

Exploring the biological processes underlying mutational signatures identified in patients with inherited disorders and in patients exposed to mutagens (Scotland)

PIS (Relative/Welfare Attorney), Version 2. 02/07/2014

PARTICIPANT INFORMATION SHEET Nearest Relative/Guardian or Welfare Attorney

Investigating mutational signatures in cancer and other inherited disorders (Scotland)

You are being invited to consider giving your permission for your relative to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Please ask me if there is anything that is not clear or if you would like more information. Thank you for reading this.

What is the purpose of the study?

The purpose of this study is to understand how and why damage accumulates in DNA.

Almost all the cells in the body contain a copy of the human genetic code (or DNA). This DNA is constantly damaged and this can lead to errors in the genetic code. Usually, these errors are corrected by a person's DNA repair toolkit that exists in cells. Occasionally, some errors are missed or become permanent changes. These changes are called mutations.

We are studying mutations that have built up in cells to understand how and why they cause health problems like cancer, brain diseases and aging.

Why has the patient been chosen?

Your relative been identified by his/her doctor as having a condition with symptoms that are probably due to damage occurring to the genetic material (or DNA) in his/her cells. In this study, we are inviting people with the patient's symptoms to understand how and why damage builds up in the DNA of cells.

However, they currently lack the capacity to make an informed decision about whether they can take place in a research study. We are therefore asking you as their nearest relative, welfare attorney or guardian if you will give consent on their behalf to join this study. This is permissible under the Adults with Incapacity (Scotland) Act 2000.

Do they have to take part?

No. It is up to you to decide whether they take part in the research or not. If you decide that they should take part you are free to change your mind at any time and without giving a reason and this will not alter their care in any way, now or at any stage in the future.

What will happen to your relative if they take part in the research?

The doctor will talk to you and the patient about all that will happen to make sure that

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you understand everything and give you time to ask questions. If you are happy for the patient to take part, you will be asked to sign a form in the presence of the doctor to give consent for the patient to be involved in the study.

If the patient takes part in this study, he/she will be asked to provide a sample of blood/saliva (spit). From this sample we will make special cells called 'stem cells' that can be grown and kept indefinitely. These cells will be made at the Wellcome Trust Sanger Institute, Hinxton, Cambridge, UK, and stored in a cell bank. The cells will be studied in many different ways to find out why damage to DNA builds up in your cells. From time to time, we may make contact with the patient's doctor to find out whether his/her health has changed.

All that is required in this study is a blood/saliva (spit) sample from the patient. This will be taken by a doctor or nurse at a time that is convenient for both of you. We shall also record some relevant clinical details in our password-protected records.

If you decide that your relative will take part in the research, you/they will not receive payment but we will pay reasonable travel expenses incurred as a result of participation in the study.

If your relative regains capacity they will be asked to give their consent to continue with the study.

What are the possible benefits of taking part?

The study will not benefit the patient directly, but we may be able to understand in more detail, how his/her genetic makeup actually causes the symptoms of the condition that he/she has. This may not lead directly to new treatments, but will be a crucial step towards it.

What are the possible disadvantages and risks of taking part?

The risks associated with blood sampling are very small as the procedures are done under sterile conditions, and by experienced doctors or nurses. Nevertheless, mild bruising can sometimes result.

Although it is highly unlikely, there is a possibility that he/she could be identified by studying the genetic information. However, this is only possible if this information is matched to other personal, identifiable data.

What if there is a problem?

If you have a concern about any aspect of this study please contact Dr Serena Nik-Zainal on 01223-834244 or by email at signatures@sanger.ac.uk who will do their best to answer your questions.

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

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What happens when the study is finished?

The patient's anonymised blood/saliva (spit) samples will be sent to researchers at the Wellcome Trust Sanger Institute in Hinxton, Cambridge, UK. These researchers will extract cells and make them into special cells or stem cells that can grow indefinitely. They will look for any patterns of damage in the DNA of the patient's cells.

When the special stem cells are made from the patient's sample, they will be stored in a regulated cell storage facility and kept indefinitely. These anonymised stem cells will become part of a useful resource for research studies. Only the patient's medical condition, age and whether the patient is male or female will be associated with the anonymised stem cells.

To enable the patient's contribution to provide the greatest benefit to research we would like to be able to share:

- 1) anonymised genetic data with other researchers. The information we obtain about the patient's DNA will be placed in a secure electronic data archive called the European phenome-Genome Archive (EGA) (a database). The EGA is kept and maintained by the European Bioinformatics Institute (EBI) in Hinxton, Cambridge, UK.
- 2) anonymised stem cells with a regulated cell storage facility.

The anonymised stem cells and the anonymised genetic data will be kept indefinitely in regulated facilities accessible only by legitimate researchers.

If you withdraw the patient from the study, we will retain any data and results of analyses that we have obtained up until the time of the withdrawal. If you request us to do so, we will destroy any identifiable data and any remaining samples but we cannot destroy the stem cells we have already made.

Will taking part in the study be kept confidential?

All the information we collect during the course of the research will be kept confidential and there are strict laws which safeguard the privacy of the patient at every stage. If the patient joins the study, some parts of their medical records may be looked at by responsible and authorised clinicians/researchers. The data collected for the study will be stored in a password-protected electronic data archive and only looked at by authorised persons involved in running the research. They may also be looked at by authorised persons from the Addenbrooke's Hospital NHS Trust Research and Development Department to check that the study is being carried out correctly. All will have a duty of confidentiality to the patient and nothing that could reveal the patient's identity will be shared outside the research site.

Procedures for handling, processing, storage and destruction of personal, identifiable data are compliant with the UK Data Protection Act 1998.

Once a sample is collected it will be anonymised. Throughout the processing and

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handling of the patient's sample, it will always be anonymised. The stem cells produced from the patient's sample and the genetic data produced will also remain anonymised.

With your consent we will inform the patient's GP that you are taking part.

To ensure that the study is being run correctly, we will ask your consent for responsible representatives from the Sponsor (Genome Research Limited) and NHS Institution to access the patient's medical records] and data collected during the study, where it is relevant to them taking part in this research. The Sponsor is responsible for overall management of the study and providing insurance and indemnity.

What will happen to the results of the study?

The results will be published in scientific journals and/or presented at scientific meetings. Your relative will not be identifiable in any published results.

The raw genetic information that is produced by analysing the patient's DNA will be deposited and stored indefinitely in a central electronic data archive (a database). This archive enables anonymised data to be shared with the research community. The archive is called the European Genome-phenome Archive (EGA) and is run by the European Bioinformatics Institute, Hinxton, Cambridge, UK. Access to the anonymised information stored in this archive will only be accepted via applications from appropriately qualified researchers who sign a legally-binding Data Access Agreement in which they commit to:

- a) use the data only for research purposes;
- b) protect the data confidentiality;
- c) provide appropriate data security;
- d) not attempt to identify individual participants from whom data were obtained;
- e) not redistribute the data or any parts of the data that could be used to identify the research participant.

For the data to be useful to researchers, some information about the medical problem being studied will also be linked to the genetic information. Personal identifiable data such as the patient's name, date of birth and address will not be shared with researchers.

Who is organising the research and why?

The study is organised by medical doctors and researchers at Wellcome Trust Sanger Institute. It is funded by research grants from the Wellcome Trust.

Who has reviewed the study?

The study proposal has been reviewed by the National Research Ethics Service Committee East of England - Norfolk. All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee. A favourable ethical opinion has also been obtained from Scotland A REC. NHS management approval has also been obtained.

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If you have any further questions about the study please contact Dr Serena Nik-Zainal on: (01223 494947) or email: signatures@sanger.ac.uk

If you wish to make a complaint about the study please contact Addenbrooke's Hospital Patient Advice and Liaison Service on 01223-216756.

Thank you for taking the time to read this information sheet