

**ROBERT GUTHRIE BIOCHEMICAL & MOLECULAR GENETICS LABORATORY**

**Georgirene D. Vladutiu, Ph.D., Director**  
THE BUFFALO GENERAL HOSPITAL  
KALEIDA HEALTH  
100 High Street, Room A762, Buffalo, NY 14203  
Telephone: (716) 859-7741 • Fax: (716) 859-7749  
[www.rgbmgl.org](http://www.rgbmgl.org)

Mutation Analysis for  
Metabolic Myopathy  
Page 1 of 4

CLIA License #33D0685375 • New York State Laboratory Permit # PFI2005

**REQUEST FOR LABORATORY ANALYSIS**

**PATIENT INFORMATION**

Please include Your accession # NP \_\_\_\_\_  
Name: \_\_\_\_\_  
Address: \_\_\_\_\_  
City/State/Zip: \_\_\_\_\_  
Phone: \_\_\_\_\_  
Sex \_\_\_\_\_ DOB \_\_\_\_\_ Age \_\_\_\_\_ Race \_\_\_\_\_  
Ethnicity \_\_\_\_\_  
Diagnostic Code(s) **(Required)**: \_\_\_\_\_

**REFERRING PHYSICIAN INFORMATION:**

Date of Request: \_\_\_\_\_  
Name: \_\_\_\_\_  
Address: \_\_\_\_\_  
City/State/Zip: \_\_\_\_\_  
Phone: \_\_\_\_\_ Fax: \_\_\_\_\_  
E-Mail: \_\_\_\_\_  
Mail Results to: Referring Physician   
Or Institution   
Or other physician

**INSTITUTION INFORMATION:** (For billing and resulting):

Guarantor: \_\_\_\_\_  
Contact Person: \_\_\_\_\_  
Department: \_\_\_\_\_  
Address: \_\_\_\_\_  
City/State/Zip: \_\_\_\_\_  
Phone: \_\_\_\_\_

**OTHER PHYSICIAN INFORMATION:**

Name: \_\_\_\_\_  
Address: \_\_\_\_\_  
City/State/Zip: \_\_\_\_\_  
Phone: \_\_\_\_\_  
Fax: \_\_\_\_\_

The referring institution will be billed.

**SPECIMEN INFORMATION:**

Tissue Submitted: [ ] Whole Blood [ ] Autopsy Specimen Collection Date: \_\_\_\_\_  
[ ] Skeletal Muscle (type) \_\_\_\_\_ [ ] Biopsy  
[ ] Cardiac Muscle Specimen Storage Prior to Shipment:  
[ ] Liver [ ] Liquid Nitrogen  
[ ] Other: \_\_\_\_\_ [ ] -70° C  
[ ] -20° C

This patient has consented to the testing of his/her tissue or body fluid for an inborn error of metabolism.  
The implications of genetic testing have been discussed with the patient. **(Required)**

Physician's initials \_\_\_\_\_  
Date: \_\_\_\_\_

OFFICE USE ONLY	
Date Received _____	Amount Received _____
ID Number _____	Comments _____
Initials _____	_____

Patient Name: \_\_\_\_\_ Current Medications & Dosage: \_\_\_\_\_  
 Reason for Referral: \_\_\_\_\_ Current Supplements: \_\_\_\_\_  
 Cholesterol-Lowering Drugs \_\_\_\_\_  
 and Dosage (if applicable): \_\_\_\_\_

Please √ appropriate choices

FAMILY HISTORY		GENERAL CHARACTERISTICS		NEUROMUSCULAR ABNORMALITIES				
<input type="checkbox"/>	50	Consanguinity in family	<input type="checkbox"/>	1760	Respiratory distress	<input type="checkbox"/>	6051	Headache
<input type="checkbox"/>	51	On cholesterol-lowering drug	<input type="checkbox"/>	1761	Multiple congenital anomalies	<input type="checkbox"/>	6052	Migraine
<input type="checkbox"/>	100	Mental retardation	<input type="checkbox"/>	1765	Hypoglycemia	<input type="checkbox"/>	6075	Visual loss
<input type="checkbox"/>	125	Psychomotor retardation	<input type="checkbox"/>	1770	Cerebral palsy	<input type="checkbox"/>	7000	Ophthalmoplegia
<input type="checkbox"/>	150	Metabolic disorder, hx of	<input type="checkbox"/>	1775	Visual impairment	<input type="checkbox"/>	7050	Rhabdomyolysis
<input type="checkbox"/>	175	Viral infection, assn. with	<input type="checkbox"/>	1777	Behavior problems	<input type="checkbox"/>	8000	Heat stroke
<input type="checkbox"/>	200	Affected child	<input type="checkbox"/>	1801	Neurofibromatosis	<input type="checkbox"/>	8050	Malignant hyperthermia
<input type="checkbox"/>	201	Affected parent	<input type="checkbox"/>	1802	Fascio-scapulo-humeral disease	<input type="checkbox"/>	8075	<b>Normal</b> neurologic exam
<input type="checkbox"/>	202	Affected sibling	<input type="checkbox"/>	1805	Diabetes	<input type="checkbox"/>	8076	Abnormal neurologic exam
<input type="checkbox"/>	250	Ethnic predilection	<b>NEUROMUSCULAR ABNORMALITIES</b>					
<input type="checkbox"/>	275	No family hx of present illness	<input type="checkbox"/>	2000	Muscle pain	<b>LABORATORY STUDIES</b>		
<input type="checkbox"/>	280	Hearing impairment	<input type="checkbox"/>	2050	Muscle weakness	<input type="checkbox"/>	10000	Metabolic acidosis
<input type="checkbox"/>	281	Diabetes, history of	<input type="checkbox"/>	3000	Muscle cramps	<input type="checkbox"/>	10025	<b>No</b> metabolic acidosis
<b>GENERAL CHARACTERISTICS</b>		<input type="checkbox"/>	3010	Fibromyalgia	<input type="checkbox"/>	10030	Respiratory acidosis	
<input type="checkbox"/>	1000	Hepatomegaly	<input type="checkbox"/>	3025	Fatigue	<input type="checkbox"/>	10050	Hypoglycemia
<input type="checkbox"/>	1025	Hepatitis	<input type="checkbox"/>	3030	Lethargy	<input type="checkbox"/>	10055	<b>No</b> hypoglycemia
<input type="checkbox"/>	1026	Liver failure	<input type="checkbox"/>	3050	Stiffness	<input type="checkbox"/>	10075	Neutropenia
<input type="checkbox"/>	1027	Hepatic dysfunction	<input type="checkbox"/>	3060	Abnormal gait	<input type="checkbox"/>	10076	Neutrolytic anemia
<input type="checkbox"/>	1050	Splenomegaly	<input type="checkbox"/>	3065	History of falling	<input type="checkbox"/>	10100	Hyperammonemia
<input type="checkbox"/>	1100	Cardiomegaly	<input type="checkbox"/>	3066	Clumsiness	<input type="checkbox"/>	10125	<b>No</b> hyperammonemia
<input type="checkbox"/>	1125	Cardiomyopathy	<input type="checkbox"/>	3075	Ataxia	<input type="checkbox"/>	10150	Lactic acidemia
<input type="checkbox"/>	1140	Other cardiac abnormalities	<input type="checkbox"/>	3080	Dystonia	<input type="checkbox"/>	10155	<b>Normal</b> lactate
<input type="checkbox"/>	1145	Kidney abnormalities	<input type="checkbox"/>	3085	Spastic diplegia	<input type="checkbox"/>	10160	Lactate unknown
<input type="checkbox"/>	1146	Renal failure	<input type="checkbox"/>	3090	Dysphagia	<input type="checkbox"/>	10200	Ketosis
<input type="checkbox"/>	1147	Gastrointestinal problems	<input type="checkbox"/>	3092	Dysarthria	<input type="checkbox"/>	10225	<b>No</b> ketosis
<input type="checkbox"/>	1148	Hyperthyroidism	<input type="checkbox"/>	4000	Exercise intolerance	<input type="checkbox"/>	10250	Elevated CK Unit:
<input type="checkbox"/>	1149	Hypothyroidism	<input type="checkbox"/>	4001	<b>Normal</b> EEG	<input type="checkbox"/>	10260	<b>Normal</b> CK
<input type="checkbox"/>	1150	Unusual hair or nails	<input type="checkbox"/>	4004	Abnormal EEG	<input type="checkbox"/>	10265	CK unknown
<input type="checkbox"/>	1175	Apnea	<input type="checkbox"/>	4005	Abnormal brain MRI/CT	<input type="checkbox"/>	10266	Elevated aldolase
<input type="checkbox"/>	1200	Developmental delay	<input type="checkbox"/>	4007	<b>Normal</b> EMG	<input type="checkbox"/>	10267	<b>Normal</b> aldolase
<input type="checkbox"/>	1215	Microcephaly	<input type="checkbox"/>	4010	Abnormal EMG	<input type="checkbox"/>	10275	Elevated CSF protein
<input type="checkbox"/>	1221	Motor delay	<input type="checkbox"/>	4012	<b>Normal</b> EKG	<input type="checkbox"/>	10276	Elevated CSF lactate
<input type="checkbox"/>	1222	Motor regression	<input type="checkbox"/>	4013	Abnormal EKG	<input type="checkbox"/>	10277	<b>Normal</b> CSF protein
<input type="checkbox"/>	1225	Short stature	<input type="checkbox"/>	4015	Demyelination	<input type="checkbox"/>	10280	Elevated liver enzymes
<input type="checkbox"/>	1250	Coarse facies	<input type="checkbox"/>	4017	Nerve dysfunction	<input type="checkbox"/>	10285	<b>Normal</b> liver enzymes
<input type="checkbox"/>	1275	Dysmorphic features	<input type="checkbox"/>	4019	<b>Normal</b> ischemic exercise test	<input type="checkbox"/>	10286	Iron deposition in hepatocytes
<input type="checkbox"/>	1276	Congenital malformations	<input type="checkbox"/>	4020	Abnormal ischemic exercise test	<input type="checkbox"/>	10300	Elevated pyruvate
<input type="checkbox"/>	1300	Corneal clouding	<input type="checkbox"/>	4025	<b>Normal</b> brain MRI	<input type="checkbox"/>	10310	<b>Normal</b> pyruvate
<input type="checkbox"/>	1325	Retinal degeneraton	<input type="checkbox"/>	4030	Encephalopathy	<input type="checkbox"/>	10315	Pyruvate unknown
<input type="checkbox"/>	1350	Cataracts	<input type="checkbox"/>	4050	Myoglobinuria	<input type="checkbox"/>	10316	Lactate/pyruvate >25
<input type="checkbox"/>	1375	Skeletal anomalies	<input type="checkbox"/>	4051	<b>No</b> pigmenturia	<input type="checkbox"/>	10318	Lactate/pyruvate <25
<input type="checkbox"/>	1400	Umbilical hernia	<input type="checkbox"/>	4052	Myoglobinemia	<input type="checkbox"/>	10320	Lactate/pyruvate normal
<input type="checkbox"/>	1425	Inguinal hernia	<input type="checkbox"/>	5000	Seizures	<input type="checkbox"/>	10325	Elevated plasma acylcarnitine
<input type="checkbox"/>	1450	Failure to thrive	<input type="checkbox"/>	5001	Tremor	<input type="checkbox"/>	10330	Plasma carnitine deficiency
<input type="checkbox"/>	1500	Vomiting	<input type="checkbox"/>	5050	Stroke	<input type="checkbox"/>	10335	<b>Normal</b> plasma carnitine
<input type="checkbox"/>	1550	Recurrent Infections	<input type="checkbox"/>	6000	Myoclonus	<input type="checkbox"/>	10350	Elevated urine organic acids
<input type="checkbox"/>	1600	Fasting-induced symptoms	<input type="checkbox"/>	6025	Choreoathetoid movements	<input type="checkbox"/>	10355	<b>Normal</b> urine organic acids
<input type="checkbox"/>	1625	<b>Normal</b> intelligence	<input type="checkbox"/>	6026	Hypertonia	<input type="checkbox"/>	10360	Abnormal plasma amino acids
<input type="checkbox"/>	1650	Intellectual impairment	<input type="checkbox"/>	6027	Parkinsonism	<input type="checkbox"/>	10366	Abnormal urinary mucopolysaccharides
<input type="checkbox"/>	1660	<b>Normal</b> hearing	<input type="checkbox"/>	6028	Decreased tone	<input type="checkbox"/>	10365	<b>Normal</b> plasma amino acids
<input type="checkbox"/>	1675	Hearing impairment	<input type="checkbox"/>	6030	<b>Normal</b> ophthalmologic exam	<input type="checkbox"/>	10370	Chromosome abnormality
<input type="checkbox"/>	1700	Progressive course	<input type="checkbox"/>	6035	<b>Abnormal</b> ophthalmologic exam			Type:
<input type="checkbox"/>	1725	Non-progressive course	<input type="checkbox"/>	6050	Ptosis	<input type="checkbox"/>	10371	<b>Normal</b> chromosomes
<input type="checkbox"/>	1750	Hypotonia						

Patient Name: \_\_\_\_\_

Please ✓ appropriate choices

MOLECULAR STUDIES			MUSCLE HISTOLOGY		
<input type="checkbox"/>	10375	MELAS mutation present	<input type="checkbox"/>	11281	Ring Fibers
<input type="checkbox"/>	10376	MELAS mutation absent	<input type="checkbox"/>	11285	Vacuolar myopathy
<input type="checkbox"/>	10377	MERRF mutation present	<input type="checkbox"/>	11286	Rimmed vacuoles
<input type="checkbox"/>	10378	MERRF mutation absent	<input type="checkbox"/>	11287	Nemaline rods
<input type="checkbox"/>	10379	mtDNA deletion present	<input type="checkbox"/>	11280	<b>Normal</b> biopsy
<input type="checkbox"/>	10380	mtDNA deletion absent	<b>MUSCULAR HISTOCHEMISTRY</b>		
<input type="checkbox"/>	10381	NARP mutation present	<input type="checkbox"/>	12000	Phosphorylase absent
<input type="checkbox"/>	10382	NARP mutation absent	<input type="checkbox"/>	12025	Phosphorylase present
<input type="checkbox"/>	10383	LHON mutation present	<input type="checkbox"/>	12050	Myoadenylate deaminase absent
<input type="checkbox"/>	10384	LHON mutation absent	<input type="checkbox"/>	12055	Myoadenylate deaminase present
<input type="checkbox"/>	13230	CPT2 mutation present	<input type="checkbox"/>	12100	Cytochrome c oxidase absent
<input type="checkbox"/>	13231	CPT2 mutation absent	<input type="checkbox"/>	12125	Cytochrome c oxidase present
<input type="checkbox"/>	13240	Myophosphorylase mutation present	<input type="checkbox"/>	12400	Cytochrome c oxidase increased
<input type="checkbox"/>	13241	Myophosphorylase mutation absent	<input type="checkbox"/>	12150	Succinate dehydrogenase absent
<input type="checkbox"/>	13250	Myoadenylate deaminase mutation present	<input type="checkbox"/>	12175	Succinate dehydrogenase present
<input type="checkbox"/>	13151	Myoadenylate deaminase mutation absent	<input type="checkbox"/>	12410	Succinate dehydrogenase increased
<input type="checkbox"/>	13152	Other mutation: Specify	<input type="checkbox"/>	12200	Phosphofructokinase absent
			<input type="checkbox"/>	12225	Phosphofructokinase present
			<input type="checkbox"/>	12275	Lipid storage absent
			<input type="checkbox"/>	12250	Lipid storage present
			<input type="checkbox"/>	12325	Glycogen storage absent
			<input type="checkbox"/>	12300	Glycogen storage present
			<input type="checkbox"/>	12350	NADH reactions absent
			<input type="checkbox"/>	12375	NADH reactions present
			<input type="checkbox"/>	12450	NADH reactions increased
			<input type="checkbox"/>	12376	NADH: targetoid
			<input type="checkbox"/>	12377	NADH: moth eaten
<b>MUSCLE HISTOLOGY</b>			<b>ELECTRON MICROSCOPY</b>		
<input type="checkbox"/>	11000	Ragged red fibers	<input type="checkbox"/>	13000	Membrane-bound glycogen
<input type="checkbox"/>	11010	<b>No</b> ragged red fibers	<input type="checkbox"/>	13050	Glycogen pools
<input type="checkbox"/>	11012	Increased trichrome staining	<input type="checkbox"/>	13051	<b>Normal</b> glycogen
<input type="checkbox"/>	11025	Esterase-positive fibers	<input type="checkbox"/>	13100	Abnormal number mitochondria
<input type="checkbox"/>	11050	Fiber type grouping	<input type="checkbox"/>	13125	Abnormal structure mitochondria
<input type="checkbox"/>	11070	Type 1 fiber predominance	<input type="checkbox"/>	13130	<b>Normal</b> mitochondria
<input type="checkbox"/>	11075	Type 2 fiber predominance	<input type="checkbox"/>	13150	Inclusions absent
<input type="checkbox"/>	11100	Fiber atrophy	<input type="checkbox"/>	13155	Inclusions present
<input type="checkbox"/>	11105	Fiber hypertrophy	<input type="checkbox"/>	13165	Vacuoles absent
<input type="checkbox"/>	11125	Fiber size variation	<input type="checkbox"/>	13160	Vacuoles present
<input type="checkbox"/>	11150	Central cores	<input type="checkbox"/>	13166	Lipid droplets
<input type="checkbox"/>	11175	Myopathic features	<input type="checkbox"/>	13176	Acute necrosis
<input type="checkbox"/>	11180	Neuropathic features	<input type="checkbox"/>	13177	<b>No</b> abnormalities
<input type="checkbox"/>	11185	Inflammatory infiltrates			
<input type="checkbox"/>	11200	Fiber necrosis/regeneration			
<input type="checkbox"/>	11250	Denervating process			
<input type="checkbox"/>	11265	Few internal nuclei			
<input type="checkbox"/>	11270	Moderate internal nuclei			
<input type="checkbox"/>	11275	Many internal nuclei			
<input type="checkbox"/>	11276	<b>No</b> increase in internal nuclei			

I, the referring physician, will provide for genetic counseling of this patient if a hereditary disorder is identified as a result of the requested testing to insure that the results and implications are understood by the patient. **(Required)**

Referring Physician's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

Patient Name: \_\_\_\_\_

**METABOLIC MYOPATHY MUTATION PROFILES**

PROFILE	MUTATIONS	FREQUENCY OF MUTANT ALLELES (5)
<input type="checkbox"/> Exercise Intolerance Mutation Profile (8 mutations) <ul style="list-style-type: none"> <li>● CPT II (<i>CPT2</i> gene) Mutation Profile (4 mutations) <ul style="list-style-type: none"> <li>S113L 60</li> <li>Q413fs 20</li> <li>P50H &lt;10</li> <li>G549D 5</li> </ul> </li> <li>● Myophosphorylase (<i>PYGM</i> gene) Mutation Profile (2 mutations) <ul style="list-style-type: none"> <li>R50X 60-80</li> <li>G205S 10</li> </ul> </li> <li>● Myoadenylate Deaminase (<i>AMPD1</i> gene) Mutation Profile (2 mutations) <ul style="list-style-type: none"> <li>Q12X 95</li> <li>P48L 95</li> </ul> </li> </ul>		
<input type="checkbox"/> Exercise Intolerance Mutation Profile (8 mutations) + Expanded <i>CPT2</i> Gene Mutation Analysis (2 additional <i>CPT2</i> gene mutations*)	R503C* R631C*	<5 <5
<input type="checkbox"/> Carnitine Palmitoyltransferase II ( <i>CPT2</i> gene) Mutation Profile (6 mutations)	S113L Q413fs P50H R503C R549D R631C	60 20 <10 < 5 < 5 < 5
<input type="checkbox"/> Myophosphorylase ( <i>PYGM</i> gene) Mutation Profile (2 mutations)	R50X G205S	60-80 10
<input type="checkbox"/> Myoadenylate Deaminase ( <i>AMPD1</i> gene) Mutation Profile (2 mutations)	Q12X P48L	95 95
<input type="checkbox"/> <i>CPT2</i> Gene Sequence Analysis		

**PREREQUISITES FOR ANY METABOLIC MYOPATHY MUTATION PROFILE:**

**CLINICAL:**

Patient should have evidence of pain, cramps, or stiffness with exertion ± myoglobinuria. Non-metabolic causes should be ruled out. A clinical summary must accompany all specimens sent for analysis.

**LABORATORY:**

Laboratory-based evidence for a metabolic myopathy should exist which may include but not be limited to elevated serum creatine kinase, an abnormal ischemic exercise test result, and an abnormal EMG. A summary of prior laboratory test results must accompany all specimens for analysis.

**CONSENT FORM (Required; see “Forms”)**

An informed consent and a HIPAA form must be signed by the patient and accompany the specimen.

**SPECIMEN REQUIREMENT:**

10 cc whole blood in EDTA (lavender top) shipped to arrive within 24 hours of collection at room temperature by overnight carrier. 50-100 mgs skeletal muscle biopsy snap frozen in liquid nitrogen and stored at -70°C until shipment on dry ice by overnight carrier.