

For Information

Donating Cells for Stem Cell Research into Motor Neuron Disease

An invitation to contribute to stem cell research to study Motor Neuron Disease

The objective of this research is to create a new opportunity to study the human disease variously known as motor neuron disease, amyotrophic lateral sclerosis (ALS) and Lou Gehrig's disease. New methods for the study of genetic diseases such as Motor Neuron Disease are being developed. These involve the production of embryo stem cells. We are approaching you to give you information about how you can help this medical research by donating tissue samples. This leaflet explains the reasons for this research (which promises benefit for people who have this or other serious diseases), what it involves, how it is regulated, and your rights if you participate. Please take time to read and consider this information carefully before deciding whether or not you want to contribute. Please ask us about anything that is not clear, or if you would like further information.

You do not have to take part in this research and if you choose not to participate you do not have to say why. Your treatment and subsequent medical care will not be affected in any way, whether or not you decide to participate. If you do agree to take part, you can still change your mind and withdraw your consent to the use of your cells at any time until they have been used for the purpose of any project of research. The cells will be regarded as so used after they are under the control of the researchers and are being cultured / grown for use in research. If researchers generate stem cells or stem cell lines from the cells, you cannot withdraw your consent to the use of these stem cells or stem cell lines; so it is important to make your decision before the samples leave the clinic.

What are stem cells?

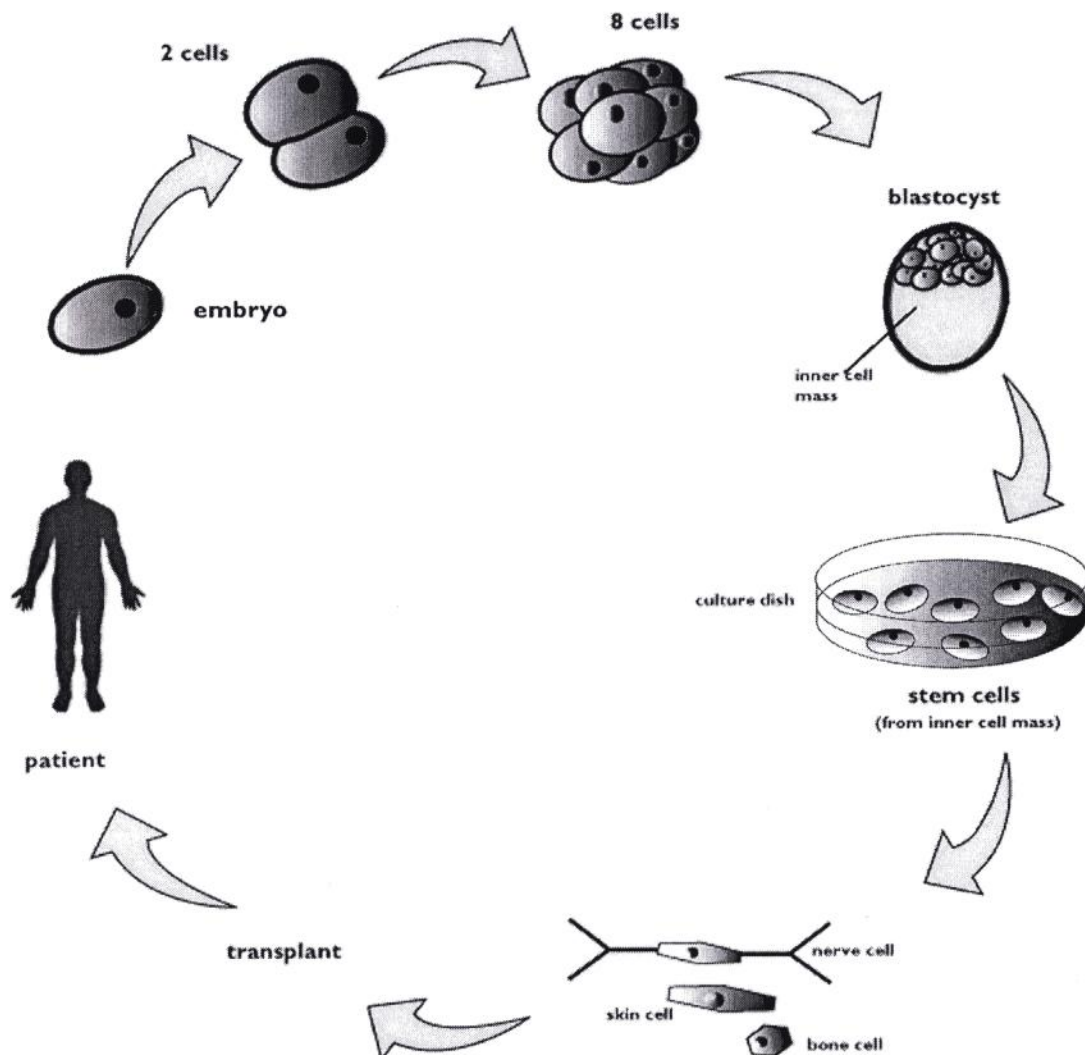
After fertilisation embryos keep on dividing to generate the many different cell types that comprise the human body. After five days a hollow ball of cells called the blastocyst forms. The outer blastocyst layer forms the placenta while an inner group of around 50 stem cells (inner cell mass) will form the developing embryo's tissues. If isolated and cultured under the right conditions these stem cells can form any cell type of the human body, and may in future be used for transplantation (see diagram).

What are stem cell lines?

Stem cell lines come from stem cells which have been grown in culture. They continue to multiply and under appropriate culture conditions they can survive indefinitely.

Why are stem cells important for medical research?

Stem cells have the ability to form all of the different tissues of an adult. Under appropriate culture conditions they can be induced to form those tissues that may be studied in the laboratory. This ability provides new opportunities to study diseases in the laboratory. These opportunities are especially important if the disease affects organs from which samples cannot be obtained from a patient, such as the nervous system or heart. If the genetic information in the cells would cause a person to have a disease then they provide a new opportunity to study that disease. For the first time, researchers would be able to study cells that were becoming abnormal by comparing them with cells that were not liable to the disease. It will also be possible to assess in the laboratory the effects of drugs before they are used in the treatment of patients.



How are stem cells obtained?

Fertilised eggs are grown in the laboratory for about seven days. At this time, embryos form a hollow ball of cells called the blastocyst. This contains around 50 'stem cells', each of which has the unique potential to develop into any cell type in the body. Stem cells will be removed from the blastocysts for further culture. These will not be able to develop into a fetus; however, the stem cells can carry on multiplying in culture and will be studied to discover more about their unique properties. For example, researchers would like to know how stem cells can grow into different cell types, such as nerve or muscle cells, and how their genes regulate this process. Some stem cells may die naturally during these studies, but others may be maintained as 'cell lines'. The embryo is destroyed during the process of making stem cell lines.

Embryo formation by cell nuclear replacement

Two cells are required for the formation of embryos by cell nuclear replacement. These are an unfertilised egg and a cell from another tissue, usually of another person. The genetic information of the oocytes is removed before it is replaced by the genetic information from the other cell. We are asking you to provide cells for this purpose. Almost all of the characteristics of the resulting embryo will be determined by the genetic information from the donor cell, including being liable to develop Motor Neuron Disease. The embryo produced in this way must then be stimulated to begin

HFEA Application, Wilmut, MRC Draft cell donor Consent Form for CNR research cell v4.doc

development in ways that mimic an effect of the spermatozoa during fertilisation. Oocytes that were not fertilised during IVF treatment will be used in cell nuclear replacement to produce embryos from which embryo stem cell lines would be derived.

The value of stem cells obtained by cell nuclear replacement to study Motor Neuron Disease

Opportunities that are not available in any other way will be provided by the derivation of embryo stem cells by cell nuclear replacement. The cells would have the characteristics of the person who provided the cell from which the genetic information was transferred. In the case of a research proposal to study Motor Neuron Disease this means that they would have the characteristics of cells of a person who has developed that disease. Research workers would be able for the first time to study the factors that cause the development of the disease. They would be able to assess in the laboratory possible methods for treatment or prevention of the disease before subsequent use with patients. **We would ask you to consider donating cells for use in this research.**

What will happen to donated cells?

The cells will be examined in the laboratory and cultured for a few hours. They may then be frozen and stored. After being thawed and cultured briefly to allow them to recover from freezing and thawing the genetic information in the cells would be transferred to oocytes from which the genetic information had been removed. The resulting embryo would then be stimulated to begin development and grown in the laboratory for about a week at which time they would be cultured for stem cell derivation. Legally, researchers can only grow embryos in the laboratory up to a maximum of 14 days.

What will happen to stem cell lines?

The stem cell lines will be created and used in the research project that is described in the attached consent form. Stem cell lines will also be preserved in a stem cell bank, which the UK Medical Research Council has established together with the Biotechnology and Biological Sciences Research Council as a resource to help doctors and scientists to develop new treatments for disease. Keeping cell lines in a stem cell bank that can be accessed by many scientists will help to reduce the number of embryos that are needed for research. The stem cell lines will be characterised, standardised, frozen and stored for future use in approved research projects, perhaps many years later. Such research projects may help us to understand and develop treatments for serious diseases or injuries, or they could have other health related goals, e.g. development of drugs and diagnostics. All scientists who want to use banked stem cell lines derived from embryos will have to seek approval from a high level Stem Cell Steering Committee that reports to the Medical Research Council; approval will only be given if i) the research is necessary and of high quality, ii) the scientists are following UK legal and ethical guidelines, and iii) the scientists provide evidence that they have secured all essential licences or accreditations from relevant UK ethical and regulatory authorities. International scientists will be permitted to access cell lines stored in the bank, but only where they are able to demonstrate that their projects meet all the conditions (i) – (iii) which apply to UK scientists.

Your consent to donate will therefore cover both the research project in which stem cell lines are created and any future research on those stem cell lines.

If you decide to donate cells for stem cell research you cannot restrict the use of cell lines derived from your cells to specific research projects. This policy was recommended in the House of Lords report (2001) and is aimed at reducing the total number of embryos required for stem cell research. It is also consistent with existing guidelines for donating human tissues for research.

Are there personal or financial benefits?

You will receive no financial reward from future commercial application of such research. Similarly, since this is long term research it is unlikely to be of immediate medical benefit to you.

New methods arising from stem cell research might be patented by academic researchers or commercial companies. However, the research and development process involves many stages and the contribution of your individual embryo(s) to any future profits will be impossible to quantify.

Additional tests

It is routine practice for couples providing cells for research to be given a blood test for HIV 1 and 2, and for Hepatitis B and C. It may also be necessary to test your blood sample for HTLV (Human T-Cell Lymphotropic Virus) and other conditions. The implications will be fully explained during counselling.

Legal and ethical safeguards

The Human Fertilisation and Embryology Authority (HFEA) is authorised to approve and license research on embryos no more than 14 days old and for strictly limited purposes. For a research license to be granted the HFEA must be satisfied that the goal of the research cannot be achieved in any other way (including research on adult stem cells) and that there are no existing stem cell lines in the bank that would be suitable for the proposed research. Furthermore, the researchers must demonstrate that ethical approval has been obtained, and that the use of human embryos is 'necessary or desirable' for at least one of the following purposes:

- Advancing infertility treatment, or improving contraception techniques
- Increasing knowledge about embryo development, and the causes of miscarriages and birth defects
- Developing methods to detect abnormalities in embryos before implantation
- Increasing knowledge about serious disease, and using this knowledge to develop treatments

The law does **not** allow research that involves using human embryos for any purposes not covered by an HFEA license. The research described on the attached consent form has already been approved by the HFEA and by the lead researcher's Local Research Ethics Committee. The HFEA patient information sheet relating to embryo research accompanies this leaflet. The requirements of research (e.g. the conditions used to culture embryos) will not affect your treatment in any way.

Protecting your confidentiality

The HFE Act imposes strict requirements about patient confidentiality. Personal information will be coded to ensure anonymity and confidential records will be maintained securely in a restricted area;

The following personnel will have access to your consent and medical history forms:

- Staff at the clinic where you donate cells
- The principal investigator licensed by the HFEA to conduct the research
- The Secretary to the Stem Cell Steering Committee; this is because the consent form must be carefully checked by the Secretariat as part of the researcher's application to the Steering Committee to deposit stem cell lines derived from embryos in the UK Stem Cell Bank.

The following personnel will never have access to your consent and medical history forms without your permission:

- Researchers other than the HFEA licence holder
- Members of the Stem Cell Steering Committee
- Staff of the UK Stem Cell Bank

Your GP, with your permission, will be notified by the clinic that you have decided to contribute to the research

Will researchers discover new information about your health?

It is important that you appreciate that any cell lines derived from your donated cells carry your genes and future research on these cell lines may include genetic analyses. For instance researchers may determine the genetic make-up of the stem cell lines (a process called 'finger printing'). However the researchers will not have access to details to link this information to you personally.

It is possible that tests performed on your stem cell line may reveal information about your health status. You can choose to receive i) no feedback under any circumstances; ii) feedback on clinically confirmed results of analytical tests for conditions [a] for which there are treatment options either currently available or potentially available in the future [b] which have no known current treatment options¹.

If you do wish to receive feedback, the professional Clinical Advisor to the Stem Cell Bank (who will only be given access to your National Insurance number via the Secretariat of the Stem Cell Steering Committee) will ask your GP to organise clinical verification of the research results; your GP will do this, inform you about the implications and arrange professional counselling as appropriate. These procedures will be carried out in strict confidence.

Genetic test results may also have implications for your children, but they will only be able to seek feedback on these results from the family GP if you give permission.

You may change your mind about receiving feedback at any time by contacting the Secretary to the Stem Cell Steering Committee, Medical Research Council, 20 Park Crescent, London W1B 1AL.

Information about the outcome of the research project

Information about the UK stem cell initiative, including the results of research using embryonic stem cells and stem cell lines will be published on the web page of the UK stem cell bank (www.ukstemcellbank.org.uk). Copies of this information will also be available at IVF clinics and the HFEA.

It will not be possible for any research results publicised in this way to be linked back to the original donors of the embryos.

How to give consent

To allow research using your cells, you will need to sign the consent form that accompanies this leaflet, having read the details of the specific research project in which the stem cell lines are created. The signed consent form will be retained by the clinic; however, if a stem cell line has been derived a copy will also be lodged with the Secretary to the Stem Cell Steering Committee; you will receive a copy of the completed form for your own records. It is important that you understand that your consent also covers research using banked stem cell lines created from your cells.

¹ You should be aware that positive results for analytical tests may possibly impact on applications for insurance

Further information: Medical information and insurance – Joint Guidelines from the British Medical Association and the Association of British Insurers, December 2002 (www.bma.org.uk), The use of genetic information in insurance: Interim recommendations of the Human Genetics Commission (www.hgc.gov.uk)

Once the cell has been used in the project described on the consent form you will have no control over any future use of the embryonic cells, or of the stem cell lines created from your cells. Your consent also covers any genetic information derived from the stem cell lines.

Withdrawing your consent

You can decide not to take part in this research, and may withdraw from participating even after you have already agreed to, without it affecting your treatment in any way. If you change your mind, your consent can be withdrawn at any time until the cells have been used for the purpose of any project of research. A cell will be regarded as so used after it is under the control of the researchers at Roslin Institute and it is being cultured/grown for use in research. If you wish to withdraw your consent you should discuss with your clinician. You do not have to give a reason for changing your mind.

To withdraw your consent you must write to [address of clinic]:

Name:

Address:

.....

Tel no.: **Email:**

Signature (member of clinic staff):

If you have any questions or concerns about this research, we will be happy to discuss them with you.

THANK YOU FOR TAKING THE TIME TO READ THIS LEAFLET*

Further information: www.mrc.ac.uk, www.hfea.gov.uk, www.royalsoc.ac.uk, House of Lords report (www.parliament.the-stationery-office.co.uk/pa/ld200102/ldselect/ldstem/83/8301.htm), Chief Medical Officer's Expert Advisory Group on Therapeutic Cloning (<http://www.doh.gov.uk/cegc/stemcellreport.htm>)

(5a)

FOR OFFICE USE ONLY:

Bank accession number

Steering Committee application number

Consent for Donating Cells to Stem Cell Research

The stem cell lines created in this research project will be deposited in the UK Stem Cell Bank and may be used in other research projects.

HFEA licence No

Patient code No

Patient NI No

Embryo code No

Title of Proposed Research: Derivation of human embryo stem cells by cell nuclear replacement for technology development and the study of Motor Neuron Disease

Researcher holding an HFEA Licence Professor Ian Wilmut

Address Roslin Institute
Roslin
Midlothian.....
EH259PS.....

Telephone Number 0131 527 4219

Email address

Other researchers involved in the study

Ethics Committee Code No.

Further information is available from (A person who is not involved in the study):

Name

Address

OR OFFICE USE ONLY:

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Information the researcher wishes to include about the specific research project:

We propose to develop methods for the derivation of stem cells from embryos produced by cell nuclear replacement. These methods will provide new opportunities for the study of inherited diseases in which the genetic cause has not yet been identified.

We propose to use the new methods to study Motor Neuron Disease. The project will make embryo stem cells from cells donated by patients with Motor Neuron Disease whose condition cannot be linked to known genetic errors that cause the disease. This would provide the first opportunity to study in cells from such patients the development of the disease, and ways to treat it. This research is not possible by any other means and would be a unique contribution to an international collaboration with experts in Motor Neuron Disease.

The methods developed in this project will also have other applications. They could be used to investigate differences between people in their response to medicine that lead to death of a significant number of patients, even if the medicine is prescribed and used appropriately. In the longer term cells produced in this way could be used to treat degenerative diseases such as Parkinson's disease, heart disease or diabetes. Cells produced by cell nuclear replacement would offer advantages in the treatment of degenerative diseases as they would be genetically identical to the donor who would not require treatment to prevent rejection.

Details of any tests that may be performed either on the embryos or on cells derived from the embryos as part of this research project:

The purpose of the research is to compare cells derived from patients with Motor Neuron disease with those from embryos not known to be vulnerable to the disease. The cells would be differentiated into neural populations and comparison made of the appearance of the cells and the functioning of genes in the cells. Although motor neurons become abnormal it is not known if the initial abnormality is in those cells. Comparisons will be made of motor neurons cultured alone or with other cells from patients with motor neuron disease. Similar mixed cultures will be used to discover if healthy cells are able to prevent cells liable to the disease from becoming abnormal. The results of this study will provide invaluable information for the development of treatment for the disease by cell transplantation. The availability of cells liable to motor neuron disease in the laboratory will make it possible to assess the value of drugs in preventing development of the disease before the drugs are tested in patients. None of these opportunities are available in any other way.

Source of research funding:

We are seeking funding from several sources.

Benefits (scientific or financial) which may accrue from the research to researchers and/or their host departments:

The authors expect to publish the results in scientific journals and to be invited to present them at meetings. It may be appropriate to seek patents for new treatments according to the requirements of the funding agents. Any income from such patents would be distributed according to an Institute policy that rewards all of the staff involved in the research before applying the remainder to further research.

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1. Have you understood the information provided?

If you have, please initial all of the appropriate boxes;

- I have read and understood the information sheet and the consent form about this study; and have had the opportunity to discuss it with an independent person. ☐
- I have discussed the project with.....(insert name) who is an independent member of clinic staff not involved in the research project. ☐
- I understand that I am under no obligation to take part in this study and that a decision not to participate will not alter the treatment that we would normally receive. ☐
- I understand that I have the right to withdraw from this study without giving any reason, at any stage up until the cells have been used for the purpose of any project of research. A cell will be regarded as so used after it is under the control of the researchers and it is being cultured/ grown for use in research; to withdraw from the study will not affect my treatment in any way. ☐
- I understand that cell lines produced in this research will be deposited in the UK stem cell bank ☐
- I understand that I will not benefit financially if this research leads to the development of a new treatment. ☐
- I understand that the research projects involving the cells may include genetic and other tests and that the results of these tests may have implications for me personally. ☐

2. Do you wish to donate cells for stem cell research?

If you do wish to donate, please provide consent and initial all of the boxes;

- I consent to donate cells to the research project in which stem cell lines are created and to future research on those stem cell lines, as approved by the Stem Cell Steering Committee ☐

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- I agree that a copy of the consent forms may be maintained securely in a restricted area by the Secretary to the Stem Cell Steering Committee ☐
- I agree that notice about my participation in this study may be sent to my General Practitioner ☐
- I agree that the following tests will be performed on my blood samples where required: HIV 1 and 2, Hepatitis B and C and other tests on the same blood sample which have been explained during implications counselling. ☐

3. Do you wish to receive feedback on research results which have implications for your health?

Please initial the following boxes as appropriate, each partner can make different choices.

- I do not wish to receive feedback under any circumstances ☐
- I wish to receive feedback on clinically confirmed results of analytical tests for conditions for which there are treatment options either currently available or potentially available in the future² ☐
- I wish to receive feedback on clinically confirmed results of analytical tests for conditions for which there are no known current treatment options² ☐

4. Changing your mind about receiving feedback

Please initial the box;

- I understand that I can change my mind about receiving feedback at any time by sending a letter to the Secretary to the Stem Cell Steering Committee at MRC Head Office, 20 Park Crescent, London W1B 1AL ☐

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² You should be aware that positive results for analytical tests may possibly impact on applications for insurance. Further information: Medical information and insurance – Joint Guidelines from the British Medical Association and the Association of British Insurers, December 2002 (www.bma.org.uk), The use of genetic information in insurance: Interim recommendations of the Human Genetics Commission (www.hgc.gov.uk)

Name and address of GP:

.....
.....

Name of Donor **DoB**

Signature of Donor **Date**

**Name of Countersigning
Witness from Clinic**

**Signature of Countersigning
Witness from Clinic** **Date**

Clinic Number

**Name of Person Responsible
holding an HFEA Licence**

**Signature of Person Responsible
holding an HFEA Licence** **Date**

THANK YOU FOR AGREEING TO TAKE PART IN THIS IMPORTANT RESEARCH

Copies: Donor; IVF Clinic Case notes; Secretary to the Stem Cell Steering Committee
Version 23