

Research Licence Committee Meeting

28 November 2007

21 Bloomsbury Street London WC1B 3HF

MINUTES Item 2

**Research Project R0179: Derivation of Embryonic Stem Cell Lines from Interspecies Embryos produced by Somatic Cell Nuclear Transfer
Centre for Stem Cell Biology and Developmental Genetics, Institute of Human Genetics, university of Newcastle Upon Tyne (0296)**

Members:

Emily Jackson – Chair, Lay Member
Richard Harries, Lay Member
Clare Brown, Lay Member
Maybeth Jamieson, Consultant Embryologist, Glasgow Royal Infirmary
Neva Haites, Professor of Medical Genetics, University of Aberdeen

In Attendance:

Trish Davies, Director of Regulation/
Deputy Chief Executive
Chris O’Toole, Head of Research Regulation
Claudia Lally, Committee Secretary

Observing:

David Gomez, legal adviser to the HFEA

Providing Clinical Advice:

William Ledger, Professor of Obstetrics and Gynaecology, University of Sheffield

Providing Legal Advice:

Graham Miles, Morgan Cole Solicitors

Conflicts of Interest: members of the Committee declared that they had no conflicts of interest in relation to this item.

The following papers were considered by the Committee:

- papers for Licence Committee (116 pages)
- the following papers were tabled:
 - written legal advice by Morgan Cole (6 pages)
 - Decision tree (2 pages)
 - Invited comments on the creation of human-animal Cytoplasmic hybrid embryos (16 pages)

1. The papers for this item were presented by Chris O’Toole, Head of Research Regulation. Dr O’Toole informed the Committee that this is an application to create embryos by inserting human nuclei into enucleated animal oocytes by the technique of somatic cell nuclear transfer (SCNT). These embryos will be used to study how the nucleus is reprogrammed during embryonic development. The

project will also attempt to derive embryonic stem cell lines from the embryos created and these will be compared with stem cell lines from embryos created from IVF. Dr O'Toole presented the main findings of the inspection report. She confirmed that the proposed Person Responsible has completed the Person Responsible Entry Programme (PREP) assessment to the satisfaction of the Executive and that the premises are suitable, secure and well equipped.

2. Dr O'Toole informed the Committee that the application asks for the project to be licensed under the Human Fertilisation and Embryology (Research Purposes) Regulations 2001 s2 a,b and c:

- To increase knowledge about the development of embryos
- To increase knowledge about serious disease
- To enable any such knowledge to be applied in developing treatments for serious disease.

Dr O'Toole confirmed that two out of the two peer reviewers agreed that the project should be licensed under these three purposes and all three agreed that they are satisfied that the research project should be approved in its current form.

3. Dr O'Toole reported that the proposed Person Responsible for the project has said that the project does not require to be approved by the Local Research Ethics Committee (LREC) due to the fact that the human nuclei to be used in the research will not be obtained from tissues or cells donated in this country but taken from commercially available tissue to be imported from an organisation called Cambrex, based in the USA. The centre has requested a statement from its LREC to confirm that LREC permission is not required for this project. Dr O'Toole asked the Committee to consider the letter from Cambrex at page 60 of the papers stating that the consent procedure fulfils USA legal requirements. Dr O'Toole also reported that a further letter has been provided from Cambrex (dated 17 November 2007) which sets out how the company complies with the Human Tissue Act 2004. Dr O'Toole informed the Committee that, these reassurances notwithstanding, the centre has not provided a consent form of the type completed by the donors nor a copy of the information given to donors prior to consent being obtained.

4. Before proceeding to its decision about whether to grant this application for a licence the Committee made a number of preliminary comments about the proposed arrangements for the procurement of human nuclei for use in the project. The Committee agreed that they were not satisfied that the use of imported tissue from the USA removed the obligations of the centre to ensure that donors to the project had properly consented and were fully informed about the aims of the project. In particular, the Committee felt that the providers of the genetic material should explicitly consent to the creation, use and destruction of embryos. The Committee called to mind a currently licensed research project where donors are invited to donate skin cells to a research project involving Somatic Cell Nuclear Transfer, and noted that the patient consent process for those donors is as rigorous as for donors of gametes to projects of research. The

Committee considered that for the purposes of this type of research, involving the creation of embryos, a donor of genetic material in the form of cells or tissue should be treated in the same way as a provider of gametes.

5. The Committee began its formal consideration of the proposed research. In reference to the legal advice prepared by Morgan Cole, the Committee considered whether this research project is one for which a licence may be granted under the 1990 act. The Committee took into account that a licence may be granted which authorises bringing about the creation of embryos *in vitro* or keeping or using embryos for the purposes of a project of research. The Committee noted that the question before them was whether the organism that would be created by inserting human nuclei into enucleated animal oocytes would be an embryo covered by the Human Fertilisation and Embryology Act 1990.

6. Following consideration of the written legal advice and advice from Professor Ledger and Professor Haites, the Committee concluded that that this precise project of research involves the creation and use in research of a “live human embryo” within the meaning of section 1 of the Human Fertilisation and Embryology Act 1990, and that, consequently, this research project is prohibited except in pursuance of a licence granted by the Authority.

7. In reaching this decision, the Committee followed the approach set out by the House of Lords in the case of *R(Quintavalle) v the Secretary of State for Health [2003] UKHL 13*. In particular, the Committee took into account the following points:

a) in enacting the 1990 Act, Parliament opted for a strict regime of control in this area, and did not intend any activity within this field to be unregulated: there was to be no free for all;

b) an embryo created by this method falls within the same genus of fact as other embryos covered by the 1990 Act, in particular, such an embryo has a full human nuclear genome and is live.

8. The Committee next considered whether the proposed research is prohibited by any of the provisions of the 1990 Act. The Committee agreed that it was satisfied that the proposed project is not prohibited as the law now stands.

9. The Committee considered whether the project of research appears either necessary or desirable for one or more of the purposes as set out in paragraph 3(2) of Schedule 2 to the 1990 Act or in paragraph 2(2)(a) of the Human Fertilisation and Embryology (Research Purposes) Regulations 2001. The Committee considered the stated aims of the project and the fact that the project had not been considered by a Local Research Ethics Committee. In considering these aspects of the application, members of the Committee came to the

conclusion that they did not have sufficient information to reach a decision at this time. In reaching this conclusion the Committee took into account the following considerations:

a) the Committee noted that the application had been submitted over a year ago and agreed that this is a considerable amount of time in this fast moving area of research. The Committee concluded that it would be useful if the prospective Person Responsible could be invited to submit an addendum to section 11 of the application which states how the project fits into the current state of knowledge on the subject. The Committee suggested that the addendum then be forwarded to the peer reviewers for information;

b) the Committee agreed that it was not usual for them to consider a research proposal without Research Ethics Committee approval and decided that they would be uncomfortable to proceed without this, particularly in the absence of a statement from the LREC confirming that the project lay outside its jurisdiction.

10. The Committee expressed its hope that the applicant would be able to take on board the Committee's comments sufficiently quickly to enable the application to be brought back before the Committee at its meeting on 9 January 2008.

Signed..... Date.....
Emily Jackson (Chair)

Research Licence Committee Meeting

9 January 2008

21 Bloomsbury Street London WC1B 3HF

MINUTES Item 2

**Research Project R0179: Derivation of embryonic stem cell lines from interspecies embryos produced by somatic cell nuclear transfer
Centre for Stem Cell Biology and Developmental Genetics, Institute of Human Genetics, university of Newcastle Upon Tyne (0296)
Initial Application**

Members:

Emily Jackson – Chair, Lay Member

Clare Brown, Lay Member

Present via teleconference phone:

Maybeth Jamieson, Consultant

Embryologist, Glasgow Royal
Infirmary

Neva Haites, Professor of Medical
Genetics, University of Aberdeen

Providing clinical advice

William Ledger, Professor of

Obstetrics and Gynaecology,
University of Sheffield

In Attendance:

Trish Davies, Director of Regulation/

Deputy Chief Executive

Chris O'Toole, Head of Research
Regulation

Claudia Lally, Committee Secretary

Observers from the Regulation

Department:

Joanne McAlpine

Barbara Lewis

Elaine Suthers

Providing Legal Advice:

Graham Miles, Morgan Cole Solicitors

Conflicts of Interest: members of the Committee declared that they had no conflicts of interest in relation to this item.

The following tabled papers were considered by the Committee:

- research application considered on 28 November 2007 (23 pages)
- inspection report dated 26 September 2007 (16 pages)
- peer reviews considered on 28 November (12 pages)
- minutes of Licence Committee meeting on 28 November 2007 (4 pages)
- summary for Licence Committee by Dr O'Toole and Ms Davies dated 8 January 2008 (2 pages)
- addendum to section 11.1 of the application form (1 page)
- recent comments from Peer Reviewers in response to addendum (5 pages).

1. The papers for this item were presented by Chris O'Toole, Head of Research Regulation. Dr O'Toole reminded the Committee that this is an application to create embryos by inserting human nuclei into enucleated animal oocytes by the technique of somatic cell nuclear transfer (SCNT). These embryos would be used to study how the nucleus is reprogrammed during embryonic development. The project would also attempt to derive embryonic stem cell lines from the embryos created and these will be compared with stem cell lines from embryos created from IVF. Dr O'Toole further reminded the Committee that the proposed Person Responsible has completed the Person Responsible Entry Programme (PREP) assessment to the satisfaction of the Executive and that the premises are suitable, secure and well equipped.
2. Dr O'Toole reminded the Committee that at its meeting on 28 November 2007 the Licence Committee adjourned its consideration of this application on the grounds that it did not have sufficient information to come to a decision. As part of its preliminary consideration of the application the Committee stated that it was not satisfied with the proposed source of human nuclei (from a tissue bank in the USA) and the associated consent arrangements.
3. Dr O'Toole informed the Committee that following the Licence Committee meeting on 28 November, the centre has changed this aspect of its application and now proposes to use two alternative sources of human nuclei: cells obtained from a human embryonic stem cell line derived in their institution, and dermal fibroblasts donated by patients recruited by dermatologists in Newcastle.
4. The Committee considered this new proposal. In relation to the first proposed source of material the Committee noted that the centre would firstly require permission from the UK Stem Cell Bank. The Committee asked whether the consent arrangements for donors of material for the creation of stem cells would be compatible with use in this project. Dr O'Toole replied that it is a condition of the UK Stem Cell Bank Steering Committee that consent forms signed by donors of material to be used in the creation of stem cell lines unequivocally state that donors have no control over any future uses of stem cell lines derived from donated material. This was noted by the Committee who agreed that they were satisfied that no new patient information and consent arrangements would be required in relation to material derived from this source.
5. The Committee noted that use of material from the second source, namely patients who would be asked to donate dermal fibroblasts, would require patient information and consent forms. These have not yet been produced by the centre, and so the Committee had not yet had the chance to consider them. Obtaining skin cells from patients would also require Local Research Ethics Committee (LREC) approval. The Committee agreed that research using material from the second source, could not commence without both LREC approval, and the Committee's approval of patient information and consent forms. However, since use of cells from the first source, i.e. the pre-existing stem cell line, did not

require LREC approval, the Committee agreed that the absence of LREC approval in relation to the second source should not prevent further consideration of the application.

6. The Committee carefully considered all of the written material submitted, including the addendum to the application setting out how the applicant considers the proposed research fits into the current state of knowledge, particularly in the light of developments in relation to reprogramming of somatic cells that have taken place since the application was submitted. The Committee noted that all three peer reviewers had seen this addendum, and that they all specifically state that they remain supportive of the application.

7. The Committee considered the issue of whether this research project, in its amended form, is one for which a licence may be granted under the Human Fertilisation and Embryology Act 1990. Taking into account that a licence may be granted which authorises bringing about the creation of embryos *in vitro* or keeping or using embryos for the purposes of a project of research, the Committee considered the question whether the organism that would be created by inserting human nuclei into enucleated animal oocytes would be an embryo covered by the Human Fertilisation and Embryology Act 1990.

The decision of the Committee

8. The Committee affirmed that that this precise project of research does involve the creation and use in research of a “live human embryo” within the meaning of section 1 of the Human Fertilisation and Embryology Act 1990, and that, consequently, this research project is prohibited except in pursuance of a licence granted by the Authority.

9. In reaching this decision, the Committee followed the approach set out by the House of Lords in the case of *R(Quintavalle) v the Secretary of State for Health [2003] UKHL 13*. In particular, the Committee took into account the following points:

a) in enacting the 1990 Act, Parliament opted for a strict regime of control in this area, and did not intend any activity within this field to be unregulated: there was to be no free for all;

b) an embryo created by this method falls within the same genus of fact as other embryos covered by the 1990 Act, in particular, such an embryo has a full human nuclear genome and is live.

10. The Committee applied the decision tree for research applications. The Committee identified the activities under consideration as the creation of human embryos and the use of human embryos in research. The Committee agreed that

as the law now stands these activities are not prohibited under the Human Fertilisation and Embryology Act 1990. The Committee recognised that the future of research, including research involving cytoplasmic hybrid embryos, may be affected by the Bill which is currently before Parliament. Although the law might change and the applicants need to be aware of that possibility, the Committee is under a legal duty to consider this application and apply the law as it stands.

11. The Committee considered whether the project of research appears either necessary or desirable for one or more of the purposes as set out in paragraph 3(2) of Schedule 2 to the 1990 Act or in paragraph 2(2)(a) of the Human Fertilisation and Embryology (Research Purposes) Regulations 2001. The Committee considered the stated aims of the project and the evaluation of the project by the three peer reviewers. The Committee noted that the that all three peer reviewers were of the opinion that the proposed research is necessary or desirable for the purpose of increasing knowledge about the development of embryos. Two of the peer reviewers additionally thought that the research was necessary or desirable for increasing knowledge about serious disease and enabling any such knowledge to be applied in developing treatments for serious disease. The Committee agreed that in the context of the project of research these activities are necessary or desirable for the following purposes:

- Human Fertilisation and Embryology (Research Purposes) Regulations 2001:
2(2)(a) to increase knowledge about the development of embryos.
- Human Fertilisation and Embryology (Research Purposes) Regulations 2001:
2(2)(b) to increase knowledge about serious disease
- Human Fertilisation and Embryology (Research Purposes) Regulations 2001:
2(2)(c) to enable any such knowledge to be applied in developing treatments for serious disease.

The Committee based its decision on the fact that scientific understanding of the process of cell differentiation and of reprogramming is still at an early stage yet these processes are fundamental to our understanding of the optimal way of producing pluripotent cells and of then driving differentiation safely down specific routes. Until scientific knowledge in this area is more complete, the Committee believes that it is important for researchers to have the ability to use different model systems to obtain a fuller understanding of the molecular and cellular events involved. During the development of an embryo, cellular differentiation begins and the research proposed in this application provides new models to explore and learn more of this process. This research will also extend our knowledge of the above processes and hence, will in the longer term, inform our understanding of the molecular and cellular events involved in disease processes

and inform the development of evidence based approaches to studies exploring potential novel therapies for diseases. The Committee were of the view that, increasing understanding in this area is an important step to increasing understanding about how diseases develop and opening up new avenues for treatment. For these reasons, the Committee was satisfied that the proposed research is, in fact, both necessary and desirable for the specified purposes.

12. The Committee agreed that they were satisfied that the proposed creation and use of human embryos was necessary for the purposes of this research. The Committee were satisfied that the proposed research could not be undertaken without the use of human embryos and was also satisfied that the proposed work justified the creation of human- animal cytoplasmic embryos, given the lack of available human oocytes. The Committee considered the emergence of new technologies for the reprogramming of adult somatic cells and agreed that, while very promising, these new technologies do not obviate the need for the basic research into differentiation of pluripotential embryonic stem cells as proposed in this application.

13. The Committee further considered the patient information and consent forms in relation to the use of donated dermal fibroblasts, and the absence of LREC approval in relation to this second source of material. The Committee decided that a condition should be placed on the licence requiring that research using material from this source should not commence before the Committee has had a chance to scrutinise the patient information and consent form, and has seen evidence of LREC approval of this aspect of the research proposal.

14. The Committee agreed that the requirements for the grant of a licence under Section 16 of the Human Fertilisation and Embryology Act 1990 were satisfied, and decided to grant a licence for the research for a period of one year. The following condition is to apply to the licence:

Research involving the use of dermal fibroblasts donated by patients is not to commence until such time that:

- This Licence Committee has seen and approved the appropriate patient information and consent forms; and
- the Executive has received evidence that the research has been approved by a Local Research Ethics Committee.

15. The Committee noted that the centre has not paid a licence fee and therefore stated that a final licence must not be issued until this fee has been received.

Signed..... Date.....
Emily Jackson (Chair)