

Patient ID SA00149317	Patient Name VALIDATIONTESTING, HAEV1	Birth Date 1967-08-08	Gender F	Age 54
Order Number SA00149317	Client Order Number SA00149317	Ordering Physician CLIENT,CLIENT	Report Notes	
Account Information C7028846 DLMP Rochester		Collected 04 Nov 2021 12:00		

Hemolytic Anemia Summary Interp

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MCR

This summary interpretation integrates additional testing results with initial findings reported in the Hemolytic Anemia Evaluation.

HEMOGLOBIN ELECTROPHORESIS:

There is a hemoglobin variant present that cannot be positively identified by hemoglobin electrophoresis methods. Molecular testing was performed to clarify these results.

MOLECULAR GENETICS:

The following alterations were detected:

Gene: HBB

DNA change: codon 28, CTG>CCG, heterozygous

Protein Change: p.Leu28Pro (p.L28P)

HGVS: c.86T>C, p.L29P

Classification: Hb Genova

OSMOTIC FRAGILITY:

Osmotic fragility testing: Increased red blood cell lysis EMA binding test (band 3 assay): Normal staining pattern

RBC ENZYMES:

All Red Blood Cell enzyme values are normal or elevated. See Interpretation

INTERPRETATION:

These results confirm heterozygous Hb Genova. Hb Genova is an unstable beta globin variant that is associated with congenital hemolytic anemia. The severity of hemolysis is variable, ranging

from moderate to severe. This variability is seen even among members of the same family with the variant (1, 2). In one family, hemoglobin levels were observed between 7.1 to 11.4 g/dL, reticulocytes were 17–24%, and MCVs were 85–95 fL (1). Reticulocytes and splenomegaly are common. Heinz bodies are evident on peripheral blood smear. Hematologic status has been observed to worsen during pregnancy, and in some cases may require transfusion (1). This phenotype is inherited in an autosomal dominant pattern but apparently some sporadic mutations have been reported twice in individuals with no family history of congenital hemolytic anemia (3, 4). Clinical correlation is necessary. A genetic consultation may be of benefit.

It is not uncommon for an individual with unstable hemoglobin variants to be erroneously diagnosed with hereditary spherocytosis prior to detection and identification of the hemoglobin variant (2). Increased osmotic fragility can be seen as a result of unstable hemoglobins as well as immune hemolytic anemia, recent blood transfusion, RBC enzyme deficiencies and some medications. Clinical correlation is necessary.

1. Acta Haematol. 1979;61(5):278–82 (PMID 111455)
2. Hemoglobin. 1983;7(6):591–4 (PMID 6668191)
3. Acta Haematol. 1990;83(1):39–41 (PMID 2105568)
4. Acta Haematol. 1980;63(4):222–5 (PMID 6771953)

Reviewed By

MCR

JENNIFER MAIN

Received: 05 Nov 2021 14:12

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Hemolytic Anemia Evaluation

Hemolytic Anemia Interpretation

MCR

EVAL INCOMPLETE UNTIL SUMMARY INTERP ISSUED

Molecular testing is added. A summary interpretation with correlation of protein and molecular results will be reported when all testing under the profile is complete. Time to issuance of the

final report is dependent on the complexity of the case. If the Hemolytic Anemia Summary Interpretation (Test ID HAEV0) is not viewable 30 days after receipt of this protein interpretation, please call Mayo Clinic Laboratories to inquire and request a copy of the full report at 1–800–533–1710.

Performing Site Legend

Code	Laboratory	Address	Lab Director	CLIA Certificate
MCR	Mayo Clinic Laboratories - Rochester Main Campus	200 First Street SW, Rochester, MN 55905	William G. Morice M.D. Ph.D	24D0404292

Patient ID SA00149317	Patient Name VALIDATIONTESTING, HAEV1	Birth Date 1967-08-08	Gender F	Age 54
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RBC ENZYME INTERPRETATION:

All RBC enzyme activity levels are normal or elevated. Elevated activity levels can be present in neonates or due to reticulocytosis.

OSMOTIC FRAGILITY/EMA BINDING INTERPRETATION:

Osmotic fragility testing: Increased red blood cell lysis in 2 of 4 NaCl concentrations EMA binding test band 3 assay) by flow cytometry: Normal staining pattern

Interpretation: The Osmotic Fragility and Band 3 results are not supportive of a diagnosis of hereditary spherocytosis. Other causes for an increased osmotic fragility to consider are immune

hemolytic anemia, recent blood transfusion, G6PD or Pyruvate Kinase deficiency, unstable hemoglobins and some medications. Corroborative data includes family history and/or testing of blood relatives, Coombs' test and blood smear erythrocyte morphology results.

HB ELECTROPHORESIS INTERPRETATION:

Hb F increased. In addition, a small peak is present by electrophoresis that cannot be definitively excluded.

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Hb Variant, A2 and F Quantitation, B

Result Name	Value	Unit	Reference Value	Performing Site
Hb A		%	95.8–98.0	MCR
Hb A + Hb Variant = 88.0%				
 Hb F	9.0	%	0.0–0.9	MCR
Hb A2	3.0	%	2.0–3.3	① MCR

Result Name	Value	Unit	Reference Value	Performing Site
HPLC Hb Variant, B	See Interpretation			① MCR
 Hb Stability, B	Abnormal			② MCR
REFERENCE VALUE Expected result is normal				

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Osmotic Fragility

Result Name	Value	Unit	Reference Value	Performing Site
 Osmotic Fragility, 0.50 g/dL NaCl High	54	%hemol	3–53	MCR
Osmotic Fragility, 0.60 g/dL NaCl	45	%hemol	14–74	MCR
Osmotic Fragility, 0.65 g/dL NaCl	34	%hemol	4–40	MCR
 Osmotic Fragility, 0.75 g/dL NaCl High	14	%hemol	1–11	2 MCR

Result Name	Value	Unit	Reference Value	Performing Site
Shipping Control Vial	Received			MCR
Band 3 Fluorescence Staining, RBC	Normal			2 MCR
REFERENCE VALUE Expected result is normal				
G6PD Enzyme Activity, B	9.7	U/g Hb	8.0–11.9	2 MCR
PK Enzyme Activity, B	8.3	U/g Hb	5.5–12.4	2 MCR
Glucose Phosphate Isomerase, B	49.5	U/g Hb	40.0–58.0	2 MCR
Hexokinase, B	1.2	U/g Hb	0.7–1.7	2 MCR
Adenylate Kinase, B	250	U/g Hb	195–276	2 MCR
Phosphofructokinase, B	8.9	U/g Hb	5.8–10.9	2 MCR
Phosphoglycerate Kinase, B	199	U/g Hb	142–232	2 MCR
Triosephosphate Isomerase, B	1297	U/g Hb	1033–1363	2 MCR
Glutathione, B	52.1	mg/dL RBC	46.9–90.1	2 MCR

Pyrimidine 5' Nucleotidase, B

Result Name	Value	Unit	Reference Value	Performing Site
Pyrimidine 5' Nucleotidase, B	Normal			2 MCR
REFERENCE VALUE Expected result is normal				

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Morphology Review

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Morphologic review of blood smear shows a subset of spherocytes.

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Isoelectric Focusing, B

Result Name	Value	Unit	Reference Value	Performing Site
Isoelectric Focusing, B	See Interpretation			1 MCR

Received: 05 Nov 2021 14:12

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Hb Variant by Mass Spec, B

Result Name	Value	Unit	Reference Value	Performing Site
Hb Variant by Mass Spec, B	See Interpretation			2 MCR

Received: 05 Nov 2021 14:12

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Beta Globin Gene Sequencing, B

Beta Globin Gene Sequencing Result

Positive. See interpretation

Interpretation

Beta Globin Sequencing: Positive

Gene: HBB

Legacy: Beta 28, CTG>CCG, Leu>Pro

HGVS: c.86T>C, p.L29P

Genomic: Heterozygous

Classification: Hb Genova mutation

See HAEV0/Hemolytic Anemia Summary Interpretation for correlation of these results with protein analysis and any provided clinical phenotype. If detected, alterations classified as Benign or

MCR

② MCR

Likely Benign are not included in this report but are available upon request. Alterations are reported in Legacy and HGVS nomenclatures and by genomic location. Genetic counseling may be of benefit to assist in the interpretation of these results.

Signing Pathologist: JENNIFER MAIN

ADDITIONAL INFORMATION

Bi-directional sequence analysis was performed to test for the presence of a mutation in all coding regions and non-coding portions of the beta hemoglobin gene (HBB) with reported mutations. HGVS mutation nomenclature is based on human assembly GRCh37(hg19) and RefSeq accession number NM_000518.4.

Received: 08 Nov 2021 07:48

Reported: 08 Nov 2021 11:12

Laboratory Notes

- This test has been modified from the manufacturer's instructions. Its performance characteristics were determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.
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Report Status: Final