MAYO CLINIC LABORATORIES

Patient ID	Patient Name		Birth Date	Sex	Age
SA00155016	VALIDATIONSOFT, TESTING		1975-04-01	M	47
Order Number	**Client Order Number**	**Ordering Physician**	**Report Notes**		
SA00155016	SA00155016	CLIENT,CLIENT			
Account Information		**Collected**			
C7028846 DLMP Rochester		30 Oct 2022 06:00			

Isoelectric Focusing, B

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

Received: 31 Oct 2022 10:39 **Reported:** 31 Oct 2022 10:49

Erythrocytosis Summary Interp

Erythrocytosis Summary Interp

MCR

This report is issued to summarize testing performed under the Erythrocytosis Evaluation.

MOLECULAR RESULTS:

Beta Globin Sequencing: Positive
The following alteration was detected:

Gene: HBB
Legacy: Beta 145, TAT>CAT, Tyr>His
HGVS: c.436T>C, p.T146H
Genomic: g.5246836A>G
Heterozygous
Classification: Hb Bethesda mutation

SUMMARY INTERPRETATION:

These results confirm heterozygous Hb Bethesda. Hb Bethesda is a high-oxygen-affinity beta globin variant associated with hereditary erythrocytosis (1, 2). Hb Bethesda is categorized as familial erythrocytosis type 6, autosomal dominant, although it has also been reported as a de novo variant (3). In this lab's experience, Hb Bethesda is associated with hemoglobin levels of 16–21 g/dL, hematocrits between 50 and 61%, and p50s of 14 to 25. Headaches, plethora (1), fatigue, and one unprovoked DVT (4) have been reported. Whether Hb Bethesda contributes to these events is not known. Clinical correlation is necessary.

1) Intern Med. 2015;54(18):2389–93 (PMID 26370867)
2) Intern Med. 1994 Apr;33(4):242–7 (PMID 8069021)
3) J Clin Invest. 1972 Sep;51(9):2229–309 (PMID 4639015)
4) Am J Hematol. 2021 Dec 1;96(12):1647–1654 (PMID 34633117)

GENETIC COUNSELING INFORMATION:

These results may have relevance for this individual's relatives or descendants. Hb Bethesda and the erythrocytosis it causes are inherited in an autosomal dominant manner although there is at least one report of the variant arising de novo (3). Hb Bethesda may pose some reproductive risk to offspring, depending on the genotype of the other parent, because it may cause more severe, symptomatic erythrocytosis when co-inherited with a beta thalassemia mutation. Homozygous Hb Bethesda and another high-oxygen affinity hemoglobin variant would also be expected to result in more severe erythrocytosis or hemolysis. A genetic consultation may be of benefit.

Reviewed By MCR

JENNIFER MAIN

Received: 31 Oct 2022 10:39 **Reported:** 31 Oct 2022 11:11

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	Patient Name		Birth Date	Sex	Age
SA00155016	VALIDATIONSOFT, TESTING		1975-04-01	M	47
Order Number	**Client Order Number**	**Ordering Physician**	**Report Notes**		
SA00155016	SA00155016	CLIENT,CLIENT			
Account Information		**Collected**			
C7028846 DLMP Rochester		30 Oct 2022 06:00			

Erythrocytosis Evaluation

Erythrocytosis Interpretation

MCR

There is a beta hemoglobin variant present. Molecular testing has been added to further evaluate and a discussion of the results will be reported in a separate summary interpretation when all testing under the Erythrocytosis Evaluation profile is complete. If all testing is complete and the Erythrocytosis Summary Interpretation (Test ID REVE0) is not viewable, please call Mayo Clinic Laboratories to request a copy of the full report at 1–800–533–1710.

Methodologies utilized in this interpretation include: capillary electrophoresis, HPLC, IEF, mass spectrometry

Reviewed By

MCR

JENNIFER MAIN

Hb Variant, A2 and F Quantitation,B

Result Name	Value	Unit	Reference Value	Performing Site
⚠ Low **Hb A**	**55.0**	%	95.8–98.0	MCR
Hb F	0.5	%	0.0–0.9	MCR
Hb A2	2.5	%	2.0–3.3	MCR
⚠ Abn **Variant 1**	**42.0 Beta variant**	%	0.0	1 MCR

Result Name	Value	Unit	Reference Value	Performing Site
HPLC Hb Variant, B	See Interpretation			1 MCR
Hb Variant by Mass Spec, B	See Interpretation			2 MCR

Received: 31 Oct 2022 10:39

Reported: 31 Oct 2022 10:52

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	Patient Name		Birth Date	Sex	Age
SA00155016	VALIDATIONSOFT, TESTING		1975-04-01	M	47
Order Number	Client Order Number	Ordering Physician	Report Notes		
SA00155016	SA00155016	CLIENT,CLIENT			
Account Information		Collected			
C7028846 DLMP Rochester		30 Oct 2022 06:00			

Hb Stability, B

Result Name	Value	Unit	Reference Value	Performing Site
Hb Stability, B	Normal			2 MCR

REFERENCE VALUE
Expected result is normal

Received: 31 Oct 2022 10:39

Reported: 31 Oct 2022 10:51

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	Patient Name		Birth Date	Sex	Age
SA00155016	VALIDATIONSOFT, TESTING		1975-04-01	M	47
Order Number	**Client Order Number**	**Ordering Physician**	**Report Notes**		
SA00155016	SA00155016	CLIENT,CLIENT			
Account Information		**Collected**			
C7028846 DLMP Rochester		30 Oct 2022 06:00			

Beta Globin Gene Sequencing, B

Beta Globin Gene Sequencing Result

MCR

Positive. See interpretation

Interpretation

[2] MCR

Beta Globin Sequencing: Positive

Gene: HBB
Legacy: Beta 145, TAT>CAT, Tyr>His
HGVS: c.436T>C, p.T146H
Genomic: g.5246836A>G
Heterozygous
Classification: Hb Bethesda mutation

See REVE0/Erythrocytosis Summary Interpretation for correlation of these results with protein analysis and any provided clinical phenotype. If detected, alterations classified as Benign or Likely Benign, silent or intronic variants not known or predicted to be clinically significant 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: 31 Oct 2022 10:48 **Reported:** 31 Oct 2022 10:55

Laboratory Notes

[1] 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.

[2] This test was developed and its performance characteristics 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.

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