

Laboratory of Molecular Neurogenetics
 Department of Pathology
 Ali Naini, Ph.D., DABCC
 www.columbiamitodiagnostics.org



COLUMBIA UNIVERSITY
 MEDICAL CENTER

630 West 168th Street
 VC 15th Floor, Room 208
 New York, NY 10032
 Tel: 212-305-3947
 Fax: 212-305-3986

REQUEST FOR GENETIC TESTING FOR Mitochondrial diseases

(Must be completely filled out; Informed consent MUST be signed by patient, parent/legal guardian or legal next of kin.)

PATIENT INFORMATION:		REQUESTING PHYSICIAN:	
Last Name:	First Name:	Last Name:	First Name:
Date of Birth:	Gender: <input type="checkbox"/> Male <input type="checkbox"/> Female	Institution:	
Address:		Address:	
City, State, and ZIP:		City, State, and ZIP:	
Telephone:		Telephone:	Fax:
CUMC MRN (Unit number):			
INSTITUTIONAL BILLING(PREFERRED): CHARGES WILL BE BILLED TO THE SUBMITTING INSTITUTION/PHYSICIAN		ALTERNATE BILLING INFORMATION:	
Institution:		Bill to: <input type="checkbox"/> CREDIT CARD <input type="checkbox"/> PATIENT (SELF PAY) <input type="checkbox"/> OTHER:	
Department:		Cardholder's Name:	
Address:		Credit Card Number:	
Contact:		Card Type: <input type="checkbox"/> AMEX <input type="checkbox"/> MASTERCARD <input type="checkbox"/> VISA <input type="checkbox"/> OTHER:	
Telephone: Fax:		Expiration Date:	
TEST ORDERED (FILL IN COMPLETELY):		TISSUE SUBMITTED	
<input type="checkbox"/> Mitochondrial DNA Point Mutations (Please specify mutation(s) on Pages 4-5) <input type="checkbox"/> Southern Blot for multiple deletions of mitochondrial DNA <input type="checkbox"/> Mitochondrial DNA depletion <input type="checkbox"/> Gene Sequencing <input type="checkbox"/> Mitochondrial Enzyme Analysis <input type="checkbox"/> Thymidine Phosphorylase activity <input type="checkbox"/> Coenzyme Q10 level		<input type="checkbox"/> BLOOD <input type="checkbox"/> MUSCLE <input type="checkbox"/> OTHER: _____ Date Specimen Collected: _____ Date Specimen Sent: _____ Blood & Fluid Precautions? <input type="checkbox"/> Yes <input type="checkbox"/> No	
REASON FOR TESTING:			
<input type="checkbox"/> Diagnostic <input type="checkbox"/> Possible diagnosis of _____ <input type="checkbox"/> History of _____ <input type="checkbox"/> Positive family history of _____			
Other relevant Clinical Information:			IDC9 Code(s):
<p>Note to Health Care Practitioner: It is New York State Law, and Columbia University Policy that an informed consent be obtained prior to performing genetic predisposition testing and maintained in the patient's medical record. Please use the appropriate disease/gene information/informed consent sheet, ensure that the patient/legal guardian understands its contents, and obtain the person's signature.</p>			

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INFORMED CONSENT / ADVANCE BENEFICIARY NOTICE :

Please read the following carefully and discuss with your ordering physician/person obtaining consent before signing consent.

1. Mitochondrial diseases are diagnosed using one or a combination methodologies: biochemical (protein amount and/or activity), and molecular genetic (DNA sequence and/or configuration determined by various molecular methods such as PCR or gene sequencing).
2. The purpose of this analysis is to test for genetic disorders of mitochondria related diseases, in which mitochondria fail to create enough energy to prevent cell injury or cell death in tissue, such as liver, muscle, brain, heart, kidney, endocrine, lungs.
- 2a. You (or the person for whom you are signing) may want genetic counseling before signing for consent.
3. This is a test for genetic susceptibility ("genetic predisposition"). The risk of having the disorder may be altered by family history and/or other factors. If the test is positive for the disorder or for an increased risk of the disorder, you may wish to have further independent testing, consult your physician or have genetic counseling.
4. The condition being tested is mitochondrial defects that affect or could lead to mitochondrial diseases.
5. A positive test increases the likelihood of having mitochondrial disease. A negative result does not exclude the possibility of disease, as other mutations or tissues other than those tested could be affected. Because levels of mitochondrial DNA mutations vary in different tissues, the risk of developing a mitochondrial disease cannot be determined based on a DNA test of a single tissue.
6. The results of the above test become a part of the patient's medical record, and may be made available to individuals/organizations with legal access to the patient's medical record, on a strict "need-to-know" basis, including, but not limited to the physicians and nursing staff directly involved in the patient's care, the patient's current and future insurance carriers, and others specifically authorized by the patient/authorized representative to gain access to the patient's medical records.
7. No additional tests will be performed on this sample, without specific, signed authorization by the patient. After 60 days, unless consent is given the sample will be destroyed – please see below.
8. Medicare/Insurance Carriers may not pay for the test, in which case, the patient/responsible party will be billed for the test.

Requesting Physician or Licensed Nurse Practitioner:

Name: _____ **Title:** _____

Name of person obtaining consent: _____ **Signature:** _____

Date: _____

I have read and fully understood the above, and give my consent for this testing.

Patient name: _____

Patient signature: _____

Date: _____

If consent is given by parent or legally authorized representative:

Name: _____ **Relationship:** _____

Signature: _____ **Date:** _____

Consent for sample retention:

I consent to the retention of this blood for: (check and initial on appropriate line)

_____ My specimen may be used for routine laboratory use only. After 60 days, unless consent is given the sample will be destroyed.

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MITOCHONDRIAL DISEASE PATIENT DATA ENTRY FORM

Patient Name: _____ Date: _____

CLINICAL INFORMATION: Clinical diagnosis: _____ Age of onset: _____

Clinical features (circle appropriate responses; Y = yes; N = no; NA = information not available)

Symptoms

1st symptom: _____			
Perinatal insult	Y	N	NA
Developmental delay	Y	N	NA
Retarded in school	Y	N	NA
Exercise intolerance	Y	N	NA
Nausea/vomiting	Y	N	NA
Gastrointest. pseudoobstruction	Y	N	NA
Headache	Y	N	NA
Migraine headache	Y	N	NA
Stroke	Y	N	NA
Episodic coma	Y	N	NA
Dementia	Y	N	NA
Seizures	Y	N	NA
Myoclonus	Y	N	NA

Other: _____

Signs

Floppy baby	Y	N	NA
Asthenia	Y	N	NA
Short stature	Y	N	NA
Hirsute	Y	N	NA
Congestive heart failure	Y	N	NA
Resp. insufficiency	Y	N	NA
Diabetes mellitus	Y	N	NA
Hypothyroidism	Y	N	NA
Hypoparathyroidism	Y	N	NA
Optic atrophy	Y	N	NA
Ophthalmoplegia	Y	N	NA
Ptosis	Y	N	NA
Retinopathy	Y	N	NA
Cerebral blindness	Y	N	NA
Cerebellar signs	Y	N	NA
Hearing loss	Y	N	NA
Proximal limb weakness	Y	N	NA
Neuropathy	Y	N	NA

State neuropathy type: _____

Other: _____

LABORATORY STUDIES:

Elevated lactate	Y	N	NA
Elevated pyruvate	Y	N	NA
Elevated CSF protein	Y	N	NA
ECG - Heart Block	Y	N	NA
ECG - Pre-excitation	Y	N	NA
EMG/NCS - Myopathic	Y	N	NA
EMG/NCS - Neurogenic	Y	N	NA
Axonal	Demyelinating	Mixed	NA
Heart block	Pre-excitation		NA

Other: _____

IMAGING STUDIES:

Angiogram	Normal	Abnormal	NA
MRI	Normal	Abnormal	NA
SPECT	Normal	Abnormal	NA
CBF	Normal	Abnormal	NA
CT	Normal	Abnormal	NA
BG calcification:	Y	N	NA

Other: _____

Positive family history: Y N NA
 If yes, please explain:

Died: Y N
 Autopsy: Y N

IMPORTANT: TO ASSIST IN DETERMINING THE MOST RELEVANT TESTS, PLEASE ATTACH COPIES OF MUSCLE HISTOLOGY AND BIOCHEMISTRY REPORTS, IF AVAILABLE

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I. PCR/RFLP ANALYSES TO DETECT MTDNA POINT MUTATIONS - \$225 PER MUTATION

Clinical Phenotype	Nucleotide	Comment	Test Requested
MELAS/MERRF/NARP battery (6 most frequently observed mutations*)			<input type="checkbox"/>
MELAS	3243*	Frequent	<input type="checkbox"/>
"	3256*		<input type="checkbox"/>
"	3271*		<input type="checkbox"/>
"	3291		<input type="checkbox"/>
"	5814		<input type="checkbox"/>
"	8356	MERRF overlap	<input type="checkbox"/>
"	13513*		<input type="checkbox"/>
MELAS battery (7 mutations)			<input type="checkbox"/>
MERRF	8344*	Frequent	<input type="checkbox"/>
"	8356*	MELAS overlap	<input type="checkbox"/>
"	8363		<input type="checkbox"/>
"	3243*	MELAS overlap	<input type="checkbox"/>
MERRF battery (4 mutations)			<input type="checkbox"/>
NARP/Leigh syndrome (MILS)	8993*	T→G; T→C	<input type="checkbox"/>
"	9176		<input type="checkbox"/>
"	13513*		<input type="checkbox"/>
NARP/MILS battery (3 mutations)			<input type="checkbox"/>
PEO	3243*		<input type="checkbox"/>
"	3256		<input type="checkbox"/>
"	# 5703		<input type="checkbox"/>
PEO battery (3 mutations)			<input type="checkbox"/>
LHON	3460		<input type="checkbox"/>
"	11778	Frequent	<input type="checkbox"/>
"	14484		<input type="checkbox"/>
LHON battery (3 primary mutations)			<input type="checkbox"/>
Cardiomyopathy	3243		<input type="checkbox"/>
"	3260		<input type="checkbox"/>
"	3303		<input type="checkbox"/>
"	4269		<input type="checkbox"/>
"	4300		<input type="checkbox"/>
"	8363		<input type="checkbox"/>
"	9997		<input type="checkbox"/>
Cardiomyopathy battery (7 mutations)			<input type="checkbox"/>

This mutation is difficult to detect in blood; a muscle biopsy is preferred

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POINT MUTATIONS ASSOCIATED WITH OTHER DISORDERS

Aminoglycoside-induced deafness	1555	<input type="checkbox"/>
Diabetes (often with deafness)	3243	<input type="checkbox"/>
Myopathy (sometimes with cardiomyopathy)	3250	<input type="checkbox"/>
Myopathy, ptosis, psychiatric problems	3251	<input type="checkbox"/>
Retinopathy, diabetes, dementia	3252	<input type="checkbox"/>
Seizures, PEO, diabetes, deafness	3256	<input type="checkbox"/>
Cardiomyopathy, deafness, epilepsy	4269	<input type="checkbox"/>
Chorea, dementia, ataxia, deafness	5549	<input type="checkbox"/>
Sensorineural deafness	7445	<input type="checkbox"/>
Sensorineural deafness, ataxia, myoclonus	7471	<input type="checkbox"/>
GE reflux, ADD, asthma	10044	<input type="checkbox"/>
LHON, dystonia	14459	<input type="checkbox"/>
Diabetes, myopathy	14709	<input type="checkbox"/>

II. SOUTHERN BLOT TO DETECT MTDNA REARRANGEMENTS \$ 500

Clinical Phenotype:

Sporadic Kearns-Sayre syndrome; Sporadic PEO; Familial PEO

III. QUANTITATIVE PCR TO DETECT MTDNA DEPLETION \$ 500

IV. GENE SEQUENCING (PER GENE) \$ 500

V. MITOCHONDRIAL ENZYME ANALYSIS \$ 550

Panel of 6 enzymes:

Cytochrome *c* oxidase; Succinate cytochrome *c* reductase;
 NADH-cytochrome *c* reductase; NADH-dehydrogenase;
 Citrate synthase; Succinate dehydrogenase

VI. THYMIDINE PHOSPHORYLASE ASSAY \$ 400

MNGIE syndrome (Mitochondrial neurogastrointestinal encephalomyopathy)

VII COENZYME Q10

Blood	\$ 100 <input type="checkbox"/>
Muscle	\$ 200 <input type="checkbox"/>

Rather than specifying any specific tests, check here to authorize any and all testing to be performed by Columbia-Presbyterian Medical Center, based on the information provided.