ALBERTA PRECISION LABORATORIES
Leaders in Laboratory Medicine

Mitochondrial DNA Testing in Alberta

Mitochondrial DNA testing through the Genetics & Genomics (G&G) North Molecular Genetics Laboratory includes:

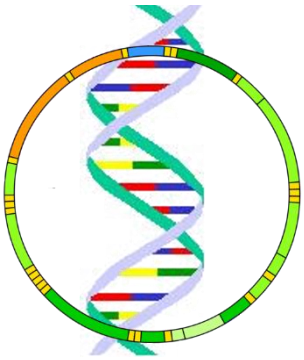
1. MNM variant panel
   - Includes common pathogenic variants for MELAS, MERRF, and NARP (see Table 1 for list of variants)
   - Available on fresh/frozen muscle, urine, or buccal (in that order of preference). In very young children with a severe phenotype, blood may be considered if urine or a buccal are not feasible.

2. LHON variant panel
   - Includes common pathogenic variants for LHON
   - Available on blood

3. Full sequencing
   - Available on fresh/frozen muscle and urine
   - Ordering is restricted to Medical Geneticists and Neuromuscular specialists
   - Full sequencing is available **ONCE per family** (please ensure the most appropriate individual and sample type is selected).

4. Deletion/Duplication Studies
   - Available on fresh/frozen muscle
     - Exception: Testing for suspected cases of Pearson syndrome should be performed on blood as mtDNA deletions are usually more abundant in blood than in other tissues.
   - Ordering is restricted to Medical Geneticists and Neuromuscular specialists.
   - **Southern blot analysis** will be performed. If negative, the lab will proceed with PCR-based assay on muscle in individuals with a "positive" Blue Native PAGE result. Please send a copy of the patient's Blue Native PAGE result to the laboratory.

5. Familial Variant
   - Testing for familial pathogenic variants will be performed by NGS as a lower level of heteroplasmy can be detected. The level of heteroplasmy can be reported. No other variants will be reported.



Mitochondrial conditions are caused by pathogenic variants in nuclear or mitochondrial genes. Testing for mitochondrial gene variants is available in the G&G North MGL. Nuclear mitochondrial testing requires funding pre-approval through the Genetic Resource Centre.

Table 1: Frequently Seen Mitochondrial Disorders:

Disorder	Variants	Test
Chronic progressive external ophthalmoplegia (CPEO)	Deletion/duplication	Deletion/duplication analysis/Southern
Kearns-Sayre syndrome (KSS)	Deletion/duplication	Deletion/duplication analysis/Southern
Pearson Syndrome	Deletion/duplication	Deletion/duplication analysis/Southern
Leigh Syndrome	m.8993T>G m.8993T>C	MNM variant panel
Neurogenic weakness with ataxia and RP (NARP)	m.8993T>G m.8993T>C	MNM variant panel
Leber hereditary optic neuropathy (LHON)	m.11778G>A m.14484T>C m.3460G>A	LHON variant panel
Mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes (MELAS)	m.3243A>G m.3271T>C m.3697G>A m.13513G>A m.13514A>G m.3252A>G	MNM variant panel
Myoclonic epilepsy with ragged-red fibres (MERRF)	m.8344A>G m.8356T>C m.8363G>A m.8361G>A	MNM variant panel

Heteroplasmy

- Individuals with mitochondrial disorders can have a mix of mutant and wildtype mtDNA in each cell (heteroplasmy)
- The percentage of heteroplasmy varies between individuals, between tissue types and may change over time

Due to variable pathogenic variant loads in different tissues, it is important that mtDNA testing be performed on the appropriate tissue type