MAYO CLINIC LABORATORIES

Patient ID	Patient Name		Birth Date	Gender	Age
SA00140481	VALIDATIONTESTING, MEV1		1983-03-30	M	37
Order Number	**Client Order Number**	**Ordering Physician**	**Report Notes**		
SA00140481	SA00140481	CLIENT,CLIENT			
Account Information		**Collected**			
C7028846 DLMP Rochester		23 Nov 2020 12:00			

Methemoglobin Summary Interp

Methemoglobin Summary Interp

MCR

Gene: HBA1
Legacy: Alpha1 58, CAC>TAC, His>Tyr
HGVS: c.175C>T, p.His59Tyr
Genomic: g.227007C>T
Heterozygous
Classification: Hb M-Boston mutation

SUMMARY INTERPRETATION:

These results confirm Hb M-Boston, a low oxygen affinity alpha chain M-hemoglobin variant that arises from a His>Tyr substitution at the distal heme coordination residue (Nishikura 1975 PMID 235745). Heterozygous states are associated with cyanosis which may be apparent at birth and most have otherwise harmless clinical presentations (Upadhye 2015 PMID: 25079170). Patients should be aware to notify medical personnel that their Hb M variant can be associated with brown-colored blood and may interfere with pulse oximetry readings to minimize unnecessary clinical evaluations if they are otherwise asymptomatic. Clinical correlation is necessary.

GENETIC COUNSELING INFORMATION:

These findings may have relevance to this individual's relatives or descendants. Hb M-Boston and the cyanosis it can cause are inherited in an autosomal dominant manner although there is at least one report of Hb M-Boston arising de novo thus family history may be negative (Upadhye 2015 PMID: 25079170). The impact is unknown when co-inherited with an alpha thalassemia mutation or another low-oxygen affinity hemoglobin variant, although it may be tolerated to a certain degree. A genetic consultation may be of benefit.

Reviewed By MCR

JENNIFER MAIN

Received: 24 Nov 2020 08:12 **Reported:** 24 Nov 2020 08:43

Methemoglobinemia Evaluation

Methemoglobinemia Interpretation

1 MCR

1) The methemoglobin level is elevated. In addition, there is a beta chain hemoglobin variant detected by protein analysis which may be associated with the increased methemoglobin level. Clinical correlation is required. Molecular testing has been added for confirmation of variant identification. See below.

2) Methemoglobin reductase (cytochrome b5 reductase) activity was within normal limits.

3) Molecular testing of the beta globin gene has been added and a discussion of results will be reported in a separate summary interpretation when all testing under the Methemoglobinemia Evaluation profile is complete. If all testing is complete and the Methemoglobin Summary Interpretation (Test ID MEV0) is not viewable, please call Mayo Clinic Laboratories to request a copy of the full report at 1–800–533–1710.

Reviewed By MCR

JENNIFER MAIN

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

MAYO CLINIC LABORATORIES

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Hb Variant, A2 and F Quantitation,B

Result Name	Value	Unit	Reference Value	Performing Site
⚠ Low **Hb A**	**71.5**	%	95.8–98.0	MCR
Hb F	0.5	%	0.0–0.9	MCR
Hb A2	3.0	%	2.0–3.3	MCR
⚠ Abn **Variant 1**	**25.0 Hb M-Boston**	%	0.0	2 MCR

Result Name	Value	Unit	Reference Value	Performing Site
HPLC Hb Variant, B	See Interpretation			2 MCR
⚠ High **Methemoglobin, B**	**10.0**	%	0.0–1.5	MCR
Sulfhemoglobin, B	0.0	%	0.0–0.4	1 MCR
Cytochrome b5 Reductase, B	9.0	U/g Hb	7.8–13.1	1 MCR

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Alpha Globin Gene Sequencing, B

Alpha Globin Gene Sequencing, B

MCR

see interpretation

Interpretation

[1] MCR

Alpha-1 Globin Sequencing: Positive
Alpha-2 Globin Sequencing: Negative

Gene: HBA1
Legacy: Alpha1 58, CAC>TAC, His>Tyr
HGVS: c.175C>T, p.His59Tyr
Genomic: g.227007C>T
Heterozygous
Classification: Hb M-Boston mutation

The most common alpha thalassemia mutations are not excluded as this method does not detect large deletion or duplication events. If the normal allele is absent, this method cannot distinguish between a homozygous state (the same alteration on both alleles) and a hemizygous state (the detected alteration present on one allele in combination with the absence of the genomic location, e.g. a large deletion, on the other allele). If multiple alterations are present, this method cannot distinguish between cis (same allele) or in trans (different alleles) configurations. These limitations have implications for clinical phenotype, inheritance and genetic counseling. If alpha globin gene deletion/duplication testing is desired, please order Alpha-Globin Gene Analysis (test code ATHAL). Additional sample required.

Alterations are reported in Legacy and HGVS nomenclatures and by genomic location. For more information about these findings, please see HbVar: A database of Human Hemoglobin Variants and Thalassemias at http://globin.cse.psu.edu.
Classification of hemoglobin disorders by genetic data alone may result in incomplete conclusions which may significantly impact overall disorder classification and expected phenotype. Correlation with hemoglobin electrophoresis results, red blood cell indices and clinical/family history is required. If detected, alterations classified as Benign or Likely Benign are not included in this report but are available upon request. 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 alpha-1 hemoglobin (HBA1) and alpha-2 hemoglobin (HBA2) genes with reported mutations. HGVS mutation nomenclature is based on human assembly GRCh37(hg19) and RefSeq accession number NM_000518.4.

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Laboratory Notes

[1] 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.

[2] 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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