Patient Information Sheet

Furthering our understanding of early human development for the generation of stem cells

We would like to invite you to donate your fresh or frozen embryos for a research project that is focused on furthering our understanding of early human embryo development. You may have embryos in an upcoming fresh cycle or in storage that are no longer required for clinical purposes and would otherwise be discarded. Before you decide whether or not to donate, it is important for you to understand why the research is being done and what it will involve. Please read the following information carefully, discuss it with others if you wish, and feel free to ask us if there is anything that is not clear or if you would like more information before making a decision. You are invited to take as much time as you need to decide whether or not you wish to participate in research focused on an important aspect of early human development. Thank you for taking the time to read this document.

What is the purpose of this study?
The research, which is being done at the Francis Crick Institute, is concerned with early human embryo development. We hope that the results of these studies will benefit medical knowledge in a number of important ways, including:

- Improving our understanding of the conditions that are important for growing human preimplantation embryos in a petri dish. We hope that ultimately these insights could lead to improvements in the treatment of infertility and benefit other patients trying to have a baby through the use of IVF.

- Furthering our understanding of how early human embryo cells become more specialised during early development. The first critical step in this process is when a small subset of cells are set aside to form eventually the foetus, whilst another subset of early cells differ in their fate to become the placenta, which supports the development of the foetus throughout the pregnancy. We are interested in how these specialisation events occur and are regulated before implantation. Understanding the genes that are essential for this first important specialisation process could provide insight into some causes of pregnancy failures and birth defects. Understanding this important switch in cell fate may also provide a deeper understanding of stem cell formation.

- Developing stem cell lines that can be taken out of the embryo and multiplied in the laboratory for many years. This can help us study and understand more fully devastating human diseases at the cellular level in the laboratory and potentially develop new drug treatments.

If you wish to contribute to this research, you may donate any of your surplus embryos that are currently kept in storage at [name of clinic]. Donating your embryos to this research project will help to increase our knowledge of an aspect of human biology that is currently poorly understood.

What is being asked of us?
You may wish to donate any embryos left over from your fertility treatment that are no longer required and would otherwise be disposed of by the embryology laboratory. This applies to embryos that are not used for your treatment in a fresh cycle and are not suitable for freezing, as well as any frozen embryos that you decide you no longer wish to keep in storage. If you choose to donate your extra embryos to this study, we kindly ask you to sign the attached consent form (page 5) allowing us to undertake Human Fertilisation and Embryology Authority (HFEA) licensed research using these embryos.

What are the possible risks of taking part in the study?
There are no physical risks to you. You may experience uncertainty or anxiety when making decisions regarding any surplus embryos from your fertility treatment. Counselling is routinely available from [name of counsellor], who is independent from the study team, to support you and your partner. Embryos that you choose to donate will be sent to the Francis Crick Institute, where the research team will verify that you have agreed to donate them. Your identity and participation in the research will be kept strictly anonymous.

What will happen to our embryos if we take part?

The main laboratory procedures that your embryos will be used for include:

- Growing embryos for no more than 14 days to study the way that embryos divide and grow. We will look at different ways of growing embryos to find the best methods.

- Studying how different culture conditions affect embryo quality with the aim of improving culture methods and better understanding embryo development.

- Biochemical studies to understand the biological properties of the embryos.

- Studying the genetic composition of embryos.

- Altering how a gene’s coded information is converted into structures in a cell (gene “expression”) to examine how this affects embryo quality with the aim of understanding how early human embryo cells become more specialised. This work may provide the research team with crucial information on the best conditions for developing stem cells.

- The resulting genetically modified embryos may be used to produce stem cells.

- If an embryo is used for the purpose of producing stem cells, the early embryonic cells will be separated so that the embryo is no longer intact. These separated cells may die naturally, or they may survive and multiply indefinitely as stem cells. These stem cells can be used to further study many types of diseases, which can be replicated in the laboratory to look at their cause and progression as well as search for treatments.

Will we benefit ourselves from the research?

No, this research will not lead to any direct benefits to you, medically, financially or otherwise. It is possible that future patients will benefit from the insights achieved through the research.

It is possible that discoveries resulting from research on donated embryos or stem cells that may be generated from them could result in patents or licenses being awarded to the researchers or to commercial organisations. You will not receive any financial benefit from research discoveries arising from the embryos you donate or from stem cells generated from them.

Data and results

Will our taking part in research be kept confidential?

Yes. The proposed research includes careful procedures to protect your identity. The research is done under a licence from the HFEA and with approval from Cambridge Central Research Ethics Committee. Both organisations impose strict requirements about maintaining your confidentiality. The embryos will be coded and your identity will remain confidential. The information identifying your embryos will be visible to a member of the research team when he or she verifies that consent for the research has been obtained, but your identity will not be recorded by them. If stem cells are generated in the research, a sample of these will be deposited with the UK Stem Cell Bank. In this case only, it will be
necessary for your treatment clinic to provide a copy of your consent form in confidence to the Secretary of the UK Stem Cell Steering Committee. Your identity will not be disclosed to the staff of the UK Stem Cell Bank or to anyone else.

**What will happen to the results of the study?**
Whenever possible we will publish the results of our studies in scientific journals. We will also present data at scientific conferences. You will not be identified personally in any way in any publication or presentation.

**Will we get any results or updates on the progress of the research project?**
You will not receive any information from either the study or on the genetic testing of the embryos that you donate or about stem cells that may be generated from them. This is because the steps taken to protect your confidentiality will make your identity unknown to the researchers.

**Some background on our research**

Your donated embryos will make an important contribution to our research programme at the Francis Crick Institute. We would like you to understand the different areas of interest that are under active investigation at our Institute and to give you an appreciation of the wider context in which your embryos are such a valuable resource.

**Points that you should know about the research**
- Embryos are used in our research programme. These embryos (tiny clusters of cells not visible to the eye) are surplus to IVF and would otherwise be discarded.

- No embryos used for research will ever be used to establish a pregnancy.

- No embryos used for research will ever be grown past 14 days.

- In addition to growing the embryos, we will perform a range of biochemical and genetic studies to help us to understand their biological properties.

- Some of our research involves ‘genome editing’. This includes the use of specific techniques (such as CRISPR/Cas9) to specifically alter the DNA sequence. Changes to the DNA sequence may cause a gene to become active or inactive, thereby allowing us to study its function in the early embryo in greater detail. This can lead to significant insights into the earliest stages of human development, prior to implantation.

- After the embryos have been genetically modified their development will be stopped prior to 14 days post-fertilisation. We will perform biochemical and genetic studies and derive stem cell lines from these embryos.

- None of the research on embryos will involve animal testing.

- Any stem cells lines derived in this research project will be deposited in the UK Stem Cell Bank. They may be made available to other research groups nationally and internationally.

- Some of the stem cell lines could in the future be used to develop new treatments for diseases. In this way, the stem cells could be used indefinitely in a wide variety of research projects, and it is not possible to foresee all the potential research opportunities they would provide.
Management of this research

Can I change my mind later and withdraw my consent?
You are free to choose whether or not to participate in this research. You can also decide to withdraw from participation after you have consented, without affecting your medical care in any way.

You are free to withdraw your consent at any time. If you withdraw your consent after transfer of embryos to the Francis Crick Institute, any embryos remaining unused will be destroyed. However, they cannot be returned to the treatment clinic or transferred elsewhere. Once the embryos that you donate become part of the research programme and are being cultured/ grown for use in research, they can no longer be withdrawn. It is important to point out, however, that the embryos might be used at any time up until their expiry date, unless you specify otherwise. In order to withdraw consent you must contact Mr. Michael Summers (contact details below).

How is this research authorised and funded?
This project is approved by the Cambridge Central Research Ethics Committee. Research using human gametes and embryos is regulated by the HFEA. This work has been approved by the HFEA (Licence R0162).

This research is funded by the Medical Research Council, Wellcome Trust and Cancer Research UK. Future funding could also include sources from other public funding agencies, private donors and companies.

Contact for further Information
More information about stem cell research in the UK can be found on the web page of the UK Stem Cell Bank: www.UKstemcellbank.org.uk

Please refer to the HFEA website for information about licensed human embryo research: http://www.hfea.gov.uk

If you would like to discuss the project of research and the possibility of donating material to the project, please contact: [Details of contact at clinic]

If you would like to receive counselling, please contact: [Details of counsellor]

You may contact [clinic contact name] to withdraw consent at any time.
Title of proposed research: Towards understanding early human development for the generation of stem cells

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<tr>
<th>RESEARCH CONSENT FORM</th>
<th>Both Partners</th>
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<tr>
<td><strong>We have read this Consent Form and Information Sheet and had the opportunity to ask questions and receive counselling.</strong></td>
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<tr>
<td><strong>We understand that we are under no obligation to take part in this study and that our decision whether or not to participate will not alter our treatment in any way.</strong></td>
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<tr>
<td><strong>We understand that we have the right to withdraw from this study at any stage until the point the donated embryos are transferred to the Francis Crick Institute and used for research. Once the embryos that you donate become part of the research programme and are being cultured/grown for use in research, they can no longer be withdrawn.</strong></td>
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<tr>
<td><strong>We understand that a sample of any stem cells derived from the donated embryos will be deposited in the UK Stem Cell Bank. In this event the treatment clinic will send a copy of this consent form to the Secretary to the UK Stem Cell Steering Committee, who will maintain strict confidentiality about our identity and participation in the study.</strong></td>
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<td><strong>We understand that if stem cells are generated from the donated embryos, the stem cells could be distributed widely to other researchers well into the future and could be used for research by commercial organisations.</strong></td>
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<td><strong>We understand that we will not benefit financially or otherwise from the research discoveries, which could be published or patented by the researchers, or from the future uses of any stem cells generated in the study.</strong></td>
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<td><strong>We understand that the research project may include genetic and other tests. We understand that as a consequence of steps taken to protect our identity and confidentiality, we will not receive any information about the outcome of the study of embryos that we donate, whether they form stem cells or otherwise.</strong></td>
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<td><strong>We agree to participate in this study.</strong></td>
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Medical number of patient: ____________________________ Date of birth: ____________________________

Full name – female patient (printed): ____________________________________________________________

Signature: __________________________________________ Date signed: ____________________________

Full name – husband/partner (printed): __________________________________________________________

Signature: __________________________________________ Date signed: ____________________________

Witness (printed) __________________________________________________________

Signature: __________________________________________ Date signed: ____________________________

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