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

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A founder variant is a pathogenic variant observed in 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 Métis 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.

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

Gene	Disorder	MOI	DNA Nucleotide Change	Predicted Protein Change	% of Pathogenic Variants in Gene [1]	Carrier Frequency	Ethnicity (Specific Region)	Reference Sequences	References
HEXB	Sandhoff disease	AR	c.115delG	p.Val39TrpfsTer25	>95%	1/27	Métis (N Saskatchewan)	NM_000521.4 NP_000512.2	Fitterer et al [2014]
SLC25A15	Hyperornithinemia-hyperammonemia-homocitrullinuria syndrome	AR	c.562_564delTTC	p.Phe188del	~100% [1]	1/19	Métis (N Saskatchewan) [2]	NM_014252.4 NP_055067.1	Sokoro et al [2010]

Included if ≤3 pathogenic variants account for ≥50% of variants identified in a specific ethnic group
AD = autosomal dominant; AR = autosomal recessive; MOI = mode of inheritance; N = northern
1. To date, additional pathogenic variants in this gene have not been reported in individuals from the specified region.
2. Carrier frequency reported in the population residing in Northern Saskatchewan which is predominantly Métis, but also includes individuals of Cree, Dene, and French Canadian ancestry.

References

Fitterer B, Hall P, Antonishyn N, Desikan R, Gelb M, Lehotay D. Incidence and carrier frequency of Sandhoff disease in Saskatchewan determined using a novel substrate with detection by tandem mass spectrometry and molecular genetic analysis. Mol Genet Metab. 2014;111:382–9. PubMed PMID: 24461908.

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