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Resources for Genetics Professionals — Genetic Disorders Associated with Founder Variants Common in the Choctaw Population

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A founder variant is a pathogenic variant observed at high frequency in a specific population due to the presence of the variant in a single ancestor or small number of ancestors. The presence of a founder variant can affect the approach to molecular genetic testing. When one or more founder variants account for a large percentage of all pathogenic variants found in a population, testing for the founder variant(s) may be performed first.

The table below includes common founder variants – here defined as **three or fewer variants that account for >50% of the pathogenic variants identified in a single gene in individuals of a specific ancestry** – in individuals of Choctaw ancestry. Note: Pathogenic variants that are common worldwide due to a DNA sequence hot spot are not considered founder variants and thus are not included.

Table. Genetic Disorders Associated with Founder Variants Common in the Choctaw Population

Gene	Disorder	MOI	DNA Nucleotide Change	Predicted Protein Change	% of Pathogenic Variants in Gene	Carrier Frequency	Ethnicity (Specific Region)	Reference Sequences	References
MPL	Congenital amegakaryocytic thrombocytopenia (OMIM 604498)	AR	c.268C>T	p.Arg90Ter	40%	Unknown	Choctaw (Mississippi)	NM_005373.3 NP_005364.1	Newman et al [2017]
			c.1609C>T	p.Arg537Trp	60%				

Included if ≤3 pathogenic variants account for ≥50% of variants identified in a specific ethnic group
AR = autosomal recessive; MOI = mode of inheritance

References

Newman LA, Luter MA, Davis DB, Abdul-Rahman OA, Johnson JM, Megason GC. Congenital amegakaryocytic thrombocytopenia: a case series indicating 2 founder variants in the Mississippi band of Choctaw Indians. J Pediatr Hematol Oncol. 2017;39:573–5. PubMed PMID: 28697167.

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Revision History

- 1 June 2023 (sw) Revision: reference sequences updated
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