Participant Information Sheet
Mitochondrial DAMPs as mechanistic biomarkers
of m**u**co**s**al inflammation **i**n **C**rohn's disease and Ulcerative Colitis
MUSIC Study

You are being invited to take part in the MUSIC study. Before you decide whether or not to do this, it is important for you to understand what the MUSIC study is and what it involves. Please take time to read the following information carefully. Talk to others about the study if you wish. Contact us if there is anything that is not clear or if you would like more information. Take plenty of time to decide whether or not you wish to take part.

In Inflammatory Bowel Diseases, Crohn's disease (CD) and Ulcerative Colitis (UC), the most important goal in treatment is complete mucosal healing - the full return to normal and healthy gut lining with the healing of all ulcers seen during active disease. For IBD patients, such restoration of normal gut will lead to a good future prognosis, a return to normal bowel habit, energy levels and long term remission.

Although we have a few strong drugs for IBD (for example 'biologics' and immunesuppressants), doctors do not have good simple tests that can reliably indicate how well these powerful drugs are working. In general, 50% of patients who feel better on these drugs, continue to have gut inflammation when their bowels are examined using an internal camera test (ileo-colonoscopy). In other words, symptoms are poor guides to whether the bowel wall has healed or not.

Currently, your doctors use blood and stool tests to monitor how well controlled your IBD is. They are also are poor guides to how severe the inflammation is on the gut wall and whether it has improved or healed in response to medical treatment.

Patients who carry on with treatments that are not fully healing the inflamed gut wall from active IBD are unnecessarily exposed to the risks associated with these long term immune-suppressive drugs, long term bowel wall damage due to under-treated inflammation and miss the opportunity to try a different treatment that might be better.

What is the purpose of the study?

The MUSIC Study aims to investigate a new approach by measuring damage-associated molecular patterns (DAMPs) or 'danger signals' in the blood and stools, as a new test to inform IBD patients (and their doctors) whether their affected and inflamed bowel gut linings have healed in response to their respective drug treatments.

Recently, we found that DAMPs arising from the mitochondria are increased in patients with active IBD. Mitochondria are the 'batteries' or 'powerstations' that are found in, 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***.

Of interest, our on-going research indicate that DAMPs are released from the inflamed part of the gut that is affecting by IBD. When our immune cells encounter these signals, they confuse them with bacteria, become activated and trigger a prolonged inflammatory response, which is destructive to our own tissue.

Typically, doctors find out how well a prescribed treatment for active flare of IBD has worked, by asking the patient whether he/she feels better and if bowel symptoms have improved. They also check blood or stool tests (C-reactive protein and calprotectin) for inflammation. The current evidence showed that such approaches are not fully informative on whether the bowel wall has healed or not.

The best way to find out whether the bowel wall has healed is by carrying out an ileo-colonoscopy (a camera test to examine the bowel lining of the lower small and large bowel). However, this is not always possible within the NHS or the waiting times are long due to lack of resources.

In the MUSIC study, we will investigate the role of DAMPs as a biomarker for inflammation and how they compared with standard approaches above. We will measure DAMPs and assess how well they reflect the state inflammation within the gut lining using the ileo-colonoscopy test at the start and during medical treatment for active IBD.

If you choose to take part, the MUSIC study will provide ileo-colonoscopy follow-up to you over a period of one year (in addition to your usual NHS clinical care). We will monitor your reported symptoms and standard blood and stool tests every 3-months and most importantly, provide an ileo-colonoscopy if this is required by your usual consultant to investigate your bowel symptoms; and a further ileo-colonoscopy at 6-months following your new treatment to check that your bowel wall has healed. If your 6-month check ileo-colonoscopy, still shows a lot of gut inflammation, a further test can be offered at 12-months.

Importantly, all these information will be given to your NHS doctor who will decide whether to change your medical treatment depending on the findings. At each of these time-points, our research aims to study how well our mitochondrial DAMP measurements perform in monitoring gut inflammation.

In the research samples obtained from you, we will carry out further scientific studies to understand how DAMPs activate inflammation in the gut in order to find new ways to block them as potential future treatment in IBD.

Why have I been asked to take part?

You have been asked to take part because you have IBD (either CD or UC).

You are currently receiving your clinical care from NHS.

You have a recent flare or your current IBD is not well-controlled requiring new or a change in medical treatment.

You have had a recent ileo-colonoscopy showing active IBD.

If you wish to take part, we will ask for your permission when you come up to your hospital appointment (clinic or endoscopy or in-patient stay).

Do I have to take part?

No, you do not have to take part or give a reason for not doing so. At your upcoming appointment, a member of your healthcare team will ask whether you would like to take part. If you would, our clinical research doctor will describe the study in detail and go through the information sheet with you. You will be asked to sign a consent form to show that you understand the risk and benefits of the study. **You can withdraw from this study at any time. Your decision will not affect your healthcare.**

What will happen if I take part?

If you agree to take part in the study, you will then be asked to sign a consent form. You should keep a copy of this Patient Information Leaflet and Consent Form for your records. In addition to your usual clinical care given by your doctor:

- You will see a research nurse or doctor who will explain the study in detail to you. Our research team will assess and record your symptoms.

- If you have not had a recent ileo-colonoscopy, you will be offered a test to assess how inflamed your bowel wall is, at the Endoscopy Unit at the Western General Hospital.

- If you have had a recent ileo-colonoscopy to assess your IBD as part of your NHS care, we will arrange a further ileo-colonoscopy approximately 6 months after treatment for active IBD. The follow-up ileo-colonoscopy will be carried out to see how well your bowel wall has healed in response to treatment. At this time, you will be seen by our research team to assess and record your symptoms.

- If your follow-up ileo-colonoscopy still shows a lot of gut inflammation, you will be offered a further test at 12 month stage to provide further monitoring.

- During your ileo-colonscopy in routine clinical practice, we will usually take up to 16 small pinches of tissue (or biopsies) from your lower small and across the length of the large bowel to provide an accurate picture of how much of the bowel wall is affected by IBD.

- For the MUSIC study, we will take up to a maximum of 16 additional biopsies (on average 8-12) from normal and affected parts of the small and large bowel for research. This will add an extra 5 minutes to your ileo-colonoscopy.

- These additional samples will allow us to study and understand the inflammatory pathways, molecular signals and genes that switched on, in the affected gut wall in IBD. This information will allow us to find new ways to heal the inflamed IBD gut.

- We will ask you to provide a blood sample every three months over a one year period. Where possible, this sample will be taken at the same time as routine blood samples, but this could possibly mean an extra blood test (a further needle prick). We will take two standard blood tubes (2x 20mls, approx.2 tablespoons).

- We will also ask you to provide a stool sample every three months over a one year period. We will provide you with stool containers where you can provide a stool specimen at your convenience which can be sent to our hospital in a specially provided envelope.

- We will ask you to provide a short report of your IBD symptoms every 3 months.

- In a small selected group of patients, we may ask to take up to 100mls of blood (1/2 cup or 6 tablespoons).

- We may also approach you again in the future to give a blood sample, which will be taken as the same time as routine blood samples requested by your doctor.

- If you have a bowel operation as a result of IBD, we will ask your consent to take additional small samples of your bowel for research.

- Give permission for approved members of the research team to access your medical records to obtain study specific clinical information.

What are the possible risks of taking part?

Although generally regarded as safe, standard ileo-colonoscopy carries a small risk. This includes causing a tear in the bowel (1 in 1200 cases), unexpected reaction to sedation, excessive bleeding from biopsy site.

As there are extra research biopsies taken, there is a slightly higher risk of excessive bleeding (<1%). Most bleeding will settle spontaneously and if there is more bleeding than expected, this can usually be treated by cauterisation or clipping during the same procedure by the Endoscopist.

There is possibility of some pain or bruising from giving an extra blood sample.

What are the possible benefits of taking part?

All the medical IBD information (your ileo-colonoscopy results and your routine NHS blood and stool tests to measure how active or well-controlled your IBD is) will be given to your NHS doctor who will decide whether to change your medical treatment depending on the findings.

Our research into DAMPs aims to identify a new way to monitor the actual level of gut inflammation, potentially replacing the need for subsequent repeated colonoscopies in IBD.

We will offer reasonable travel expenses to cover your hospital trip(s) for your ileo-colonoscopy and additional hospital visits for clinic review.

Will my taking part be confidential?

Your participation in this study will be recorded in your medical notes and your usual IBD doctor and GP will be informed.

The information gathered for research purposes will be confidential. Only members of the research team will be able to identify you. They will abide by the Data Protection Act 2018 at all times and make sure your name, address, and any other information that would identify you are

removed from your medical information before it is given to any researchers. The information held on computer will be kept secure, and all written information will be held in locked filing cabinets within University of Edinburgh, under the direct responsibility of Dr Gwo-tzer Ho (the Chief Investigator of this study).

In order for to monitor and audit the study we will ask your consent for responsible representatives from the sponsors and NHS institution to access your medical records and data collected during the study, where it is relevant to you taking part in this research. The Sponsors are responsible for overall management of the study and providing insurance and indemnity. With your consent we will inform your GP that you are taking part in our study.

Will my medical notes be used?

Medical research is of more value if the researcher has information about the medical history of the person who donated the tissue. We would like your permission to use and store information from your medical notes now, and possibly in the future as a follow up. All information collected and stored will be kept strictly confidential. Your personal information like your name and address will be removed from your medical notes before being given to anyone for their research. Only the research team and your Healthcare team will be able to link your information to your research data.

What will we study on your research samples?

In your blood and stool samples, we measure the DAMP levels to see how well they are linked to whether your bowel inflammation has healed or not.

We will also carry out a number of protein and gene studies on your gut biopsies to understand how DAMPs are released in the bowel wall and type of inflammation processes they cause.

We know that genetics play an important role in increasing your risk of developing IBD. We will carry out genetic testing of your DNA from your donated research blood. These genetic variations may explain differences in the level of DAMPs and how they activate the immune system. This in turn helps in finding out who may benefit from future new drugs and treatments that block the effects of DAMPs.

The results of these tests cannot be traced back to you, and will only ever be used for research.

I have participated in the study…what happens next?

The clinical data obtained from your 1-year research follow-up will be passed to usual consultant. Following this, your clinical care of your IBD will continue as usual and carried out by your consultant.

Where will my blood, stool and tissue samples be used?

We will recruit participants into our study for 3 years. The samples collected will be kept within the Gut Research Unit, Centre for Inflammation Research, Queens Medical Research Institute, University of Edinburgh and Wellcome Trust Clinical Research Facility, Western General Hospital under the oversight of the Lothian Gastroenterology Bioresource, University of

Edinburgh and be processed every 2-3 months; or for certain experimental work, be used immediately in the Gut Research Unit, University of Edinburgh. Here, we will carry out new biomarker analysis from blood, stools and biopsies working together and in combination with our studies in Edinburgh. Your anonymised samples that are not directly used by our research will be transferred to South East Scotland SAHSC BioResource under the guardianship of NHS Lothian or disposed in accordance to the Human Tissue Authority Code of Practice, at the end of our research study. Your anonymised samples may also be used by clinical, academic or commercial researchers, and maybe used in countries out with the United Kingdom undertaking similar research in partnership with our group.

What will happen to the results of the study?

The overall results of the project will be made widely available. They will be published in medical journals but anonymously so results cannot be traced back to individuals. We will also provide fact sheets to communicate the most important research findings to the general public and bowel disease patients. We will set up a webpage for this study where we can update the participants of the progress and the publications that will come out from this work.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people called a Research Ethics Committee. The committee has the responsibility for scrutinising all proposals for medical research on humans, has examined and raised no objections from the point of view of research ethics. It is a requirement that your records in this research, be made available for scrutiny by monitors from NHS Lothian, whose role is to check that research is properly conducted and the interests of those taking part are adequately protected.

Identifiable Data for future research

University of Edinburgh and NHS Lothian are the co-sponsors for this study based in Scotland. The co-sponsors are responsible for any identifiable information about you for 5 years and are strictly governed by UK Policy Framework for Health and Social Care Research guidelines. In this study, we will use your Community Health Index (CHI) number, which uniquely identifies a patient within NHS in Scotland. Future information is provided in the accompanying leaflet Data Protection Information Sheet.

What if there is a problem?

If you have a concern about any aspect of this study please contact <insert name and contact details here> who will do their best to answer your questions

In the unlikely event that something goes wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against the NHS but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you (if appropriate)

Further Information

If you have any further questions about the study please contact Dr Gwo-tzer Ho on: Tel 0131 6511033 or email: gwo-tzer.ho@luht.scot.nhs.uk. *If you would like to discuss this study with someone independent of the study team please contact:* Dr Alan Shand on: 0131-537-1770 or email: alan.shand@luht.scot.nhs.uk.

Complaints

If you wish to make a complaint about the study please contact:

Patient Experience Team
2 – 4 Waterloo Place, Edinburgh, EH1 3EG
feedback@nhslothian.scot.nhs.uk
0131 536 3370

Thank you for taking the time to read this Information Sheet and for considering taking part in this study.

Data Protection Information Sheet

The EU General Data Protection Regulation (GDPR), along with the UK Data Protection Act, governs the processing (holding or use) of personal data in the UK.

You are receiving this as you are considering being a participant on this clinical research study. The information below details what data will be held about you and who will hold or store this.

University of Edinburgh and NHS Lothian are the co-sponsors for this study based in Scotland. We will use information from you and/or your medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. The co-sponsors will keep identifiable information about you for 5 years.

As a University and NHS organisation, we use personally-identifiable information to conduct research to improve health, care and services. As a publicly-funded organisation, we have to ensure that it is in the public interest when we use personally-identifiable information from people who have agreed to take part in research. This means that when you agree to take part in a research study, we will use your data in the ways needed to conduct and analyse the research study. Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

Providing personal data directly e.g. verbally, in a questionnaire or from your care provider

University of Edinburgh and NHS Lothian as co-sponsors, will use your name, Community Health Index (CHI) number, contact details, and medical details to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Individuals from University of Edinburgh and NHS Lothian and regulatory organisations may look at your medical and research records to check the accuracy of the research study. NHS Lothian will pass these details to University of Edinburgh along with the information collected from you and your medical records. The only people in University of Edinburgh and NHS Lothian who will have access to information that identifies you will be people who need to contact you to if further samples or follow-up clinical data are required or audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS/ CHI number or contact details.

University of Edinburgh and NHS Lothian will keep identifiable information about you from this study for 5 years.

B: Where participants are providing information indirectly e.g. being obtained from previously collected medical records or database. NOTE that special category data includes identifiers such as a name, an identification number, location data, an online identifier or to one or more factors specific to the physical, physiological, genetic, biometric, mental, economic, cultural or social identity of that natural person

Providing personal data indirectly e.g. from your medical records

2. If the sponsor will receive personal data

University of Edinburgh will collect information about you for this research study from you and your hospital medical files. This information will include your name/ NHS/ Community Health Index (CHI) number/contact details and health information, which is regarded as a special category of information. We will use this information solely for research purposes specific to the GI-DAMPs study.

C. Where data is intended to or likely to be used for future research

Use of data for future research

When you agree to take part in a research study, the information about your health and care may be provided to researchers running other research studies in this organisation and in other organisations. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research**.**

Your information could be used for research in any aspect of health or care, and could be combined with information about you from other sources held by researchers, the NHS or government.

Where this information could identify you, the information will be held securely with strict arrangements about who can access the information. The information will only be used for the purpose of healthcare research, or to contact you about future opportunities to participate in research. It will not be used to make decisions about future services available to you, such as insurance.

Where there is a risk that you can be identified your data will only be used in research that has been independently reviewed by an ethics committee and/ or the sponsor.

Contact for further information

You can find out more about how we use your information and our legal basis for doing so in our Privacy Notice at www.accord.scot.

For further information on the use of personal data by NHS sites, please link to the Health Research Authority (HRA) website; https://www.hra.nhs.uk/information-about-patients/.

If you wish to raise a complaint on how we have handled your personal data, you can contact our Data Protection Officer who will investigate the matter. If you are not satisfied with our response or believe we are processing your personal data in a way that is not lawful you can complain to the Information Commissioner's Office (ICO) at https://ico.org.uk/.

Data Protection Officer contact information:

University of Edinburgh
Data Protection Officer
Governance and Strategic Planning

NHS Lothian
Data Protection Officer
NHS Lothian

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