



MOLECULAR REQUISITION

SHIP SAMPLES TO: **NSO SPECIMEN HUB**
415 Smyth Road Ottawa, ON K1H 8M8

Lab Use Only

PATIENT INFORMATION		ORDERING PROVIDER	
Health Card Number	Sex <input type="checkbox"/> Male <input type="checkbox"/> Female <input type="checkbox"/> Ambiguous <input type="checkbox"/> Unknown	Date of Birth yyyy mm dd	Name
Patient's Telephone Contact Number	MRN/Hospital Number		Email
Patient's Last Name	Patient's First Name		Phone Fax
Patient's Address		Institution	
Ethnicity: _____ <input type="checkbox"/> Fetal Sample		Phone Fax	
For STAT requests please indicate how a shorter TAT will change patient management: Ongoing pregnancy; result needed for decision making within 6wks (i.e. termination or birth) Estimated due date: Positive newborn screens where molecular results are essential for treatment decisions Expedited results will directly impact management decisions For inquiries please contact nsomolecular@cheo.on.ca		Copy results to clinician/practitioner: Name Phone Fax Copy results to clinician/practitioner: Name Phone Fax	

TEST REQUESTED see FAQ section on NSO website for more information	SPECIMEN TYPE
Targets of Newborn Screening – targeted panel (complete Section 1) Primary Immune Deficiencies – augmented exome slice (complete Section 2; whole blood or DNA) Mitochondrial Diseases – augmented exome slice (complete Section 3; whole blood or DNA) TREC (DBS only; for out-of-province newborn screening samples only) SMA - ddPCR/MLPA CFTR common mutation panel (for carrier testing and CF newborn screen positive only) Familial Variant Testing (complete table below) Maternal Cell Contamination (MCC) studies (for prenatal and umbilical cord blood testing)	Whole Blood (room temp, EDTA tubes) Adult 1x5mL, Children 1x4mL, Infant ≤2yo 1x3mL Umbilical Cord blood (maternal sample for MCC studies required) EDTA blood DBS DNA (>5 µg with at least [50ng/ µL]) Source: _____ DBS (Dried bloodspot - Whatman 903) Other: _____ Contact NSO prior to sending
<input type="checkbox"/> Variant reinterpretation (must attach NSO report issued >=1 year ago)	

SPECIMEN COLLECTION			
Date of collection (YYYY/MM/DD)		Time of Collection (24HR)	
# Tubes (if applicable)		Specimen ID	

Please contact us if this is a precious sample. For more information on precious samples and our sample retention policy, please visit our website.

AUTHORISATION	
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 ordering healthcare provider:

TESTING FOR KNOWN FAMILIAL VARIANT(S) <input type="checkbox"/> Please provide proband's report or NSO report number and family history			
Proband's Name / DOB:		Relationship to Proband:	
Gene and Variant(s): <i>Transcript (NM number) required if report not attached</i>			
Personal History: Asymptomatic Symptomatic:			
Family History:			
Name(s) and DOB of other submitted family members:			

Complete NSO's billing form if patient is not covered by OHIP; attach subsequent pages/sections as needed





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SECTION 1: MOLECULAR TESTING FOR DISEASES TARGETED BY NEWBORN SCREENING ONTARIO

Disease Targeted: _____

Gene (or choose from list below); *If a multi-gene panel is being requested, please indicate if you are suspicious of a specific gene(s):*

Clinical Indication:

Family History (please attach all relevant documents related to previous test results and clinical diagnosis):

AMINO ACID DISORDERS (requesting a panel is equivalent to requesting all related subpanels)

x	PANEL	x	SUBPANEL	GENES
	Homocystinuria		Hypermethioninemia	ADK, AHCY, CBS, GNMT, MAT1A, SLC25A13
			Hypomethioninemia	MTHFR, MTR, MTRR
	Phenylketonuria		PAH Deficiency	PAH (sequencing + reflex MLPA as needed)
			Bioppterin Deficiencies	DNAJC12, GCH1, PCBD1, PTS, QDPR, SPR
	Tyrosinemia		Elevated Succinylacetone	FAH, GSTZ1
			Elevated Tyrosine	HPD, TAT
	Urea Cycle Diseases		High citrulline	ASS1, SLC25A13
			High ASA	ASL
			Low citrulline	CPS1, NAGS, OTC
			Other	ARG1, CA5A, GLUL, GLUD1, OAT, SLC7A7, SLC25A2, SLC25A15
	Maple Syrup Urine Disease			BCKDHA, BCKDHB, DBT, DLD

ORGANIC ACID DISORDERS (requesting a panel is equivalent to requesting all related subpanels)

x	PANEL	x	SUBPANEL	GENES
	Multiple carboxylase Deficiency		Biotinidase Deficiency	BTBD
			Other	CA5A, HLCS
	Propionic / Methylmalonic acidemias		PA	PCCA, PCCB
			MMA	ACSF3, ALDH6A1, MCEE, MLYCD, MMAA, MMAB, MMUT, SUCLA2, SUCLG1
			MMA + Homocysteinemia	ABCD4, AMN, CBLIF, CD320, CUBN, HCF1, LMBRD1, MMACHC, MMADHC, TCN1, TCN2
	Isovaleric acidemia			ACADSB, FLAD1, IVD
	Glutaric aciduria Type 1			GCDH
	Isobutyryl-CoA dehydrogenase deficiency			ACAD8
	Succinic semialdehyde dehydrogenase deficiency			ALDH5A1
	b-ketothiolase deficiency			ACAT1
	Guanidinoacetate Methyltransferase Deficiency			GAMT

FATTY ACID OXIDATION DISORDERS Check here to request ALL genes noted below

x	PANEL	GENES
	Carnitine Uptake Deficiency	SLC22A5
	MCAD Deficiency	ACADM (sequencing + reflex MLPA as needed)
	LCHAD/MTP Deficiency	HADHA, HADHB
	VLCAD Deficiency	ACADVL
	MADD/Glutaric Aciduria Type2	ETFA, ETFB, ETFDH, FLAD1, SLC52A2, SLC52A3, SLC52A1
	CPT2 Deficiency	CPT2
	CACT Deficiency	SLC25A20
	CPT1 Deficiency	CPT1A
	Other FAOD	ACAA2, ACAD9, ACADL, ACADS, ECHS1, HADH

CONGENITAL ADRENAL HYPERPLASIA (if both requested, CYP21A2 will be performed first and reflex to panel)

21-Hydroxylase Deficiency	CYP21A2 (includes MLPA and long-range PCR analyses for CNVs and common rearrangements)
Other	ARMCS, CYP11B1, CYP11B2, CYP17A1, HSD3B2, POR, PRKAR1A, STAR

GALACTOSEMIA

GALT Deficiency	GALT
Other	GALK1, GALE, GALM, GLUT2 (SLC2A2)

MUCOPOLYSACCHARIDOSIS TYPE I

Mucopolysaccharidosis type I	IDUA
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PEROXISOMAL STORAGE DISORDERS Check here to request ALL genes noted below

XL-Adrenoleukodystrophy	ABCD1
Zellweger Spectrum	ACBD5, ACOX1, HSD17B4, PEX1, PEX10, PEX11B, PEX12, PEX13, PEX14, PEX16, PEX19, PEX2, PEX26, PEX3, PEX5, PEX6, PEX7





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SECTION 2: MOLECULAR TESTING FOR INBORN ERRORS OF IMMUNITY

PANEL SELECTION

Severe Combined/Primary Immune Deficiency (251 gene augmented exome slice), please visit our [website](#) for full list of genes

SUBPANELS

- ADA Deficiency (*ADA*)
- Chronic Granulomatous Disease (*CYBA, CYBB, CYBC1, G6PD, NCF1*, NCF2, NCF4*) [*limited coverage due to high homology with duplicated regions in genome; please note that this gene is not included in the full severe combined/primary immune deficiency panel]
**Additional testing to ensure full coverage of NCF1 can only be requested if patient has had an abnormal neutrophil oxidative burst index*
- Aicardi-Goutières syndrome (*ADAR, IFIH1, RNASEH2A, RNASEH2B, RNASEH2C, SAMHD1, TREX1*)

CLINICAL DETAILS

Please provide detailed information regarding patient's phenotype, age of onset of symptoms, previous tests completed, and family history:

- Age of onset:
- Family history:
- Other:

CLASSIC PRESENTATIONS

- | | |
|--|--|
| <input type="checkbox"/> ADA deficiency | <input type="checkbox"/> G6PD deficiency |
| <input type="checkbox"/> Aicardi-Goutières syndrome | <input type="checkbox"/> Hyper IgE syndrome – Autosomal Dominant |
| <input type="checkbox"/> Autoimmune lymphoproliferative syndrome | <input type="checkbox"/> Hyper IgE syndrome – Autosomal Recessive |
| <input type="checkbox"/> Chronic granulomatous disease | <input type="checkbox"/> Mendelian susceptibility to mycobacterial disease |
| <input type="checkbox"/> Common variable immunodeficiency | <input type="checkbox"/> Severe combined immunodeficiency |
| <input type="checkbox"/> Familial cold autoinflammatory syndrome | <input type="checkbox"/> Wiskott-Aldrich syndrome |
| | <input type="checkbox"/> Other (indicate if you are suspicious of a specific gene): |

LABORATORY FEATURES

- | | | |
|--|--|---|
| <input type="checkbox"/> Elevated inflammatory markers | <input type="checkbox"/> Abnormal Neutrophil Oxidative Burst Index | <input type="checkbox"/> Low or absent B cell number |
| <input type="checkbox"/> Anemia | <input type="checkbox"/> Abnormal TREC assay | <input type="checkbox"/> Agammaglobulinemia |
| <input type="checkbox"/> Neutropenia | <input type="checkbox"/> Low or absent CD4+ T cell number | <input type="checkbox"/> Increased immunoglobulins: <input type="checkbox"/> IgG <input type="checkbox"/> IgA <input type="checkbox"/> IgM <input type="checkbox"/> IgE |
| <input type="checkbox"/> Lymphopenia | <input type="checkbox"/> Low or absent CD8+ T cell number | <input type="checkbox"/> Decreased immunoglobulins: <input type="checkbox"/> IgG <input type="checkbox"/> IgA <input type="checkbox"/> IgM <input type="checkbox"/> IgE |
| <input type="checkbox"/> Thrombocytopenia | <input type="checkbox"/> Abnormal T cell function | <input type="checkbox"/> Poor specific antibody response to vaccine |
| <input type="checkbox"/> Eosinophilia | <input type="checkbox"/> Low or absent NK function | |

CLINICAL FEATURES

RHEUMATOLOGICAL/IMMUNE DYSREGULATION

- Arthritis
- Granulomas
- Hepato/splenomegaly
- Lymphadenopathy
- Recurrent fevers
- Systemic lupus erythematosus
- Vasculitis

HEMATOLOGICAL

- Autoimmune cytopenia
- Bone marrow failure
- Evan's syndrome
- Hemophagocytic lymphohistiocytosis
- Lymphoma

GASTROINTESTINAL

- Chronic diarrhea
- Celiac disease
- Enteropathy
- Inflammatory bowel disease
- Perianal abscess/fistula
- Liver/biliary disease

INFECTIONS

- Abscesses
- Candidiasis
- Epstein-Barr virus
- Mycobacterium tuberculosis
- Non-tuberculous mycobacteria
- Recurrent infections: bacterial fungal viral
- Recurrent pneumonia
- Skin and/or connective tissue infections

DERMATOLOGICAL

- Alopecia
- Bullous pemphigoid
- Dermatitis/eczema
- Psoriasis
- Urticaria
- Vitiligo
- Warts

PULMONARY

- Asthma
- Bronchiectasis
- Chronic obstructive pulmonary disease
- Interstitial lung disease

OTHER

- Developmental delay
- Endocrinopathy
- Facial dysmorphism
- Failure to thrive
- Hearing loss
- Microcephaly
- Short stature
- Unexplained weight loss





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SECTION 3: MOLECULAR TESTING FOR MITOCHONDRIAL DISEASES

Criteria for testing requires selections from at least one classic presentation OR at least one pathologic/lab feature OR at least one biochemical feature OR (at least one sign in CNS/heart/eyes/muscles AND one "other")

PANEL SELECTION

Full Mitochondrial Nuclear Gene Panel (437 gene augmented exome slice), please visit our [website](#) for full list of genes

SUBPANELS

- Mitochondrial Encephalopathy / Leigh Disease (117 genes)
- mtDNA Depletion and Deletion (19 genes)
- Progressive External Ophthalmoplegia (PEO) / Optic Atrophy (77 genes)
- Pyruvate Dehydrogenase Complex Deficiency (16 genes)
- Hydroxyglutaric Aciduria (4 genes)

Please contact laboratory to request another subset of the full nuclear gene panel

CLINICAL DETAILS

Please provide detailed information regarding patient's phenotype, age of onset of symptoms, previous tests completed, and family history:

- Age of onset:
- Family history:
- Other:

CLASSIC PRESENTATIONS

- | | |
|--|---|
| <input type="checkbox"/> Alpers disease | <input type="checkbox"/> Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS) |
| <input type="checkbox"/> Chronic progressive external ophthalmoplegia (CPEO) | <input type="checkbox"/> Mitochondrial neuro-gastro-intestinal encephalomyopathy (MNGIE) |
| <input type="checkbox"/> Gentamicin-related sensorineural hearing loss | <input type="checkbox"/> Multiple symmetric lipomatosis |
| <input type="checkbox"/> Kearns-Sayre syndrome | <input type="checkbox"/> Myoclonic epilepsy with ragged-red fibers (MERRF) |
| <input type="checkbox"/> Leber's hereditary optic neuropathy (LHON) | <input type="checkbox"/> Neuropathy, ataxia, and retinitis pigmentosa (NARP) |
| <input type="checkbox"/> Leigh disease | <input type="checkbox"/> Pearson syndrome |
| | <input type="checkbox"/> Primary lactic acidosis |
| | <input type="checkbox"/> Sensory-ataxia, neuropathy, dysarthria and ophthalmoparesis (SANDO) |
| | <input type="checkbox"/> Other (indicate if you are suspicious of a specific gene): |

PATHOLOGIC/LABORATORY FEATURES

- Ragged red fibers: _____ %
- COX-negative fibers: _____ %
- Ultrastructurally abnormal mitochondria by electron microscopy
- Muscle biopsy consistent with mitochondriopathy (affix report)

BIOCHEMICAL FEATURES

- Persistent hyperalaninemia
- Persistent abnormal excretion of lactate, pyruvate or TCA intermediates in urine
- Evidence of mtDNA depletion or multiple mtDNA deletions (affix results)
- <30% activity of any RC complex in tissue or cell line
- Increased lactate pyruvate ratio (>25) in skin fibroblasts

CLINICAL FEATURES

CENTRAL NERVOUS SYSTEM (CNS)

- Developmental delay
- Regression
- Movement disorder
- Seizures
- Hemiplegic or complicated migraine
- Peripheral neuropathy
- Sensorineural hearing loss

OTHER

- Clinical progression with stepwise exacerbation of symptoms
- Elevated alanine (PAA)
- Elevated 3-methylglutaconic acid (UOA)
- GI tract: pseudoobstruction
- GI tract: hepatopathy
- Lactic acidosis (in non-acute illness setting)

HEART

- Arrhythmias
 - Cardiomyopathy
 - Conduction block
- EYES**
- Optic atrophy
 - Pigmentary retinopathy

MUSCLES

- Hypotonia
- Rhabdomyolysis
- Fixed weakness of skeletal muscle
- Ataxia

- Proximal renal tubulopathy (Fanconi syndrome)
- Sideroblastic anemia
- Short stature (<2 SD below normal)
- Type 2 diabetes mellitus
- Unexplained failure to thrive

