

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

Gamma Globin (HBG1 and HBG2) Sequencing

ARUP test code 3001957

Specimen HBG FGS whole Blood

HBG FGS Interpretation

Positive *

Section 79-1 of New York State Civil Rights Law requires informed consent be obtained from patients (or their legal guardians) prior to pursuing genetic testing. These forms must be kept on file by the ordering physician. Consent forms for genetic testing are available at www.aruplab.com. Incidental findings are not reported unless clinically significant but are available upon request.

TEST PERFORMED - 3001957
TEST DESCRIPTION - Gamma Globin (HBG1 and HBG2) Sequencing
INDICATION FOR TEST - Not Provided

RESULT

One pathogenic variant was detected in the HBG2 gene. No pathogenic variants were detected in the HBG1 gene.

DNA VARIANT

Classification: Pathogenic
Gene: HBG2
Nucleic Acid Change: c.85C>A; Heterozygous
Amino Acid Alteration: p.Leu29Met
Commonly Known As: Hb F-M Viseu, Leu28Met
Variant Phenotype: Neonatal cyanosis

INTERPRETATION

One pathogenic variant, c.85C>A; p.Leu29Met, was detected in the HBG2 gene by sequencing. Heterozygous carriers of Hb F-M Viseu are reported to have neonatal cyanosis (see evidence for variant classification below). The clinical presentation may vary due to other genetic modifiers or coexisting conditions. Offspring of this individual have a 50 percent chance to inherit the pathogenic Hb F-M Viseu variant.

Evidence for variant classification: The HBG2 c.85C>A; p.Leu29Met variant, also known as Leu28Met in traditional nomenclature, is reported in the medical literature in several individuals with neonatal cyanosis (Bento 2013, Carreira 2015, Marks 2013). This variant is absent from general population databases (Exome Variant Server, Genome Aggregation Database), indicating it is not a common polymorphism. The leucine at codon 29 is highly conserved and computational algorithms (PolyPhen-2, SIFT) predict this variant is deleterious. Considering available information, this variant is classified as pathogenic.

RECOMMENDATIONS

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

Medical management should rely on clinical findings. Correlation with hematologic parameters and hemoglobin electrophoresis results is recommended. Hematologic and genetic consultations are recommended. At-risk family members should be offered testing for the identified pathogenic variant (Familial Mutation, Targeted Sequencing, ARUP test code 2001961).

COMMENTS

Reference Sequences: GenBank # NM_000559.2 (HBG1), NM_000184.2 (HBG2)
Nucleotide numbering begins at the "A" of the ATG initiation codon.
Likely benign and benign variants are not included in this report, but are available upon request

REFERENCES

Link to Hb F-M View in HbVar
database:http://globin.bx.psu.edu/cgi-bin/hbvar/query_vars3?mode=output&display_format=page&i=3108&.cgifields=histD
Bento C et al. Transient neonatal cyanosis associated with a new Hb F variant: Hb F viseu. J Pediatr Hematol Oncol. 2013 Mar;35(2):e77-80.
Carreira R et al. An unusual cause of neonatal cyanosis. BMJ Case Rep. 2015 Mar 9;2015. pii: bcr2014208371.
Marks A et al. Hemoglobin Shady Grove: a novel fetal methemoglobin variant. Pediatr Blood Cancer. 2013 Aug;60(8):E55-6.

BACKGROUND INFORMATION: Gamma Globin (HBG1 and HBG2) Sequencing

CHARACTERISTICS: Variants in the gamma globin genes, HBG1 and HBG2, may occasionally result in either a quantitative defect (gamma thalassemia or nondeletional hereditary persistence of fetal hemoglobin) or a qualitative abnormality (gamma variant). Gamma variants resulting in unstable, high- and low-oxygen affinity or M hemoglobin variants may result in hemolytic anemia/hyperbilirubinemia, erythrocytosis/cyanosis, or methemoglobinemia in neonates, respectively. Clinical symptoms related to gamma globin variants commonly resolve after the first six months of life given the switch from fetal hemoglobin expression to adult hemoglobin expression.

INCIDENCE: Unknown.

INHERITANCE: Autosomal dominant.

CAUSE: Pathogenic germline variants in HBG1 or HBG2.

CLINICAL SENSITIVITY: Unknown. Gamma globin variants are a rare cause of neonatal hemolytic anemia, cyanosis, erythrocytosis, or methemoglobinemia.

METHODOLOGY: Long range PCR followed by nested PCR and bidirectional sequencing of all coding regions, intron-exon boundaries, and 5' proximal promoters of the HBG1 and HBG2 genes.

ANALYTICAL SENSITIVITY AND SPECIFICITY: 99 percent.

LIMITATIONS: Diagnostic errors can occur due to rare sequence variations or repeat element insertions. Large deletions/duplications, distal regulatory region variants, deep intronic variants, and hybrid gene events will not be detected.

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

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

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
Specimen HBG FGS	21-028-103211	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
HBG FGS Interpretation	21-028-103211	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
Tracy I. George, MD, Laboratory Director

Patient: Patient, Example
ARUP Accession: 21-028-103211
Patient Identifiers: 01234567890ABCD, 012345
Visit Number (FIN): 01234567890ABCD
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