NATIONAL HEALTH LABORATORY SERVICE

Practice number: 5200296 (Lab contact number: 021 404 4449 / 021 650 1630)

NHLS LAB NUMBER BARCODE

INHERITED METABOLIC DISEASE GENETIC TEST REQUEST FORM

LOC

HOSPITAL / CLINIC	
WARD	
COPY REPORT TO	

CLIN

ICD10 CODES	CLINICAL DIAGNOSIS
. .	

PATIENT

PATIENT ID NO			ID/Passport
HOSPITAL NUMBER			
SURNAME			
FIRST NAME		SEX	M F
DATE OF BIRTH	D D / M M / Y Y Y Y	AGE	
PATIENT ADDRESS			
PATIENT TEL NO	H:	W:	C:

PRIVATE

MEDICAL AID		PLAN	
MEDICAL AID NO		DEP CODE	
MEMBER NAME		MEMBER ID NO	
MEMBER ADDRESS			
MEMBER TEL NO	H:	W:	C:

HCW

CLINICIAN NAME		HPCSA / SANC NO	
CONTACT NO		EMAIL ADDRESS	
CONSULTANT I/C		☐ I have taken informed consent from patient (see back of form)	
CONTACT NO/EMAIL			

SPEC

EDTA blood		Urine (Early morning)	Skin
Muscle		Biopsy site:	
Other		Describe:	
Date collected		Time	
Collected by:			

TEST

TEST TYPE	
Diagnostic (All biochem/clin data provided)	
Prenatal (Mutation details provided)	
Carrier testing (Fam history provided)	
Predictive (Fam history provided)	
Other:	

IMD LABORATORY GENETIC TESTS (excluding mitochondrial disease – see overleaf)

- ☐ **Alpha-1 Antitrypsin Deficiency (*Serpina1*: S and Z alleles)**
- ☐ **AMP Deaminase deficiency (*AMPD1* Full gene)**
- ☐ **Biotinidase deficiency (*BTD*)**
  - ☐ Common European mutation (p.Cys33PhefsTer36)
  - ☐ Full gene sequencing
- ☐ **Centronuclear myopathy, AR (*RYR1*)**
  - ☐ Common Indigenous African mutations (2 mutations)
  - ☐ Common SA Caucasian mutations (4 mutations)
  - ☐ Mixed ancestry panel (5 mutations)
- ☐ **Congenital adrenal hyperplasia (17-OHP required)**
- ☐ **Cystinosis (*CTNS*)**
  - ☐ Common Indigenous African mutation (c.971-12G>A)
  - ☐ Full gene sequencing (AA/UOA results required)
- ☐ **Disorders of sexual disorientation (DSD)** (Discuss with lab)
  - ☐ Androgen receptor insensitivity (*AR*)
  - ☐ Steroid 5-alpha reductase deficiency (*SRD5A2*)
- ☐ **Galactosaemia (*GALT*)**
  - ☐ Common Indigenous African mutation (p.S135L)
  - ☐ Full sequencing (Enzyme results required)
- ☐ **Other:** _____
- ☐ **Glutaric aciduria Type 1 (*GCDH*)**
  - ☐ Common Indigenous African mutation (p.A293T)
  - ☐ Full sequencing (UOA results required)
- ☐ **Glutathione synthetase deficiency (*GSS*)**
- ☐ **Glycogen storage disease**
  - ☐ Type 1A (*G6PC*) full sequencing
  - ☐ Type 5, McArdles (*PYGM*) p.R50X (European)
- ☐ **Hyperbilirubinemia (*UGT1A1*)**
  - ☐ Gilbert syndrome common variant only
  - ☐ Criggler-Najjar / Gilbert full sequencing
- ☐ **Isovaleric Acidemia (*IVD*) Afrikaner mutation (p.G123R)**
- ☐ **Lesch Nyhan Syndrome (*HPRT*)** (send 2 EDTA tubes on ice)
- ☐ **Mevalonic aciduria (*MVK*) (UOA results required)**
- ☐ **Primary hyperoxaluria (*AGXT*)**
  - ☐ Common Indigenous African mutation (p.A112D)
  - ☐ Full sequencing
- ☐ **Urea cycle disorders (AA/UOA results required)**
  - ☐ N-Acetylglutamate synthase (*NAGS*)
  - ☐ Ornithine transcarbamylase (*OTC*) gene
- ☐ **X-linked adrenoleukodystrophy (*ABCD1*)**

IMD LABORATORY - MITOCHONDRIAL GENETICS

Mitochondrial DNA (mtDNA) genetics:

- ☐ **mtDNA full sequencing (muscle preferred, blood accepted)**
  - Clinical scenario: ☐ MELAS; ☐ MERRF; ☐ LHON
  - ☐ Leigh syndrome; ☐ Other:_____
- ☐ **mtDNA large deletion screen for:**
  - ☐ CPEO **(muscle ONLY)**
  - ☐ Kearn Sayre syndrome **(muscle ONLY in >20 year old)**
  - ☐ Pearsons disease **(blood ONLY)**
- ☐ **Multiple deletion screen (muscle ONLY)**
- ☐ **mtDNA point mutation screens** (single gene/mutation only):
  - ☐ MELAS m.3243A>G only (blood **and** urine/muscle)
  - ☐ MERRF *MT-TK* only (blood **and** urine/muscle)
  - ☐ MIDD m.3243A>G (blood **and** urine/muscle)
  - ☐ NARP m.8993T>C/G (blood/urine)
  - ☐ LHON screen (3 common mutations) (blood)
- ☐ **mtDNA depletion screen (arrange with lab):**
- ☐ **Other (specify):**_____

Nuclear DNA (nDNA) genetics:

- ☐ **Leigh syndrome**
  - ☐ *SURF1*
  - ☐ PDH deficiency (*PDHA1*)
  - ☐ Full Leigh disease gene panel **(discuss with lab)**
- ☐ **CPT2 deficiency**
- ☐ **ETHE1 deficiency (UOA results required)**

mtDNA maintenance disorders:

- ☐ MPV17 neurohepatopathy
  - ☐ Common Indigenous African mutation (p.Q36X)
  - ☐ Sequencing (mRNA, **arrange**)
- ☐ POLG sequencing **(costly, discuss with lab)**
- ☐ Thymidine kinase 2 (*TK2*)
- ☐ Twinkle (c10ORf2) sequencing **(arrange)**
- ☐ MNGIE (*TYMP*) sequencing **(arrange)**
- ☐ **mtDNA depletion gene panel (discuss with lab)**

Clinical Details (Mitochondrial disease) :

Classical mitochondrial disease phenotype> Yes ☐ / No ☐

If yes, then which of the following?

☐ Alpers' syndrome	☐ Kearn Sayers	☐ MEMSA	☐ NARP/MILS
☐ CPEO	☐ Leigh syndrome	☐ MERRF	☐ Pearson's syndrome
☐ CPEO (+)	☐ LHON	☐ MIDD	☐ Pure myopathy
☐ Deaf/Dystonia	☐ LIMM	☐ MIRAS	☐ SANDO
☐ HCM	☐ MELAS	☐ MNGIE	☐ SNHL

If no, then which of the following clinical features are present?

☐ Anaemia	☐ Diabetes	☐ Growth failure	☐ Nystagmus
☐ Cardiomyopathy	☐ Dysphagia	☐ Hypotonia	☐ Renal disease
☐ Central apnoea	☐ Dystonia	☐ Learning difficulties	☐ Retinopathy
☐ Constipation	☐ Encephalopathy	☐ Liver disease	☐ Optic atrophy
☐ Deafness	☐ Endocrinopathy	☐ Migraine	☐ Seizures
☐ Dementia	☐ Failure to thrive	☐ Myalgia	☐ Stroke/stroke-like episodes
☐ Dev delay	☐ Fatigue	☐ Myopathy	

Muscle biopsy results (if available): **Histology:** _____ **Enzymology:** _____

Clinical investigations:

Blood Lactate ……(mmol/L) CSF Lactate ……(mmol/L) Serum CK ……(U/L)

ECG abnormal ☐ yes / ☐ no EEG abnormal ☐ yes / ☐ no Echo abnormal ☐ yes / ☐ no

Brain MRI/CT findings:_____

Metabolic / Biochem findings (i.e. UOA / AA results): _____

Other Relevant clinical findings and family history: _____

Ethnic origin of patient's mother _____ **Father**_____

For lab use only

Received by: .....

Labelled by: .....

Date: .....

Time: .....

CONSENT FOR DNA ANALYSIS AND INCLUSION IN RESEARCH STUDIES

PLEASE MAKE A COPY OF THIS PAGE FOR THE PATIENT

Research Lab contact number: 021 650 1630

1. I, _____, request DNA testing on myself ☐ / my child ☐ / my unborn child ☐ for disease-causing mutations in the gene/genes responsible for: _____.

2. I understand that the genetic material (DNA) for analysis is to be obtained from: blood ☐, skin ☐, muscle ☐, or any other body tissue ☐ (specify:_____) provided today.

3. I request that a portion of the sample be stored indefinitely for (Tick where applicable):

   ☐ Possible re-analysis.
   ☐ Further diagnostic testing / analysis when more information about my disorder becomes available.
   ☐ Analysis for the benefit of members of my immediate family.
   OR
   ☐ I request that no portion of the sample be stored for later use.

4. If clinically relevant, I authorise that the results may be made known to family members ☐.

5. I give consent ☐ / do not give consent ☐ that the DNA and/or a portion of the tissue samples, as well as relevant clinical and demographic information obtained for diagnostic purposes be stored indefinitely for research purposes into this or other health conditions, subject to the approval of the UCT Research Ethics Committee, provided that **all information will remain strictly confidential**.

   Information about consent for research: Research into rare metabolic disorders is paramount in helping us better understand the conditions that affect patients in South Africa and find new and effective ways to diagnose and treat these conditions. Although in some instances taking part in such studies may provide diagnostic answers to individuals / individual families, it is important to note that this is not always the case. Agreeing to make your biological samples and health information available for such research may have no direct benefits to you, but may go a long way in ensuring better diagnostic and treatment outcomes for future patients.
   What are the risks to me / my child / my family? The main concerns people have with genetic research is that, although unlikely, their genetic or clinical information may become known to third parties, such as insurance companies, possibly resulting in stigma or discrimination. Rest assured that every attempt is made to reduce the risks of such confidentiality breaches occurring. All patient samples and information are stored securely with controlled access which is strictly limited to the authorised research and diagnostic staff from the IMD laboratory who are bound by confidentiality agreements. If at any stage you change your mind about taking part in such research you may withdraw your consent with no questions asked by contacting the IMD laboratory directly.

6. I have been informed that (Delete where not applicable):
   (a) The analysis procedure is specific to the genetic condition and cannot determine the complete genetic makeup of an individual.
   (b) The IMD laboratory is under obligation to respect medical confidentiality and results are only reported to the specified doctor(s).
   (c) Genetic analysis may not be informative for some families or family members.
   (d) Even under the best conditions, current technology of this type is not perfect and could lead to incorrect results.
   (e) Where biological material or data is used for research purposes, there may be no direct benefit to me.

7. I understand that I may withdraw my consent for any aspect of the above at any time without this affecting my future medical care.

8. ALL OF THE ABOVE HAS BEEN EXPLAINED TO ME IN A LANGUAGE THAT I UNDERSTAND AND MY QUESTIONS ANSWERED BY:

Doctor / Consultant Signature: _____ Date_____

Patient (or Parent in case of a minor) Signature: _____ Date_____

Witness Signature: _____ Date_____

RECOMMENDED MITOCHONDRIAL DISEASE GENETICS TESTING STRATEGIES

Adapted from Meldau et al. (2016) SAMJ; 106(3):234-236