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Exploring biomarkers of mucosal inflammation in paediatric Crohn's disease (Mini-MUSIC)

Submission date
28/06/2023

Recruitment status
No longer recruiting

Registration date
24/03/2025

Overall study status
Ongoing

Last Edited
07/04/2025

Condition category
Digestive System

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Inflammatory bowel disease (IBD) comprising of Crohn's disease (CD), ulcerative colitis (UC) and IBD-unclassified (IBD-U) are chronic, incurable immune-mediated conditions affecting the gastrointestinal tract. Despite recent progress in identifying factors that increase one's likelihood to develop IBD (e.g. genetics), or that can trigger (e.g. drugs, stress) a flare, we do not understand why gut inflammation seen in IBD does not resolve. Paediatric IBD (PIBD) tends to be more aggressive with patients typically presenting with more extensive areas of the bowel affected while having higher hospitalisation and colectomy rates. The current gold standard for monitoring is endoscopy however, this carries issues of poor patient tolerance, associated complications and usage of finite NHS resources. These are compounded in paediatrics due to the need for patients to receive general anaesthesia for the procedure.

The Mini-MUSIC study is a multi-centre, longitudinal, translational research study set in the real-world PIBD clinical setting to investigate and develop a new biomarker (a biological signal of a normal or abnormal process, condition or disease) approach that aims to inform both patients and clinicians of the current state of the affected gut lining (how inflamed or whether the bowel wall has completely healed). This new biomarker approach will study a panel of molecular signs in PIBD patients' blood, stools and biopsies that will be correlated to clinical status, disease activity, systemic inflammatory activity and mucosal state (by non-invasive faecal calprotectin) - and in some cases, the direct appearances (via endoscopy and histopathology) of PIBD patients' gut lining will be assessed over 1 year in response to current standard nutritional and drug treatment given to them by their NHS PIBD consultant.

Who can participate?
Patients aged 6-17 years old with inflammatory bowel disease in Scotland

What does the study involve?
Patients will be followed longitudinally at three time points over the course of one year. Each visit will include a detailed clinical assessment and biological sampling (blood, stool, saliva). If patients are receiving an endoscopy as part of their standard NHS care additional biopsies will be taken.

What are the possible benefits and risks of participating?
There are no direct benefits to the participants other than the knowledge that their inclusion is contributing to the advancement of knowledge around their condition. The risks are minimal and related to biological sampling including pain around venepuncture. The current understanding is that the additional biopsies taken during endoscopy do not infer additional risk.

Where is the study run from?
Child Life and Health, Royal Hospital for Children and Young People, Edinburgh, and the Centre for Inflammation Research, Queen Mother's Research Institute, Edinburgh. The research is based in all children's hospitals across Scotland (Edinburgh, Glasgow, Dundee, Aberdeen).

When is the study starting and how long is it expected to run for?
January 2023 to December 2026

Who is funding the study?
The study is funded through a charitable donation through the Edinburgh Children's Hospital Charity (Scotland)

Who is the main contact?
Dr Gwo-Tzer Ho (Chief Investigator, Consultant Gastroenterologist), g.ho@ed.ac.uk
Professor David Wilson (Principle Paediatric investigator)
Dr David Wands (Research Fellow), dwands@ed.ac.uk

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Additional identifiers

Integrated Research Application System (IRAS)
321507

Central Portfolio Management System (CPMS)
59890

Protocol serial number
AC23012

Study information

Scientific Title
Mitochondrial DAMPs as mechanistic biomarkers of mucosal inflammation in paediatric Crohn’s disease and ulcerative colitis

Acronym
Mini-MUSIC

Study objectives

Recently, it was found that damage-associated molecular pattern (DAMPs) arising from the mitochondria are increased in patients with active inflammatory bowel disease (IBD). Mitochondria are the ‘batteries’ or ‘power stations’ that reside within and provide energy for living cells. They have evolved from bacteria around 2-3 billion years ago. As such, the mitochondria have many similarities with bacteria. When our immune cells encounter mitochondria that are released, they confuse them with bacteria, become activated and trigger a prolonged inflammatory response, which is destructive to our own tissue. Of interest, it has been shown that these signals are mitochondrial DNA and fragments of their protein, called formylated peptides.

Mitochondrial DAMPs can also be released in severe acute tissue damage or inflammation (for example, in major trauma or sepsis respectively). The hypothesis for this study is that mitochondrial DAMPs could be used as biomarkers in chronic immune-mediated conditions such as IBD.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 22/05/2023, Health and Social Care Research Ethics Committee A (HSC REC A) (Office for Research Ethics Committees Northern Ireland (ORECNI), Lissue Industrial Estate West, 5 Rathdown Walk, Lisburn, BT28 2RF, United Kingdom; +44 (0)28 95 361400; info.orecni@hscni.net), ref: 23/NI/0062

Primary study design
Observational

Study design
Multi-centre longitudinal observational cohort study

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Paediatric inflammatory bowel disease

Interventions
This is a multi-centre longitudinal observational cohort study following paediatric inflammatory bowel disease patients, aged 6-17 years, with clinical assessment and biological sampling at three-time points over one year (0, 3 and 12 months). They will undergo a clinical assessment at each time point, including height, weight and a symptom questionnaire carried out by the study team or local clinical research facility team. Biological sampling will also occur at each visit, including blood and optional saliva and stool samples. If the patient is admitted to the hospital unexpectedly for a flare of their disease or surgery then a further disease assessment with biological sampling will take place. The study ends for the participant after their 12-month visit.

Detailed clinical and phenotypic data
Biological sampling including blood (cfDNA, RNA, plasma, standard disease biomarkers - CRP/ESR/FBC); saliva for microbiome analysis; stool for microbiome analysis; and gut biopsies for transcriptomics and microbiome analysis

Primary outcomes include:
Assessing the utility of mitochondrial DAMPs as prognostic and mechanistic biomarkers in inflammatory bowel disease
Secondary outcomes include:
Assessing oral-gut microbiome signatures

Intervention Type
Other

Primary outcome(s)
Each of the following primary outcome measures will be assessed at 0, 3 and 12 months plus any additional admissions to the hospital:
1. Full blood count (FBC), erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels measured using blood tests
2. Biological sampling including blood (cfDNA, RNA, plasma, standard disease biomarkers - CRP /ESR/FBC); saliva for microbiome analysis; stool for microbiome analysis; and gut biopsies for transcriptomics and microbiome analysis

Disease course and severity will be recorded using the study's case report forms
Height will be measured using a tape measure
Weight will be measured using scales
Blood will be taken by venepuncture by the research team
Saliva will be collected in a specialised tube by the patient and given to the research team
Stool samples will be collected in a specialised tube by the patient and given to the research team

Key secondary outcome(s)
Oral-gut microbiome signatures measured using saliva and stool collected in specialised tubes by the patient and given to the research team at 0, 3 and 12 months plus during any additional admissions to the hospital

Completion date
31/12/2026

Eligibility

Key inclusion criteria
1. Aged 6 - 17 years old
2. A diagnosis of IBD (CD, UC or IBD-U)
3. All patients must have active IBD at the time of screening: Active IBD symptoms by referring clinician’s judgement in addition to one of the following criteria (within 6 weeks of screening): FC level of >100ug/g; Blood CRP >5mg/l; Endoscopic, radiological or histological evidence of active IBD
4. All new diagnosis PIBD patients will require a recent ileo-colonoscopy within 6 weeks of recruitment that has:
4.1. Clear documentation of endoscopic disease activity and extent (SES-CD for CD; Mayo Score for UC)
4.2. Photographs of endoscopic mucosal IBD disease activity
5. If patients have undergone an ileo-colonoscopy within 6 weeks but with an endoscopic report that is insufficient in endoscopic disease activity data as per (4), potential participants can still be considered providing there is:

5.1. Supporting objective evidence of IBD disease activity (FC, CRP) within 2 weeks of index endoscopic assessment
6. Patients who have evidence of an active IBD flare (as per 3) or are changing IBD therapies due to treatment failure can be included in the study without a recent ileo-colonoscopy if the referring clinician considers omitting it as their local standard of care.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
6 Years

Upper age limit
17 Years

Sex
All

Key exclusion criteria
Does not meet the inclusion criteria

Date of first enrolment
01/01/2024

Date of final enrolment
31/12/2025

Locations

Countries of recruitment
United Kingdom

Scotland

Study participating centre
Royal Hospital for Children, Glasgow
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Study participating centre
Tayside Children's Hospital
Ninewells Hospital
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Sponsor information

Organisation
Accord (United Kingdom)

ROR
https://ror.org/01x6s1m65

Funder(s)

Funder type
Charity

Funder Name
Edinburgh Children's Hospital Charity (ECHC)

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study will be available upon request from Dr David Wands, dwands@ed.ac.uk

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 1.1	15/05/2023	05/07/2023	No	Yes
Protocol file	version 1.0	18/04/2023	05/07/2023	No	No