, African-American (1:3), Mediterranean (1:30-50), Middle Eastern, Southeast Asian (1:20).

Inheritance: Autosomal recessive.

Cause: Pathogenic variants in the alpha globin gene cluster (HBZ, HBM, HBA2, HBA1, HBQ1) or regulatory region.

Clinical Sensitivity: Varies by ethnicity, at least 90 percent.

Methodology: Multiplex ligation-dependent probe amplification (MLPA) for the HBZ, HBM, HBA2, HBA1, and HBQ1 genes, the HS-40 regulatory region, and Hb Constant Spring (HbCS) HBA2 c.427T>C; p.Ter143Gln. To determine copy number of HbCS in absence of a concurrent deletion of HBA2, PCR and bidirectional sequencing for HbCS is performed.

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 variants of similar size. Non-deletional variants within the coding or regulatory regions of the alpha globin cluster genes, other than HbCS, will not be targeted. Fetuses 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 gene variants will not be detected.

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.

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VERIFIED/REPORTED DATES				
Procedure	Accession	Collected	Received	Verified/Reported
Maternal Contamination Study Fetal Spec	24-131-402420	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Maternal Contam Study, Maternal Spec	24-131-402420	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Specimen HBA DDCSFE	24-131-402420	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
HBA DDCSFE Interpretation	24-131-402420	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

Unless otherwise indicated, testing performed at:

ARUP LABORATORIES | 800-522-2787 | aruplab.com  
500 Chipeta Way, Salt Lake City, UT 84108-1221  
Jonathan R. Genzen, MD, PhD, Laboratory Director

Patient: Patient, Example  
ARUP Accession: 24-131-402420  
Patient Identifiers: 01234567890ABCD, 012345  
Visit Number (FIN): 01234567890ABCD  
Page 4 of 4 | Printed: 6/6/2024 3:10:49 PM  
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