

# Using stool samples in the diagnosis of mitochondrial disease

<b>Submission date</b> 19/04/2022	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 16/05/2022	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 08/07/2024	<b>Condition category</b> Genetic Diseases	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Mitochondria are the 'batteries' of the cell that generate the energy we need. When these batteries are faulty, it can cause conditions known as mitochondrial diseases. There are many different causes of mitochondrial diseases, and people affected experience a range of symptoms.

All cells contain genetic material called DNA. Mitochondria also contain their own separate type of DNA called mitochondrial DNA (mtDNA). Some mitochondrial diseases happen because of errors in mtDNA.

A way to diagnose some mitochondrial diseases is to look for mtDNA containing these errors. We look at how much mtDNA with errors we find compared to how much 'normal' mtDNA there is. We call this the 'mtDNA heteroplasmy' level.

Currently, to measure mtDNA heteroplasmy, we use samples of muscle or blood. This involves a muscle biopsy or blood sample and needs a visit to the hospital or clinic. It can also be painful or uncomfortable.

In this study, we will test whether we can use faecal samples (poo) to diagnose mitochondrial disease.

We will collect faecal samples from people we know have a certain type of mitochondrial disease. We will measure mtDNA heteroplasmy levels in these samples to check if they match levels previously recorded from other samples (e.g. muscle or blood).

### Who can participate?

People with a certain type of mitochondrial disease (who have a m.3243A>G mutation) can take part. The study is open to adults and children of any age.

Participants must have a confirmed genetic diagnosis of mitochondrial disease. They must also be under the care of the Newcastle Mitochondrial Disease Clinic for Adults and Children.

Fifty people (30 adults and 20 children) will be included in the study.

### What does the study involve?

Participants will complete a consent form (either online or on paper) and then provide a faecal

sample.

Collection of the samples will happen at home. Participants will send samples in by post.

Some participants will also attend a focus group or interview. We will ask them how they feel about using faecal samples to diagnose mitochondrial disease.

What are the possible benefits and risks of participating?

Participants will not directly benefit from the study. However, the results may help us develop a new, less invasive way to diagnose mitochondrial disease.

Collecting faecal samples may seem unpleasant, unhygienic or embarrassing. We will provide a special kit and gloves to make collection easy, clean and safe.

Where is the study run from?

This study is run by the Wellcome Centre for Mitochondrial Research, Newcastle University and The Newcastle upon Tyne Hospitals NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?

March 2021 to October 2023

Who is funding the study?

Medical Research Council (UK)

Who is the main contact?

Professor Grainne Gorman

grainne.gorman@ncl.ac.uk

## Contact information

### Type(s)

Scientific

### Contact name

Dr Charlotte Warren

### Contact details

Wellcome Trust Centre for Mitochondrial Research

Newcastle University Translational and Clinical Research Institute (NUTCRI)

4th Floor Cookson Building

Medical School

Newcastle University

Newcastle-upon-Tyne

United Kingdom

NE2 4HH

-

Charlotte.warren@ncl.ac.uk

### Type(s)

Principal investigator

### Contact name

Prof Gráinne Gorman

### Contact details

Wellcome Trust Centre for Mitochondrial Research  
Newcastle University  
4th Floor Cookson Building  
Medical School  
Newcastle University  
Newcastle-upon-Tyne  
United Kingdom  
NE2 4HH

-  
grainne.gorman@newcastle.ac.uk

## **Additional identifiers**

### **Clinical Trials Information System (CTIS)**

Nil known

### **Integrated Research Application System (IRAS)**

295392

### **ClinicalTrials.gov (NCT)**

Nil known

### **Protocol serial number**

CPMS 49933, MC\_PC\_19047, IRAS 295392

## **Study information**

### **Scientific Title**

A new non-invasive diagnostic method for detection of pathogenic mitochondrial DNA variants using faecal-derived DNA samples

### **Acronym**

FiND

### **Study objectives**

The aim of this study is to develop and validate the use of faecal tissue as a novel, non-invasive diagnostic tool for mitochondrial disease.

We hypothesise that faecal specimens will be comparable to other samples (such as muscle, blood, urine and buccal derived DNA) currently used in the diagnosis of mitochondrial disease.

### **Ethics approval required**

Old ethics approval format

### **Ethics approval(s)**

Approved 27/08/2021, East of Scotland Research Ethics Service REC 1 (Ninewells Hospital & Medical School, Tayside Medical Science Centre (TASC), Residency Block, Level 3, George Pirie Way, Dundee, DD1 9SY, UK; +44 (0)1382 383878; tay.eosres@nhs.scot), ref: 21/ES/0075

### **Study design**

Observational

## Primary study design

Observational

## Study type(s)

Screening

## Health condition(s) or problem(s) studied

Detection of pathogenic mitochondrial DNA variants

## Interventions

This study will involve the assessment of faecal samples from adult (n = 30) and paediatric patients (n = 20) with mitochondrial disease.

Patients will be identified for the study by the direct clinical care team at the Newcastle Mitochondrial Disease Clinic for Adults and Children through the screening of clinic lists and by interrogation of the Wellcome Centre for Mitochondrial Research Patient Cohort: A Natural History Study and Patient Registry. Interested patients or the parents/carers of paediatric patients will be provided with a copy of the relevant Participant Information Sheet (PIS) and provided with the opportunity to review the form and ask questions before consent will be taken. Once consent has been given, patients will be asked to provide a stool sample which will be sent to the Wellcome Centre for Mitochondrial Research via post. Study samples and data will be analysed within the Wellcome Centre for Mitochondrial Research. Once the study is complete any remaining tissue will be transferred to the Newcastle Mitochondrial Research Biobank (NMRB). This study will also mitigate the need for patients to attend clinical appointments where appropriate, where patients will be able to collect and post samples from their home address, facilitating equity of access to diagnosis. All faecal samples will be sent to the laboratory for subsequent analysis.

Further to this, 10 participants (adults n = 5 and paediatrics n = 5) will be selected at random and invited to participate in giving feedback. This will be used to discuss current diagnostic approaches, and how the use of faecal samples may enhance this experience. This will be carried out remotely so no site visits are required.

## Intervention Type

Other

## Primary outcome(s)

Mitochondrial DNA (mtDNA) heteroplasmy level (percentage heteroplasmy) detected from faecal samples at a single time-point, compared to mtDNA heteroplasmy levels reported from previous clinical samples.

## Key secondary outcome(s)

1. Confirmation of whether mtDNA variants that may be present can be detected via whole genome sequencing of mtDNA extracted from faecal samples
2. Determination of whether faecal samples as a diagnostic approach are acceptable to patients via collection of participant feedback during focus group discussion.

## Completion date

31/10/2023

# Eligibility

## Key inclusion criteria

1. A genetically confirmed diagnosis of mitochondrial disease, specifically, the common m.3243A>G variant.
2. Adults aged  $\geq 16$  years old
3. Paediatrics aged  $< 16$  years old
4. Have ability, in the opinion of the recruiting investigator to undergo all study assessments and investigations.
5. Capable of providing informed consent

## Participant type(s)

Patient

## Healthy volunteers allowed

No

## Age group

Mixed

## Sex

All

## Total final enrolment

47

## Key exclusion criteria

1. Currently have a confirmed bowel obstruction
2. Received surgery on the gastrointestinal tract in last 12 months
3. New drug regime within the 3 months prior to providing a faecal sample
4. Participating in any study that may influence the gastrointestinal tract three months prior to study commencement.

## Date of first enrolment

01/05/2022

## Date of final enrolment

30/04/2023

# Locations

## Countries of recruitment

United Kingdom

England

## Study participating centre

**Freeman Road Hospital**

Freeman Road  
High Heaton  
Newcastle upon Tyne  
United Kingdom  
NE7 7DN

## Sponsor information

**Organisation**

Newcastle upon Tyne Hospitals NHS Foundation Trust

**ROR**

<https://ror.org/05p40t847>

## Funder(s)

**Funder type**

Research council

**Funder Name**

Medical Research Council

**Alternative Name(s)**

Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

**Funding Body Type**

Government organisation

**Funding Body Subtype**

National government

**Location**

United Kingdom

## Results and Publications

**Individual participant data (IPD) sharing plan**

The current data sharing plans for this study are unknown and will be available at a later date

**IPD sharing plan summary**

Data sharing statement to be made available at a later date

**Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Basic results</a>		08/07/2024	08/07/2024	No	No
<a href="#">HRA research summary</a>			28/06/2023	No	No