

## Generation of Induced Pluripotent Stem (IPS) Cells for Research

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### Generation of Donor Induced Pluripotent Stem (IPS) Cells for Research

The University of Cambridge would like to invite you to take part in the above research study, which involves the donation of a small skin sample and a blood sample for the generation of Induced Pluripotent Stem Cells for use in research studies. Before you decide whether or not to participate, you need to understand why the study is being done and what it will involve for you. Please take time to read the following information leaflet carefully. Please ask us if there is anything that is not clear or if you would like more information. Talk to others about the study if you wish. Participation is entirely voluntary.

### What is the purpose of the study?

Many genes associated with different disease risks have been discovered with the help of thousands of NHS patients and healthy volunteers such as blood donors. The next step is to discover the mechanisms by which these genes modify the risk of disease, and we are planning to use IPS cells to study diseases such as cardiovascular diseases, diabetes, cancers, neurological diseases and haematological disorders amongst others. IPS cells have a great potential to make different cell types and we hope that this will help us to understand more about these different diseases.

IPS cells are believed to have the same properties as embryonic stem cells but they have the advantage of not being derived from human embryos. Another benefit of IPS cells is that it allows for the creation of cell lines that are genetically customized to an individual; this allows scientists to study the relationship between the genetic make-up (genotype) of individuals with their characteristics or traits (phenotype).

IPS cells can be grown in the laboratory from healthy individuals like yourself. Currently we can produce and isolate IPS cells from skin cells but we are also making efforts to generate them from blood as efficiently.

### Why have I been invited?

You have agreed to participate in the Cambridge BioResource or other Cambridge University / NHS Blood and Transplant led studies and to be contacted again for future biomedical and genetic studies. The reason we are contacting you now is to ask if you would be willing to participate in the above study.

### What is cell cloning?

Cloning refers to the process of making copies of your cells in the laboratory in order to obtain cells which are immortal. These immortalised and cloned cells can be stored at low temperatures for later recovery and use. The cloned cells will possess the same genetic material (DNA) as the person from which they are derived.

### What can we achieve with cell cloning?

With cell cloning we can store IPS cells indefinitely, and in the future make copies for a wide range of biomedical research studies.

Scientists and the Government have agreed not to allow “human cloning” by which they mean implanting a cloned embryo into a woman’s womb, and allowing the embryo to develop into a foetus and ultimately be born. This is currently prohibited and considered to be a criminal offence under the UK Human Reproductive Cloning Act 2001, and will be explicitly prohibited in all research studies using your cells.

### **What will happen if I decide to take part?**

If you agree to participate, a member of the Cambridge BioResource team will contact you via phone, text, e-mail or letter to arrange an appointment to attend the Addenbrooke’s biomedical campus. A nurse or doctor will see you when you attend to explain what will happen in detail and you will have the opportunity to ask any questions. If all questions have been answered to your satisfaction you will be asked to sign a consent form.

### **What samples are required for this study?**

For this study we will ask you for:

1. A small skin sample
2. A blood sample of up to 50 ml (three tablespoons), and on occasions
3. We may also ask you to donate a standard (475 ml) blood donation for research

The small skin sample, called a skin biopsy, and the small sample of blood will be collected during the same appointment. The procedure will take about 30 minutes. If you also agree to give a standard blood donation for research then a separate appointment will be arranged with you to come to the Cambridge NHSBT blood donor clinic for a routine donation.

### **What does a skin biopsy involve?**

A skin biopsy is normally taken from the upper arm. Alternatively, it may be taken from the inner lower thigh or upper calf areas. A local anaesthetic is used to numb the biopsy site so volunteers usually do not feel any pain when the skin sample is taken. A special instrument is used to take the biopsy. The instrument is gently inserted into the skin and rotated so that a small circle of skin can be carefully removed. The biopsy size is 2 mm in diameter (i.e. quarter the size of a small pea).

### **What happens after the skin biopsy?**

The biopsy site occasionally bleeds slightly straight after the procedure, but stops when pressure is applied to the site. The area is closed with Steri-strips (a type of sticky plaster) and covered with an adhesive dressing and, you will be able to go home. Steri-strips will need to be kept on the biopsy site for at least 2 days.

### **What are the possible risks involved with a skin biopsy?**

Rarely you may experience;

1. Some bleeding
2. Increased tenderness
3. Localised infection which can follow any invasive procedure
4. There may be a small scar

### **What are the possible risks of giving a blood sample?**

As a blood donor you will be aware of the risks of blood donation. Every venepuncture has a potential for problems including bruising, inflammation, and fainting.

If you are a regular blood donor then there is a small risk of iron deficiency anaemia developing as a consequence. To monitor whether you are at risk of developing anaemia the NHSBT monitors your level of haemoglobin at every donation. You will only be asked to give a small blood sample (up to 50 ml) or a standard blood donation for this study if you have not yet given your yearly recommended maximum number of blood donations.

### **Do I have to take part?**

It is entirely up to you to decide whether or not to take part. If you decide to take part you will be asked to give informed consent. You are free to withdraw your consent at any time without giving a reason.

### **How will my samples be used?**

Samples you provide will be used only for ethically approved research either in the UK or overseas. Researchers overseas, just like the researchers in the UK, will have to follow all the laws and guidelines that apply to biomedical research.

We will use your donated samples to generate IPS cells. The first step in this process is to isolate a specific type of skin cell, known as a fibroblast. A second step derives IPS cells from the fibroblasts. Because the process of generating clones of IPS cells is not simple we may not always succeed. If we succeed, the cloned IPS cells will be stored indefinitely for future use in research. The fibroblasts will also be stored indefinitely in case we wish to return to them in future to derive new IPS cells, and may also be shared with other researchers.

We will isolate, analyse, amplify, and store your DNA and RNA from your donated cells and from the derived cells (e.g. fibroblasts, IPS cells) and we will use it to identify how the behavioural pattern of your cells is programmed in your genes. Genes are made out of DNA and that is why we want to analyse your DNA in detail. RNA is derived from your DNA and shuttles between the cell nucleus and the protein production sites in your cells.

In addition to DNA and RNA, we will isolate, analyse, and store other components from your donated materials, including protein, lipid and carbohydrate molecules and any other substances that can be measured or characterised.

### **How will my IPS cells be used in the future?**

There are about 200 different cell types in your body, any of which researchers may want to generate from the stored IPS cells. Cells that are of particular interest to us include the endothelial cells which line the inside of your blood vessels, stem cells that make all of your blood cells, neuron cells and liver cells.

The IPS cells and other cells derived from them will also be deposited in a cell bank, from which they will be made available to other research and healthcare groups in the UK and overseas. These groups may be in the public or non-profit sectors, or in commercial companies, and the cells may be used for research or commercial purposes. Such researchers, just like the researchers in this project, will have to follow all the laws and guidelines that apply to biomedical research.

Data will be collected from measurements on your IPS cells and other cells derived from them, including DNA sequence data. We will archive the data we collect in a database, analyse the data to carry out research, and also make the data openly available via the internet, enabling other scientists to carry out research. Where other researchers have obtained your cells from the cell bank, the data from those studies may also be made available on the internet in a similar fashion. All data will be kept separately from your identity i.e. the researcher will not know from whom the cells have been derived.

The cell lines and data will be available for use for many years.

### **Will my information be kept confidential?**

We will protect your personal information at all times. Your skin and blood samples will be labelled with a unique sample number before being transferred to the research laboratory. Your name and contact identifiers will never appear on the samples that are stored and/or distributed to ensure that the laboratory researchers never know who you are. The consent form will be archived separately by the Cambridge BioResource team at the University of Cambridge. The database that contains your personal identifiers and contact information is not accessible to researchers and can only be used by the Cambridge BioResource staff for the purpose of contacting you for future studies.

Once IPS cells are created from your donated cells, they will also be given a unique sample identifier number which will be linked to identifiers given to the donated samples from which they were derived.

### **Are there risks associated with data from my cells being available on the internet?**

We will place anonymised data from your cell lines openly on the internet because this makes it most useful for scientific research. Because it is openly available, anyone will be able to access it, however no personal data about you other than your gender and approximate year of birth (in 5 year bands) will be available. This means that neither your name, nor contact details, nor other identifiers used for you outside this study, nor medical or other measurements made on you, will be included in the public information available on the internet.

Because each person's DNA sequence is individual, it would be possible in principle for someone who already has genetic data from you to make a match. This would not be permitted as part of a study using the cell lines derived from your sample. It would also be possible to make a match to genetic data from a close relative. Because the Y chromosome is inherited through the male line, genetic data from the Y chromosome can in some cases be used to guess a surname from a more distant relative; to prevent this from happening we will not make Y chromosome data available openly on the internet, but it will be available to *bona fide* researchers through a managed data access process. Even if a match is made, the only information about you that a user can access would be your gender, approximate year of birth, and data derived from your cells.

### **How can researchers ask for another blood sample in the future if they do not have my personal identifiers?**

If a researcher requires another blood sample they will provide the unique sample number to selected Cambridge BioResource staff who have access to the table linking your sample number with your contact identifiers. A Cambridge BioResource member of staff would then contact you to ask for a further sample but they will not be aware of the results obtained from your original sample, or the reason why another sample was required. If you are contacted for another sample or a new study you are free to decline without giving a reason.

### **Is there something wrong if I am asked to give another sample?**

No. There are many reasons why we might ask you to return to give another sample. We might want to reproduce former results or we may wish to invite you for a new study based on results which have been obtained from your donated samples.

### **What will happen to the results obtained from my samples?**

Results of this study will be made available to the public through scientific publications, including placing information on the internet, in press articles, in project leaflets and through other media. Under no circumstances would your personal information be disclosed in any publication.

### **Will any of the results obtained with my samples predict my risk for disease?**

The aim of this study is to produce IPS cells which can make different cell lines in the laboratory and analyse the variations in the genetic code (called genetic markers) that might predict different diseases. Every healthy individual carries risk markers and protective markers in their genes. However, the scientific knowledge we have about these markers is very incomplete, and in this research study we are not able to provide feedback on an individual basis.

### **Can I know the results obtained from my samples?**

As outlined above, for protection of your privacy, your samples will be kept completely separate from your contact identifiers. It is not planned to feed back any research results to participants as it would be of no direct benefit. The only occasion that any laboratory test results would be communicated back to you would be in the event that something is discovered that has an immediate impact on your healthcare (i.e. severe anaemia, very high white cell count, etc.). In this case a Cambridge BioResource staff member would inform you and contact your GP with your permission.

You may wonder if we have a clone of your cells from which all different cell types in your body can be generated, whether this could be of benefit to you or someone else in case of disease. It is hoped that in future we may be able to do this, but we must be clear that we cannot use the IPS clone generated from your cells for this purpose. This is for several reasons. Firstly, we don't know yet whether cells derived from IPS cells are safe. Secondly, we don't generate the clone under conditions of culture which are suitable for possible future applications in treatment. Finally, we don't know whether cells which have been engineered in the laboratory by manipulation of IPS cells can be used for a cure. Research is being performed on the Addenbrooke's biomedical campus and elsewhere to address these questions.

### **Who will work with my samples?**

The primary laboratories working with your samples are located on the Addenbrooke's biomedical campus as part of both the University of Cambridge and NHSBT, at the Wellcome Trust Sanger Institute and European Bioinformatics Institute in Hinxton south of Cambridge, at King's College London and University College London, and at the University of Dundee. However, as described above IPS cells derived from your samples will be available to other research and healthcare groups in the public and commercial sectors in the UK and overseas via the cell bank in which we deposit the cells. Data we and others generate will be made available openly on the internet. Again, your identity will never be known to any of these collaborators.

### **Will I be reimbursed for taking part?**

We will cover reasonable expenses for travelling to the Addenbrooke's biomedical campus.

### **What is the benefit of being involved in this project?**

There will be no direct financial or medical benefit to you if you choose to participate. However, there will be a benefit to the future development of healthcare provision, and the long-term understanding of mechanisms of many different diseases.

### **What happens if the funding for this project stops?**

This study is currently funded by the National Institute for Health Research (NIHR), the Wellcome Trust and the Medical Research Council. The IPS cell repository will distribute IPS cells and other cells derived from your donated samples to researchers. Researchers will be charged a fee for the service provided and this fee will include the costs of maintaining the collection of IPS cells. The data generated by us will be deposited at the European Bioinformatics Institute in Hinxton. This institute maintains all large datasets of biomedical interest. If funding for the biorepository ceases then all samples will be discarded following the normal procedures.

### **Who has approved this project?**

All research in the NHS is reviewed by an independent group of people called a Research Ethics Committee to protect your safety, rights, wellbeing and dignity. This study has been reviewed and was given a favourable opinion by the Cambridgeshire I Research Ethics Committee.

### **What happens if an invention is made using my sample?**

You are giving your sample as an absolute gift. An “absolute” gift is a gift which is given as a donation, i.e. without receiving a payment and without conditions. In the future, your sample may help us or others to make an invention, e.g. develop a new product to diagnose or treat disease. If an invention results from the research undertaken with your sample, you will not receive any compensation or payment. The inventors may work together with commercial companies to develop inventions for the benefit of patients and we hope that such products are brought into use by the NHS to improve healthcare.

### **Can I withdraw my consent after participating?**

Volunteers can withdraw from the study at any time and without giving a reason. If you wish to withdraw, please contact the Cambridge BioResource team on Freephone 0800 085 3650 and a withdrawal form will be sent to you. Please note that we would not be able to remove results of any tests already obtained with your sample from the databases and laboratory notebooks and we would also not be able to remove cloned cell stocks and any materials derived thereafter. We will take care however that you will not be contacted anymore by Cambridge BioResource staff in relation to any follow-up studies for this research project.

### **What arrangements have been made for indemnity?**

The NHSBT is the sponsor of this study and therefore cover is provided under the NHSBT indemnity scheme.

### **Whom do I contact if I have further questions?**

If you have any questions or wish to comment about any aspect of the this study, please contact the study coordinator Heather Lloyd-Jones BSc (Hons), RGN University of Cambridge, , Long Road, Cambridge CB2 0PT, telephone 01223 588119 or contact the Cambridge BioResource team on Freephone 0800 085 3650 or email to [nhsbt@cambridgebioresource.org.uk](mailto:nhsbt@cambridgebioresource.org.uk) .