THE UNIVERSITY of EDINBURGH

Anne Rowling Regenerative Neurology Clinic

NHS Lothian

iMSMS

THE INTERNATIONAL MS MICROBIOME STUDY

An international multi-centre case-control study of the gut microbiota and microbiome in people with multiple sclerosis

The International MS Microbiome Study (iMSMS)

Participant Information Leaflet

Version 1.1
25th January 2016

The iMSMS Study "in a nutshell"

iMSMS is an international collaborative study that seeks to characterise the "bugs" or microbes that normally live in our gut – called microbiome - to determine whether there is a difference in composition between the microbiome of people with MS (case) compared to partners (who do not have MS (called control) but otherwise share a similar environment and diet). *This study builds on accumulating evidence that implicates the microbiome and a person's genetic make up as important factors that together influence susceptibility to getting MS*. For this reason we will study not only the microbiome – by using genetic tests on stool samples that provides a "fingerprint" of your microbiome but also look at your blood genetic make up as this might in turn influence the composition of your microbiome. The study involves a clinical assessment at the Anne Rowling Clinic including blood sampling and two short questionnaires (approximately 2 hours), then collecting two stool samples at home. Your samples and data will be completely anonymised and sent to the international iMSMS centre in the USA where the analysis is undertaken.

1) The iMSMS Study Team – an introduction

Professor Siddharthan Chandran & Dr. Peter Connick at the University of Edinburgh are collaborating in an international research consortium (iMSMS) to investigate how the structure and activity of bacteria and fungi naturally found in the gut (the gastrointestinal "microbiome") may contribute to multiple sclerosis. The global iMSMS Consortium is led by Professor Stephen Hauser and Prof. Sergio Baranzini from the Department of Neurology, University of California, San Francisco (UCSF).

2) Invitation to Participate

The iMSMS study is a study for pairs of people, one with multiple sclerosis (case) and a person who lives with you who does not have MS (control). The experience of participating in iMSMS will be the same for both and this information leaflet describes what is involved.

We would be delighted for you and your study-partner to participate in iMSMS but please take enough time to be sure that you both fully understand the study and are happy to participate. What's involved, together with the uses of your samples and data are described in this information leaflet; but if anything is unclear then please ask us what we mean.

3) The aim of the iMSMS study

The gut harbors millions of microorganisms which vary substantially between individuals, and are shaped, in part, by an individual's genetic "make-up". Alterations in the microorganisms found in the gut have been associated with disease and with autoimmune conditions. By analysing and comparing microorganisms in people diagnosed with MS and in controls, we hope to better understand the role that they play in immune function and whether they might be involved in the development of multiple sclerosis.

4) Do I have to take part?

No, and if you choose not to take part this will not affect your clinical care. You are also free to withdraw from the study at any time without providing a reason and this will not affect your clinical care or legal rights.

5) What does the study involve?

Clinic visit: We will arrange a separate clinic visit, or see you after a routine clinic visit if this is more convenient for you and clinic space is available. Having given you the information on the study and allowed you enough time to review the information we will discuss the study and answer any questions you have. If both you and your study-partner are both satisfied and willing to participate, we will ask you both to complete the consent form. This is attached as an appendix so that you can read it in advance.

After the consent form is signed, we will take a brief history, recording some details about you and your health. If you have MS, this will take a little longer. We will then perform a brief standard neurological examination similar to that undertaken by your GP or specialist in normal clinical care, and ask you to complete the participant and food questionnaires (online or paper

format if preferred). A member of the research team will be able to help with the questionnaire. Finally, we will measure your height and weight, and a trained member of staff will collect a blood sample (about 80 ml or 5 tablespoons). The visit should take around two hours.

After the blood sample has been taken we will explain about taking the stool sample at home.

At home: We ask you to collect samples from two bowel movements that aren't on the same day. There are two collection methods that we use on each bowel movement. We provide you with detailed instructions and all of the equipment you need to safely and hygienically collect samples. You then post them back to us in the pre-paid and secure packaging we give you.

The two methods are:

a. **"The scoop":** We give you a collection hat that fits over the toilet bowl. This catches the stool. We then ask you to transfer a level spoonful (~1 gram, the size of a pea) of stool into a 15-ml stool collection bottle (similar to a urine specimen bottle) using the spoon attached to the cap of the bottle. The tissue paper and stool can then be flushed as normal.
b. **"The wipe":** We give you a sterile qtip (cotton buds) and ask you roll it on the toilet paper enough to "stain" the qtip. The qtip has a sealed plastic case that it fits straight back into for posting in the packaging required.

6) What happens to the blood and stool samples? All samples are **de-identified** linked only through a unique study number. Your de-identified blood and stool samples will first be processed in Edinburgh and then shipped to the central laboratory at UCSF, California, USA. There are no individual results available from the analysis. In other words you will not be identifiable and all data is fully annonymised.

7) Use of samples in future projects & contacting you about other research projects

Current knowledge of the genetics and disease-causing factors of neurological conditions is limited, however as this understanding increases and new techniques develop we could apply these techniques to the donated samples further enhancing our understanding of MS. For this reason we are seeking permission from both the person with MS (case) and their partner (control) to use some of your stored sample in future research projects which could include whole-genome sequencing. Again this would be annonymised and used only for ethically approved research into the causes and / or treatment of MS or related diseases.

Such future studies may involve collaboration with high-quality international research centres that are linked in collaborative networks to share non-identifiable data. The best research increasingly requires partnerships with other research centres, and in working together one maximises the value of the precious samples that have been donated. Ultimately we hope that

the research will lead to the involvement of pharmaceutical companies in the development of new therapies.

8) What is the purpose of the questionnaires?
The microorganisms in the gut are extremely sensitive to dietary habits. We therefore ask you to complete the food frequency questionnaire which will be critical to interpret results appropriately. The participant questionnaire about general information about your environment and family can also be done in paper format or online at the clinic visit.

9) Who will see my personal data and samples, and how will my privacy be protected?
Data from your visit to the Anne Rowling Clinic will be collected on paper and stored securely in a locked filing cabinet. In order to protect your privacy when your data is transferred onto a computer, a unique numeric code will be used in place of your name: ***this is called de-identification***. Only key Anne Rowling Clinic researchers will have access to the link between each person's name and code, and this link will be kept in a secure place. The same numeric code used to protect your data will be used to identify all samples.

Your coded data will be stored on an NHS approved computer system and only anonymised data will be shared with the iMSMS researchers outside the local (Edinburgh) research team.

- **Our privacy standards:** Our management and handling of your data is fully compliant with the Data Protection Act, NHS Lothian, and University of Edinburgh policies. All research personnel at the Anne Rowling Clinic hold NHS Lothian contracts (honorary or substantive). All of the research team hold good clinical practice certificates.

- **Who will see my data?** Non-anonymised data may be seen by: authorised Anne Rowling Clinic researchers working on the study; and by individuals from The University of Edinburgh (the Study Sponsor), from regulatory authorities, or from NHS Lothian if required for Study oversight and monitoring.

  De-identified data and specimens will be sent to the central iMSMS laboratory and may be shared in the future (appropriate permissions in place) with other qualified researchers. These researchers may include other UCSF researchers, other academic collaborators or possibly those in industry.

10) Are there any risks or disadvantages of taking part?
Giving a blood sample causes momentary discomfort. When taking blood samples there is also a small risk of bruising, and, very rarely, infection. There are no anticipated risks associated with collecting and shipping of stool samples. The risk to data is minimized as all data collected is stored in accordance with current data protection governance.

11) Will my taking part in the study be kept confidential?
We ask specific permission to let your GP and consultant(s) know that you have agreed to participate. No one else will be informed of your participation.

12) Economic Consideration
If in the future there is any commercial value from information, products or discoveries derived from this study there will be no individual payments to participants. Reasonable travel costs will be reimbursed to a maximum of £10 per subject.

13) Benefit
There is no direct benefit to you from your participation in this study. However, the knowledge that is gained from the study will help the investigators learn more about MS and immune function and it may also help to develop improved treatments for the disease in the future.

14) Alternatives
You may choose not to participate in this study without your medical care or legal rights being affected in any way.

15) What if I change my mind? You can withdraw from the study at any time without your medical care or legal rights being affected. You may also request at any time that all your biological samples be destroyed. This can be done either by calling the research team at 0131-465-9517 or by writing a letter to Professor Siddharthan Chandran, Anne Rowling Regenerative Neurology Clinic, 49 Little France Crescent, Edinburgh, EH16 4SB. If you chose to do this a sample destruction form will be sent to you to sign to sign, along with a prepaid return envelope so that we have a record of your request. Should you withdraw from the study, any information or research results collected up to that point will be maintained.

16) What happens to the results of the study?
The results will be presented to patient groups and at academic meetings, and published in academic medical/scientific journals. No patient identifiable data will ever be published. Please let us know if you are interested in receiving the results of the study when available by contacting us at the address below or indicating on the consent form that you are interested.

17) Who has reviewed the study?
The study has been reviewed by South East of Scotland Research Ethics Committee01.

18) Further questions?
If you have further questions, comments or concerns, you can call the study team on 0131-465-9517 (answerphone available if all staff are busy).

If for some reason you do not wish to speak to the investigating team, you may contact an independent Consultant Neurologist, Dr Anna Williams, Anne Rowling Regenerative Neurology Clinic, Little France Crescent, Edinburgh, EH16 4SB.

19) What if there is a problem?

All core research staff have NHS contracts and are covered by NHS public liability insurance. We do not anticipate any problems with this study but if you do have a complaint, please report this using the standard NHS complaints procedure by contacting the team below.

NHS Lothian Complaints Team: 2nd Floor, Waverley Gate, 2-4 Waterloo Place, Edinburgh, EH1 3EG, Tel: 0131 465 5708, Email: craft@nhslothian.scot.nhs.uk

For further information please contact:

Denise Cranley
Research Assistant
Anne Rowling Regenerative Neurology Clinic
49 Little France Crescent
Edinburgh
EH16 4SB

Tel: 0131-465-9517
Email: UK@imsms.org