Ontario Mitochondrial Laboratories

London Health Sciences Centre - McMaster University Mediacal Centre - Newborn Screening Ontario at CHEO
www.mitodx.ca - Phone: (613) 738-4209

Ontario Mitochondrial Disease Testing Requisition

Patient Information

Last Name: First Name: Phone:

Birthdate (dd/mm/yyyy):

Gender: ☐ Male ☐ Female ☐ Unknown

Guardian's Name:

Address:

Apt #:

City: Province:

Postal Code: Country: Canada

For Canadian Patients Only:

Provincial Health Card #:

Version:

Issuing province:

Patient Sticker

Referring Physician

Name: Phone: Fax:

Institution: Email:

Registration #:

Address:

City: Prov/State:

Postal/Zip Code: Country:

Genetic Counsellor / Nurse:

Name:

Phone: Fax:

Additional Physician:

Name:

Phone: Fax:

Specimen

Specimen Type:

(See page 8 for specimen requirements)

☐ Blood ☐ Fibroblast ☐ Urine ☐ Muscle

☐ mtDNA ☐ DNA ☐ Other:

Date of Collection(dd/mm/yy):

Hospital #: Accession #:

Last Name: First Name: Birthdate (dd/mm/yyyy):

Family Information

Specimens from this family previously sent to DNA lab:

☐ Yes ☑ No

Name of proband if different:

If Yes, please specify:

Relationship to proband:

Pedigree

Ethnicity (be specific as possible):

☐ Amish/ Mennonite/ Hutterite
☐ Ashkenazi Jewish
☐ Black/African
☐ East Asian (Japanese,Chinese)
☐ European
☐ First Nations/Inuit
☐ French Canadian
☐ Hispanic
☐ South Asian (Bengali, Indian, Filipino)
☐ Middle Eastern
☐ Other:

Consent

Please verify that the following statement is true and provide your signature:

I certify that the patient and/or legal guardian has been informed of the nature of the genetic test requested, including benefits, risks, possible results, limitations and possible implications for himself/herself and his/her family. I have answered this person's questions and have obtained informed consent for this testing.

Signature of the Referring Physician:

Last Name: First Name: Birthdate (dd/mm/yyyy):

Available Testing

Rare or Familial Mutuation Testing

Specify Gene/Mutuation:

* Please attach any supporting laboratory/pathology documents.

Select Laboratory:

- ☐ London Health Sciences Centre
- ☐ McMaster University Medical Centre
- ☐ Newborn Screening Ontario at CHEO

* Shipping instructions and specimen requirements for each laboratory are indicated on page X of this requisition.

If familial mutuation testing, please specify the following information about the proband:

Name:

Birthdate (dd/mm/yyyy):

Relationship to this patient:

Entire mtDNA Sequence by NGS

Massively Parallel Sequencing using Next Generation sequence technology. Heteroplasmic point mutations present in at least 5 % of the genomes can be detected. Suitable for patients that meet testing criteria without a specific phenotype or negative test results for a specific phenotype.

Select Laboratory:

- ☐ London Health Sciences Centre
- ☐ McMaster University Medical Centre

* Shipping instructions and specimen requirements for each laboratory are indicated on page X of this requisition.

Panels Available at Newborn Screening Ontario at CHEO

Nuclear gene NGS panels suitable for patients without a specific phenotype or a phenotype that can be caused by mutations in multiple genes.

Specimens for these panels should be sent to Newborn Screening Ontario along with a completed requisition. See page 7 for shipping instructions and specimen requirements.

- ☐ Check here if requesting the Full Panel or an additional subpanel be performed on a previously sent sample.

- ☐ Full Mitochondrial Nuclear Gene Panel (408 genes)

Subpanels:

- ☐ Mitochondrial Encephalopathy / Leigh Disease (119 genes)
- ☐ Complex I (35 genes)
- ☐ Complex IV (21 genes)
- ☐ Complexes II + III + V + CoQ + PDH Deficiencies (26 genes)
- ☐ mtDNA Depletion and Deletion (21 genes)
- ☐ Progressive External Ophthalmoplegia (PEO) / Optic Atrophy (22 genes)

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Last Name: First Name: Birthdate (dd/mm/yyyy):

Available Testing (continued)

Panels Available at London Health Sciences Centre

Targeted gene analysis including percent heteroplasmy. Suitable for defined clinical phenotypes, family studies and cascade testing.

Specimens should be sent to London Health Sciences Centre for these panels along with a completed requisition. See page 7 for shipping instructions and specimen requirements.

Kearns-Sayre Syndrome(sensitivity: 90%, tissue: muscle > blood)

- ☐ Mitochondrial DNA Deletions

LHON (Leber's Hereditary Optic Neuropathy)(sensitivity: 90%, tissue: blood)

- ☐ 11778G>A (MT-ND4)
- ☐ 14484T>C (MT-ND6)
- ☐ 14484T>C (MT-ND6)

MELAS(sensitivity: 90%, tissue: urine > blood)

- ☐ 3243A>G
- ☐ 3271 T>C
- ☐ 3291T>C
- ☐ 3260 A>G

MERRF (myoclonic epilepsy with ragged red fibers)(sensitivity: >80%)

- ☐ 8344 A>G

NARP (neurogenic muscle weakness, ataxia, and retinitis pigmentosa)(sensitivity: >50%)

- ☐ 8993T>G/C

Pearson marrow pancreas syndrome(sensitivity: 90%, tissue: blood)

- ☐ Mitochondrial DNA Deletions

Progressive external ophthalmoplegia (PEO)(sensitivity: 90%, tissue: muscle)

- ☐ Mitochondrial DNA Deletions

Hepatocerebral mtDNA depletion syndrome

- ☐ Deoxyguansine kinase deficiency (DGUOK)

Myopathic mtDNA depletion syndrome

- ☐ Thymidine kinase deficiency (TK2)

SANDO, ALPERS, SCAE,familial PEO

- ☐ Polymerase G (POLG)

Panels Available at McMaster University Medical Centre

Nuclear gene NGS panel suitable for patients without a specific phenotype or a phenotype that can be caused by mutations in multiple genes.

A specimen for this panel should be sent to McMaster University Medical Centre along with a completed requisition. See page 7 for shipping instructions and specimen requirements.

- ☐ Adult mitochondrial disease nuclear gene panel (68 genes)

Last Name: First Name: Birthdate (dd/mm/yyyy):

Clinical Information and Criteria for Testing

To be eligible for testing, the patient must satisfy any one of criteria A-D.

* Please attach any supporting laboratory/pathology documents.

Clinical Features

A Classic presentation of a recognized mitochondrial symptom complex:

- ☐ Leigh disease (subacute necrotizing encephalomyelopathy)
- ☐ Alpers disease (progressive sclerosing poliodystrophy + hepatopathy)+
- ☐ Primary lactic acidosis (in the absence of tissue hypoxia or multi-system organ failure)
- ☐ Chronic progressive external ophthalmoplegia (CPEO)
- ☐ Mitochondrial neuro-gastro-intestinal encephalomyopathy (MNGIE)
- ☐ Multiple symmetric lipomatosis (must include head and/or neck)*
- ☐ Pearson syndrome*
- ☐ Kearns-Sayre syndrome*
- ☐ Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS)*
- ☐ Myoclonic epilepsy with ragged-red fibers (MERRF)*
- ☐ Neuropathy, ataxia, and retinitis pigmentosa (NARP)*
- ☐ Leber's hereditary optic neuropathy (LHON)*
- ☐ Gentamicin-related sensorineural hearing loss*
- ☐ Sensory-Ataxia, Neuropathy, Dysarthria and Ophthalmoparesis (SANDO)+

B Clinical features satisfying B1 and any of B2 - B6 for the following conditions:

B1 At least one of the following signs in a highly oxidative tissue/organ without other known etiology:

- ☐ CNS (dev delay/regression, hypotonia, movement disorder, seizures, hemiplegic or complicated migraine)
- ☐ Pigmentary retinopathy and/or optic atrophy
- ☐ Peripheral neuropathy
- ☐ Sensorineural hearing loss
- ☐ Rhabdomyolysis and/or fixed weakness of skeletal muscle
- ☐ Cardiomyopathy and/or arrhythmias and/or conduction block
- ☐ Proximal renal tubulopathy (Fanconi syndrome)
- ☐ Type 2 diabetes mellitus
- ☐ Sideroblastic anemia
- ☐ GI tract: pseudoobstruction, hepatopathy
- ☐ Unexplained failure to thrive or short-stature (< 2 SD below normal)

AND any one of B2 - B6:

B2 ☐ Clinical progression with stepwise exacerbation of symptoms (eg. after periods of intercurrent illness)

B3 ☐ Positive family history for any of B1.

B4 ☐ Lactic acidosis (in a non-acute illness setting).

B5 ☐ Elevated alanine (plasma amino acids)

B6 ☐ Elevated 3-methylglutaconic acid (urine organic acids)

* Analysis will be initially limited to mtDNA testing

+ Analysis will be initially limited to POLG1 testing

â€¡ Percentage of normal control mean relative to citrate synthase

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Last Name: First Name: Birthdate (dd/mm/yyyy):

Clinical Information and Criteria for Testing (continued)

Pathologic and/or laboratory features (please affix relevant reports)

C Pathologic - any one of the following:

- ☐ > 2% ragged red fibers in skeletal muscle
- ☐ 1%-2% ragged red fibers if aged 30-50 years
- ☐ Any ragged red fibers if <30 years of age
- ☐ 2% subsarcolemmal mitochondrial accumulations in a patient <16 years of age
- ☐ > 2% COX-negative fibers if <50 years of age
- ☐ > 5% COX-negative fibers if >50 years of age
- ☐ Ultrastructurally abnormal mitochondria by electron microscopy
- ☐ Muscle biopsy most consistent with a mitochondriopathy per reporting pathologist (affix report)

D Biochemical - any one of the following:

- ☐ < 30% activity of any RC complex in tissue or cell lineâ€¡
- ☐ Persistent (> 2 samples on separate days) unexplained hyperlactatemia (>3.0mmol/L in freely-flowing sample drawn without tourniquet) (affix results)
- ☐ Increased lactate:pyruvate ratio (>25) in skin fibroblasts (affix results)
- ☐ Persistent (> 2 samples) hyperalaninemia >500uM (affix amino acids analyses)
- ☐ Persistent (> 2 samples) abnormal excretion of lactate, pyruvate, and/or TCA cycle intermediates in urine (affix results)
- ☐ Evidence of mtDNA depletion or multiple mtDNA deletions (affix results)
- ☐ Patient fibroblasts unable to grow with galactose as sole carbon source

* Analysis will be initially limited to mtDNA testing

+ Analysis will be initially limited to POLG1 testing

â€¡ Percentage of normal control mean relative to citrate synthase

Last Name: First Name: Birthdate (dd/mm/yyyy):

Billing Information

Instructions:

- Do not fill out the billing form for patients who have an Ontario health card and who meet the above criteria for testing.
- The referring physician should complete the appropriate section of the Billing Form to specify billing method.
- The completed requisition should be sent with specimens to the appropriate laboratory depending on the selected testing. If the selected testing will be performed at more than one laboratory, send a copy of the complete requisition to each laboratory.
- Contact Newborn Screening Ontario at (613-738-4209 or newbornscreening@cheo.on.ca) for billing inquiries.

Complete to have the healthcare provider billed:

Billing address of hospital, referring laboratory, clinic, referring physician, or medical group: (if different from requisition):

Name: Address:

Institution:

Registration #: City: Province:

Phone: Fax: Postal Code: Country:

Complete to have the patient/guardian billed directly:

Send bill to: ☐ Patient ☐ Guardian

Method of Payment:

☐ American Express ☐ Mastercard ☐ Visa

Name on credit card:

Credit card number:

Expiry Date:

Cardholder Signature (required):

Mailing Address of Patient/Guardian

(if different from requisition)

Name:

Address:

City: Prov/State:

Postal Code: Country:

Shipping Informatiom

Please ship specimens to the appropriate laboratory as specified in the Available Testing section.

London Health Sciences Centre (LHSC)
Molecular Genetics Laboratory
Victoria Hospital, Room B10-123A
800 Commissioners Road East
London, Ontario N6A 5W9
Phone: 519-685-8122
Fax: 519-685-8279

McMaster University Medical Centre (MUMC)
Molecular Genetics Laboratory, Room 2N22
1200 Main Street West, Hamilton, ON L8N 3Z5
Telephone: 905-521-2100 ex. 76944
Fax: 905-521-7913
Email: moleculargenetics@hhsc.ca

Newborn Screening Ontario (NSO)
415 Smyth Road
Ottawa, Ontario K1H 8M8
Phone: (613) 738-4209
Fax: (613) 738-4214

Specimen Requirements

Please provide specimens as indicated for the selected test(s) in the Available Testing section. If no tissue preference is specified, please send Blood according to the instructions below. Please be sure to follow all shipping instructions that pertain to each tissue type.

Specimen Type:	**Blood**
Requirements:	2 x 5ml (Adults/Children) and 2 x 3ml (Infant less than 2yrs) in EDTA (purple-top) tubes.
Shipping Instructions:	Ship at room temperature in an insulated container by overnight courier. Do not heat or freeze.
Specimen Type:	**Fibroblast**
Requirements:	Tissue culture dish 100x200mm.
Shipping Instructions:	Ship at room temperature in an insulated container by overnight courier. Do not heat or freeze.
Specimen Type:	**Urine**
Requirements:	4ml of of a random urine (no preservatives). Store the specimen frozen at -20C.
Shipping Instructions:	Ship frozen on dry ice in an insulated container by overnight courier.
Specimen Type:	**Muscle**
Requirements:	30-50 mg from muscle.
Shipping Instructions:	Ship in dish on ice.
Specimen Type:	**DNA**
Requirements:	At least 5Î¼g (minimal concentration of 50ng/uL).
Shipping Instructions:	Please contact Lab prior to shipping.
Specimen Type:	**Other**
Requirements:	Please contact Lab prior to shipping.
Shipping Instructions:	Please contact Lab prior to shipping.