Materials Submitted to NIH
From the University of New South Wales
Submission #2010-ACD-008

NOTE: Duplicative information in the submission is not included.

hESC Registry Application Database

Detailed Listing for Request #: 2010-ACD-008
June 1, 2010

hESC Registry Application Search Results

Request #: 2010-ACD-008
Status: Pending

Review: ACD

Assurance: Yes (Section II(B))
Certification: Yes
Authority: Yes

Cell Lines: 1
Available: 1

Previous #:
2009-DRAFT-043
2010-ADM-002

Email
Edit
Delete
Switch to ADM

Organization: Stem Cell Laboratory, Faculty of medicine, University of New South Wales
Org Address: Stem Cell Lab, R-406, Wallace Wurth Building, University of New South Wales, NSW 2152 Australia
DUNS: 751020900 **Grant Number(s):**
Signing Official (SO): Daniel Owens / +61293857254 / d.owens@unsw.edu.au
Submitter of Request: Kuldip Sidhu / +61293853938 / k.sidhu@unsw.edu.au
Submitter Comments: (None)

Line #1: Endeavour-2
NIH Approval #:
Available: Yes
Embryo from U.S.: No
Embryo Donated in Year(s):
Provider Name: Kuldip Sidhu
Provider Phone: +61293853938
Provider Email: k.sidhu@unsw.edu.au
Provider URL:
Provider Restrictions: Cost recovery fee $ 600 per vial will apply for supply of this cell line

NIH Restrictions:

Additional Information:

Supporting Documents:
Document 1: (PDF - 01/18/2010) Fertility clinic ethics apporval, consent froms and declaration of spare embryos by couples - Elements: 1,2
Document 2: (PDF - 01/18/2010) Research laboratory(hospital) ethics approval for derivation of six hESC lines from domnated human e - Elements: 2,4
Document 3: (PDF - 01/18/2010) National Health & Medical Research Council (NHMRC) Licence awarded to fertiity clinic for derivation - Elements: 1,2,3
Document 4: (PDF - 01/18/2010) Authority letter to submit hESC lines - Elements: 4,5,8,11,16
Document 5: (PDF - 01/18/2010) MTA with NIH - Elements: 6,7,10,16
Document 6: (PDF - 01/18/2010) Fertility clinics ethics - Elements: 4,7,9
Document 7: (PDF - 01/18/2010) Hospital ethics - Elements: 7,11,12
Document 8: (PDF - 01/18/2010) NHMRC Licence - Elements: 4,8,13,14
Document 9: (PDF - 01/18/2010) Fertility clinic patient information - Elements: 9,12,15
Document 10: (PDF - 01/18/2010) Consent for spare embryos - Elements: 10,12,15

Administrative Comments: correspondence with submitter and attachments uploaded 23 March 2010 by E. Gadbois

2

correspondence with submitter and attachments uploaded 13 April 2010 by E. Gadbois

SO certifications corrected 13 April 2010 by E. Gadbois

IIB assurance uploaded 21 April 2010 by E. Gadbois

IIB staff analysis uploaded 27 April 2010 by D. Hannemann

Administrative Attachments:
Document 1: (PDF - 03/23/2010) email correspondence
Document 2: (PDF - 03/23/2010) publication
Document 3: (PDF - 03/23/2010) clinical ART consent
Document 4: (PDF - 03/23/2010) research study consent
Document 5: (PDF - 03/23/2010) donation to research consent
Document 6: (PDF - 03/23/2010) heads of agreement
Document 7: (PDF - 03/23/2010) IVF Australia
Document 8: (PDF - 04/13/2010) email correspondence April 3 2010
Document 9: (PDF - 04/13/2010) email attachment April 3 2010
Document 10: (PDF - 04/13/2010) record of decision to switch to ACD WG
Document 11: (PDF - 04/21/2010) IIB assurance
Document 12: (DOC - 04/27/2010) IIB Staff Analysis

Status History:
Draft: 12/14/2009
Pending: 01/18/2010

Emails Sent: 01/18/2010-New_Applicaton_Email

Previous ADM Request Number: 2010-ADM-002
Switched from ADM to ACD Date: 04/13/2010
Reason for Switch to ACD Review:
The decision was made on April 9, 2010, on the basis that exculpatory language in the consent to donate embryos for research needs discussion by the Working Group.

Added By: Commons\kuldip_sidhu **On:** 12/14/2009 | **Last Updated By:** NIH\hannemannd **On:** 04/27/2010 | **Record ID:** 43

Total Record Count = 1

Administration Page

Logout of NIH Form 2890 Admin Site

From: Daniel Owens
To: HESCREGISTRY (NIH/NIDCD)
Cc: Kuldip Sidhu
Subject: RE: New hESC Registry Application Request #2010-ADM-002
Date: Tuesday, April 13, 2010 9:57:51 PM

Dear Ellen

I am writing to confirm that:

I hereby assure that the embryo from which the cell line(s) identified in item 6 of the form was derived was donated prior to July 7, 2009, and the embryo: 1) was created using in vitro fertilization for reproductive purposes and was no longer needed for this purpose; and 2) was donated by individuals who sought reproductive treatment ("donor(s)") who gave voluntary written consent for the human embryo to be used for research purposes. The applicant is advised that the Working Group of the Advisory Committee to the NIH Director will consider submitted materials taking into account the principles articulated in Section II(A) of the NIH Guidelines for Human for Human Stem Cell Research, 45 CFR 46 Subpart A, and the following points to consider: during the informed consent process, including written and oral communications, whether the donor(s) were: (1) informed of other available options pertaining to the use of the embryo ; (2) offered any inducements for the donation of the embryo ; and (3) informed about what would happen to the embryo after the donation for research.

Section IIB Assurance

If I can provide any further information or assurances, please do not hesitate to contact Dr Sidhu or myself.

Kind Regards
Daniel Owens

DANIEL OWENS
Deputy Director | UNSW Grants Management Office
Level 3, South Wing, Rupert Myers Building
The University of New South Wales | UNSW SYDNEY | NSW | 2052
T: +61 2 9385 7254 | F: +61 2 9385 9797 | M: 0411 106 636 | E: d.owens@unsw.edu.au
W: www.gmo.unsw.edu.au | CRICOS Provider No 00098G | ABN 57 195 873 179

From: HESCREGISTRY (NIH/NIDCD) [mailto:hescregistry@mail.nih.gov]
Sent: Wednesday, 14 April 2010 1:36 AM
To: Daniel Owens; Kuldip Sidhu
Cc: HESCREGISTRY (NIH/NIDCD)
Subject: RE: New hESC Registry Application Request #2010-ADM-002

Dr. Owens and Dr. Sidhu,

I am writing to inform you that NIH has reviewed this submission under Section IIA of the NIH Guidelines. We have decided that this submission requires review by the Working Group on Human Embryonic Stem Cell Eligibility Review under Section IIB of the NIH Guidelines. Could you please send us an assurance (signed or emailed by Dr. Owens) per Section IIB (see below). You do not need to take any other action at this time.

Thank you and please let me know if you have any questions.

Sincerely,
Ellen Gadbois

Ellen L. Gadbois, Ph.D.
Office of Science Policy Analysis
Bldg 1 Room 218D
National Institutes of Health
voice: 301-594-2567
fax: 301-402-0280

CREATING HUMAN EMBRYONIC STEM CELL LINES FOR THE TREATMENT OF DIABETES

Participant Information Sheet

Diabetes (Type I & II) affects 100,000 Australians and is set to become Australia's most costly and significant health issue within the next decade. The incidence of diabetes in Australia has increased by 30% in the last five years. Currently the treatment of Type I diabetes in particular involves the injection of insulin several times each day to control the level of glucose in the blood. Unfortunately, this does not always control blood glucose levels or prevent the development of complications that result in impaired vision and kidney failure.

Another treatment for diabetes is to replace the organ or a part of the organ in the body (pancreas) which produces insulin. This approach can result in normal blood glucose levels without the need to inject insulin. In Australia, for example, 26 diabetic people were transplanted with a pancreas last year. However, a shortage of donor organs (only 206 donors in Australia last year), means that this form of treatment is not available to most people. This has prompted interest in other sources of insulin-producing cells as a treatment of diabetes. Embryonic stem cells are one such source.

Embryonic stem cells are special cells that are derived from an embryo when it is 5 or 6 days of age. They are special because they have the ability to form virtually any cell type in the body. They are also self-renewable. This means they can be grown unchanged in the laboratory where their numbers will multiply. They should only change into other cell types such as nerve cells or heart cells if they receive the correct signals to do so by changing the conditions under which they are grown. This ability to change into various cell types including insulin-producing cells has led researchers to investigate whether human embryonic stem cells could be utilised as a treatment for diabetes.

At present there are only 3 human embryonic stem cell lines available in Australia. They differ in their abilities to grow in the laboratory unchanged and in their abilities to be converted into insulin-producing cells. Unfortunately, it is unlikely that these cell lines will ever be suitable for human use because they have been grown with the aid of cells from animals to help keep them in an unchanged state. The aim of the present study is to make human embryonic stem cells without the possibility of being contaminated by animal cells and convert them into insulin-producing cells that might be suitable for human use.

The present study consists of a number of important components. Donated frozen embryos will be thawed and if necessary, cultured to the blastocyst stage. We will attempt to isolate a special subset of cells (inner cell mass cells) from the embryos that reach this stage, a process that will destroy the embryo. Unfortunately, many embryos do not reach this stage and are not suitable for use. The cells taken from embryos in turn will be cultured for a number of weeks or months during which time they will be assessed to determine whether they are true embryonic stem cells. Attempts will then be made to convert these embryonic stem cells into insulin-producing cells that will be tested further under laboratory conditions. We are therefore requesting your consent to use more embryos than the number of stem cell lines we hope to establish.

Ultimately some time in the future the embryonic stem cell lines might be suitable for human trials. Indeed, if embryonic stem cells are produced with proven desirable properties their therapeutic use as a treatment for diabetes may one day become a reality. This may result in commercialisation of a product and financial gain to the researchers and/or their organizations. It is important to understand that participants in this study have no claim or interest in such commercial outcomes from this research and are donating their excess embryos for altruistic purposes.

Recently introduced legislation governing human embryo research in Australia requires couples, who wish to donate their excess embryos to research, to consent to a specific research project. We seek your consent therefore to use your donated embryos to create embryonic stem cell lines for the potential treatment of diabetes. There will be a period of two weeks from the time the project consent form is signed during which you can withdraw your consent to donate embryos. If consent is withdrawn after the embryos have entered the experimental protocol they may have already been destroyed and it will no longer be possible to retrieve the embryos.

If you are interested in participating in this study please complete the attached consent form and forward it to IVFAustralia North Shore. If you require further information or explanation of the proposal please contact Dr John Ryan on 9879 7520. Likewise, if you would like to discuss any aspect of donating your embryos with our counselling or nursing staff please contact the clinic on 9904 8900.

revision 5 – 31/5/2004

Consent form to participate in a research study

We . ...../

Of .....

have been requested to donate our excess embryo(s) for use in the following study :

CREATING HUMAN EMBRYONIC STEM CELL LINES FOR THE TREATMENT OF DIABETES

In relation to this study we have read the Participant Information Sheet, have had the opportunity of seeking further advice and have been informed of the following points.

1. Approval for this study has been given by the Research & Development Committee of IVF Australia and IVFA's Ethics Committee.
2. A licence to carry out this study has also been obtained from the NH&MRC Licensing Committee (License Number 309708) that regulates the use of excess ART embryos.
3. We acknowledge the availability of counselling services from IVF Australia and the provision of an oral explanation of the project to assist us in making a decision whether to donate our embryos.
4. That only embryos frozen before 5th April 2002 may be donated for use in this study.
5. The aim of the project is to use donated frozen human embryos to produce embryonic stem cells that will be evaluated for their capacity to be transformed into cells that produce insulin.
6. The results of this study are not of direct benefit to our future medical management.
7. The study will involve (i) The thawing of frozen embryos and their subsequent culture in vitro for a period of no more than 7 days, (ii) The isolation of cells from embryos at the blastocyst stage of development, a process that will destroy the embryo (iii) The characterisation of the cells as stem cells using various laboratory techniques and using mice as experimental models, and (iv) The investigation of the insulin production properties of the transformed stem cells.
8. That embryonic stem cells produced may be used in the treatment of human diabetes and may result in financial gain to the researchers and/or their organizations. We understand that we have no claim or interest in such outcomes from this research and are donating our excess embryos for altruistic purposes.
9. We understand that our embryos will not enter the experimental protocol for at least two weeks from the date that this consent was signed to give us time to change our mind about donating our embryos.
10. We accept that if we withdraw consent after the embryos have entered the experimental protocol that they may have already been destroyed and it will no longer be possible to retrieve the embryos.
11. Should we have a problem with any aspect of this research study we understand that we can contact Dr John Ryan, Unit Science Manager- IVF Australia North to discuss the problem on (02) 9879 7520.
12. Any person with concerns or complaints about how IVF Australia is conducting the study can contact the Chairman of IVF Australia's Ethic Committee via (02) 9929 5259.
13. Participation in this study will not result in any extra cost to us.
14. The results of the study or information regarding our medical history will not be published to reveal any identifying information about us.
15. That NHMRC inspectors may request access to participants' records.
16. We have read the "Creating human embryonic stem cell lines for the treatment of diabetes" information sheet and have had the opportunity to discuss it and the consent form.

After considering all these points we freely choose to take part and give our consent to the use of our embryo(s) in this study.

SIGNATURES

FEMALE PARTNER:	PRINTED NAME DATE	SIGNATURE ...
MALE PARTNER:	PRINTED NAME DATE	SIGNATURE .....
WITNESS:	PRINTED NAME ..... DATE	SIGNATURE .....
DOCTOR/NURSE/ SCIENTIST	PRINTED NAME ..... DATE	..... SIGNATURE .. ..

IVFAustralia

ASSISTED REPRODUCTIVE TECHNOLOGY AGREEMENT (ARTA)

We wish to attempt to produce a child with the assistance of the in-vitro fertilisation, embryo transfer and related procedures, hereafter referred to as ART, offered by IVFAustralia Pty Ltd™, its officers, employees, agents and consultants (hereafter referred to together as "IVFAustralia"):

A. WE ACKNOWLEDGE THAT:

1. We have read and understood the *ART Booklet*, Version] prior to signing this Assisted Reproduction Technology Agreement and we are aware that future versions will be available at the offices of IVFAustralia. We understand that a Specific Treatment Cycle Agreement (STCA) must also be signed prior to the commencement of EACH treatment cycle, which will define what will apply for that cycle alone.
2. We agree that until one, or both, of us notifies IVFAustralia in writing to the contrary that either of us can sign future Specific Treatment Cycle Agreements (STCA).
3. We have discussed the ART procedures and related technologies with ... . on behalf of IVFAustralia.
4. All our questions have been answered to our satisfaction.
5. The in ART procedure requires the following medical or scientific interventions or techniques:

    a) Testing of us both for infectious diseases including Hepatitis B&C and HIV
    b) medication to induce or control ovulation;
    c) taking of blood samples for pathology testing;
    d) examination of the ovaries using ultrasound;
    e) oocyte retrieval using either ultrasound or laparoscopy;
    f) laboratory techniques to prepare the oocytes and sperm for fertilisation and to attempt to achieve fertilisation;
    g) laboratory techniques to culture embryos using non-autologous media;
    h) transfer of the embryos.

6. If more than one embryo is transferred at any one cycle, a multiple pregnancy may result with the risk of complications as outlined in the booklet.
7. There may be variations to the procedure as technology develops or for any other reason. All variations will be discussed with us by IVFAustralia
8. It may be necessary to undergo ART more than once in order to achieve a pregnancy, and a pregnancy cannot ever be assured.
9. If we do not comply with all directions given us by IVFAustralia concerning the ART procedure our chances of achieving a pregnancy are likely to be reduced.
10. IVFAustralia offers counselling services that are available for either or both of us upon request.
11. The ART procedure involves risks and side effects including those discussed in the ART information booklet we were given.

B. IF APPLICABLE:

We request that IVFAustralia consider us for the application of:

1. **Intra Cytoplasmic Sperm Injection (ICSI):**

    is the technique of microinjection of spermatozoa into the egg in order to attempt fertilisation. This technique will potentially enable spermatozoa to fertilise the egg without having to penetrate the outer coats of the egg. We understand that fertilisation and pregnancy are not guaranteed. We are aware that if there is a Y chromosome problem it may be passed onto sons causing fertility problems and possibly other, as yet unknown, long-term effects.

2. **Assisted Hatching (AH);**

which is an IVF laboratory procedure that "thins" the outer coat (the "egg shell" known as the zona pellucida or simply the 'zona') of the developing embryo. It is performed when there might be reason to suspect that the normal process of zona thinning is not occurring correctly. The thinning is usually carried out immediately prior to embryo transfer.

3. **Blastocyst Culture;**

is a more complex procedure whereby the developing embryo/s are cultured *in-vitro* for up to six (6) days prior to being transferred to the uterus or cryopreserved. This may allow better discrimination of embryo quality but is still experimental and we acknowledge that many embryos do not survive the culture process or the freezing/thawing process. This prolonged culture can also be used as part of the *Pre-implantation Genetic Diagnosis* procedure, an option for which there is a separate brochure and Agreement form.

4. **Embryo Cryopreservation, Thawing and Transfer**

Embryo Cryopreservation is the freezing of embryos to enable them to be thawed and transferred to the woman's uterus in a later cycle. Not all embryos survive this process, and it may result in deterioration of or damage to the embryos. However, embryo cryopreservation permits further attempts at pregnancy in the future without the need to go through the procedure of egg retrieval and fertilisation again.

C. ***WE AGREE THAT:***

1. IVFAustralia will undertake the ART procedure for us; we request IVFAustralia to do so and we consent to the procedure and to any ancillary interventions or techniques that affect us, or either of us.

2. IVFAustralia will determine in its sole discretion which of our embryos are suitable for cryopreservation or for transfer to the uterus.

3. IVFAustralia is entitled to terminate the cryopreservation of any of our embryos and allow the embryos to regress in-vitro if any of the following occurs:

   a) we both so request IVFAustralia in writing
   b) we do not pay all cryopreservation storage charges within 30 days of the date of the account
   c) we give conflicting instructions to IVFAustralia about what should be done with our embryos
   d) either one or both of us dies without specific instructions concerning our embryos left in our will(s)
   e) at the expiration of ten years from the commencement of the cryopreservation
   f) IVFAustralia is required to do so by law.

4. If we require advice about the legal rights and liabilities arising out of the ART procedure or about the legal status of any child born as a result of the procedure, we will seek independent legal advice and will not rely in any way upon information received from or advice given by IVFAustralia.

5. We will pay the fees of IVFAustralia for the ART procedures, and other procedures that are agreed upon, including all fees and storage charges for cryopreservation and thawing of our embryos.

6. We will assume liability for all risks, consequences and side-effects resulting from the above procedures.

D. ***RELEASE AND INDEMNITY:***

1. We release IVFAustralia from and indemnify IVFAustralia against all costs, claims, demands, losses and any other liability whatsoever arising directly or indirectly from the ART and related procedures, including any ancillary interventions or techniques, that IVFAustralia undertakes on us or either of us.

E. ***FOLLOW-UP:***

1. We are aware that non-identifying information collected in the routine course of treatment may be utilised for quality assessment and research purposes.

2. We agree to identifying information being used for long term research. (Yes) No

..... **(female partner signature)** .... **(witness signature)**

..... **(male partner signature)** ..... **witness signature)**

Date: 27/07/04 ***(This Agreement form is valid for 2 years from the date of signing)***

IVFAustralia hereby agrees to undertake the ART procedure.

IVFAustralia

Dear

Date: _____

Dear IVFAustralia Administration

We wish to advise that we no longer require IVFAustralia to maintain storage of our embryos. We therefore request that the following be undertaken: (circle the preferred option number &/or delete the other options)

1. Please destroy the embryos by way of natural regression.
2. We wish to donate our embryos to another couple. (In which case you will need to contact our Clinic Counsellor to arrange for an appointment to be scheduled to discuss this further).
3. We wish to donate our embryos for the purpose of research. We understand that a specific Research Project consent form will later be required.

Signature: _____

(Please print name): _____

Signature: _____

(Please print name): _____

Please note that BOTH signatures are required.

Office use only: (matched by .....)

IVFAustralia
corporate

advanced reproductive technologies
genetic & fertility counselling
scientific & clinical research
diagnostic services

12 June 2003

Emeritus Professor Douglas M Saunders
Chair, R&D Committee
IVFAustralia
Level 1
24 Thomas Street
Chatswood NSW 2067

Dear Prof Saunders,

On 3 June 2003 the IVFAustralia Ethics Committee reviewed and approved the Ethics Application entitled:

Full Project Title
Creating human embryonic stem cell lines for the treatment of diabetes.

Chief Investigator / Supervisor
Dr John Ryan

On this date the Committee (whose membership has been previously sent to NH&MRC and is constituted according to the National Statement) considered the proposal and agreed without dissent. This decision was formally minuted and accepted. This committee accepts Professor Tuch's request that he use new stem cell lines and not previously established ones, and that his work on the treatment of juvenile diabetes is in the national interest.

The Committee now understands that this proposal will be submitted for License to NH&MRC Licensing Committee for IVFAustralia to use excess ART embryos.

Yours sincerely,

Garth Leslie

Garth Leslie
Chair
IVFAustralia Ethics Committee

[redacted] SOUTH EAST HEALTH
South Eastern Sydney Area Health Service

HUMAN RESEARCH ETHICS COMMITTEE - Eastern Section

Room G71, EBB
Cnr High & Avoca Strs
RANDWICK NSW 2031
Tel: 9382 3587
Fax: 93822813

29th September 2004

Professor Bernie Tuch
Diabetes Transplant Unit
POWH

Dear Professor Tuch

Re: **Extension of approval (REF: 02/[illegible]) for study entitled 'Human Fetal Tissue in the Culture of Human Embryonic Stem Cells(HESC)'.**

The Human Research Executive Committee at its meeting of 28th September 2004 considered the Executive Approval given on 12-08-2004 for the following for the above study and this decision was ratified.

- **Confirmation that the work will be conducted in accordance with the NH & MRC License Agreement issued to IVF Australia.**
- **Provision of a copy of the Heads of Agreement Document involving IVF Australia and the Diabetic Transplant Unit.**

Approval has been granted for the derivation of six embryonic stem cell lines from donated human embryos as per the agreement with IVF Australia. This is an extension to the above study.

In accordance with the National Health and Medical Research Council Guidelines, the Committee requires you to furnish it with a progress report every 12 months until and on completion of the study.

The Committee wish you well with the study.

Yours sincerely

Janet White
Admin Assistant
Human Research Ethics Committee

Australian Government
National Health and Medical Research Council

Research Involving Human Embryos Act 2002

Embryo Research Licensing Committee of the NHMRC

LICENCE

This licence is issued under s.21 of the *Research Involving Human Embryos Act 2002*. This licence authorises the use of excess ART embryos specified below, subject to the conditions specified in items 8 and 9 below.

1.	Licence number:	309708
2.	Licence holder:	IVF Australia Pty Ltd
3.	Licence title:	A collaborative project between IVF Australia and the Diabetes Transplant Unit, Prince of Wales Hospital to derive Human Embryonic Stem Cell Lines for the treatment of Diabetes
4.	Date of issue:	5 November 2004
5.	Licence begins:	5 November 2004
6.	Licence ends:	31 December 2005
7.	Use of excess ART embryos authorised by the licence	Isolation of the inner cell mass from excess human ART embryos in order to establish six embryonic stem cell lines.
8.	Standard conditions	All conditions that are specified in the document *Standard Conditions for Using Excess ART Embryos* as currently published on www.nhmrc.gov.au/embryo and as amended from time to time.
9.	Special conditions:	All conditions that are specified in the *Special Conditions for Licence No. 309708.*

The licence holder is reminded of the statutory provisions of the *Research Involving Human Embryos Act 2002* and the *Prohibition of Human Cloning Act 2002.*

Australian Government
National Health and Medical Research Council

Research Involving Human Embryos Act 2002

Embryo Research Licensing Committee of the NHMRC

Special Conditions for Licence No. 309708

1.	Licence number:	309708
2.	Licence holder:	IVF Australia Pty Ltd
3.	Licence title:	A collaborative project between IVF Australia and the Diabetes Transplant Unit, Prince of Wales Hospital to derive Human Embryonic Stem Cell Lines for the treatment of Diabetes

The conditions that are specified below are the special conditions that apply to this licence. The *Special Conditions* operate **in addition to** all conditions identified in the *Standard Conditions for Using Excess ART Embryos*. The *Special Conditions* prevail where there is an inconsistency between a special condition and a standard condition.

Number of embryos

Condition number	*Condition*
9101	The licence holder may remove from cryostorage and thaw up to 100 excess ART embryos subject to the conditions contained in this licence.
9102	Excess ART embryos used for this licence must have been created before 5 April 2002.
9103	1. The excess ART embryos must only be used to isolate their inner cell masses.

9104	2. The licence holder is authorised to isolate inner cell masses and these must be transferred to the Diabetes Transplant Unit, Prince of Wales Hospital ("the Diabetes Transplant Unit") only for the purpose of establishing six (6) embryonic stem cell lines and undertaking the activities and achieving the goals proposed in Attachment 1 to the application dated 1 October 2003 and lodged in accordance with s.20 of the *Research Involving Human Embryos Act 2002* ("the licence application").
9105	(1) The licence holder is authorised to use the excess ART embryos mentioned in Condition 9101 to produce 6 established stem cell lines in accordance with Condition 9104. (2) In the first stage of the licensed use, the licence holder is authorised to thaw up to 30 of the excess ART embryos to isolate inner cell masses. Should any inner cell masses be isolated, they shall be transferred to the Diabetes Transplant Unit. Should no inner cell masses result from the initial 30 embryos, a further 10 excess ART embryos may be thawed and any inner cell masses isolated from that further 10 shall be transferred to the Diabetes Transplant Unit. If no inner cell masses result from the initial 30 embryos and the further 10 embryos, then the licence holder must report promptly in writing to the Licensing Committee and no further embryos may be thawed without the written approval of the Licensing Committee. (3) Following transfer of any inner cell masses isolated in the first stage, the licence holder shall request a report from the Diabetes Transplant Unit that describes the outcome for each inner cell mass supplied. (4) The licence holder may not thaw any more excess ART embryos until the licence holder has received the report from the Diabetes Transplant Unit described in (3) above. (5) If the report from the Diabetes Transplant Unit states that fewer than 6 embryonic stem cell lines have been established according to the criteria in Condition 9106 below, the licence holder may use up to 10 more excess ART embryos to isolate inner cell masses. Any additional inner cell masses that result must be transferred to the Diabetes Transplant Unit. (6) Following the transfer in (5), the licence holder is again required to request a report from the Diabetes Transplant Unit that describes the outcome for each inner cell mass transferred and no further excess ART embryos may be thawed until that report has been received. (7) If the report referred to in (6) states that fewer than 6 embryonic stem cell lines have been established according to the criteria in Condition 9106 below, the licence holder may again thaw up to 10 more excess ART embryos to derive additional inner cell masses and transfer these to the Diabetes Transplant Unit. (8) This process of thawing batches of embryos and transferring inner cell masses in response to a report from the Diabetes Transplant Unit can continue as often as necessary, but subject to condition 9101 above, until 6 embryonic stem cell lines have been established according to the criteria in Condition 9106 below.

9106	No excess ART embryos may be removed from cryostorage and thawed after the Diabetes Transplant Unit has reported to the licence holder that it has established 6 embryonic stem cell lines according to the following criteria: • the embryonic stem cell line must possess a normal human diploid karyotype, and express antigens and genes specific for embryonic stem cells; • initial studies indicate that the cell line is pluripotent and capable of self-renewal; and • these lines must have been passaged ten times in culture and have been successfully cryopreserved on two occasions and shown to be free of contamination by adventitious agents.
9107	When 6 embryonic stem cell lines are established in accordance with condition 9106, any remaining cell lines under evaluation by the Diabetes Transplant Unit may, subject to condition 9402, continue to be used to meet the goals of the project proposed in Attachment 1 to the application dated 1 October 2003 and lodged in accordance with s.20 of the *Research Involving Human Embryos Act 2002*.

Specified sites

Condition number	*Condition*
9201	The use of excess ART embryos authorised by the licence may only be conducted at the following sites: IVF Australia North Hunters Hill Hospital 9 Mount St HUNTERS HILL NSW 2110 IVF Australia Western Sydney City West Day Surgery 30 Mons Rd WESTMEAD NSW 2145 IVF Australia Eastern Suburbs Level 1 Maroubra Day Surgery 225 Maroubra Rd MAROUBRA NSW 2035

9202	The licence holder may only hold records (other than patient records) associated with the use authorised by the licence at the following sites: IVF Australia North Hunters Hill Hospital 9 Mount St HUNTERS HILL NSW 2110 IVF Australia Western Sydney City West Day Surgery 30 Mons Rd WESTMEAD NSW 2145 IVF Australia Eastern Suburbs Level 1 Maroubra Day Surgery 225 Maroubra Rd MAROUBRA NSW 2035

9203	The licence holder may only hold patient records associated with the excess ART embryos used in accordance with this licence at the following sites: IVF Australia North Level 1 24 Thomas St CHATSWOOD NSW 2067 IVF Australia Central Coast Suite 2 213 North Albany St GOSFORD NSW 2250 IVF Australia Western Sydney 12 Caroline St WESTMEAD NSW 2145 IVF Australia Eastern Suburbs Level 1 Maroubra Day Surgery 225 Maroubra Rd MAROUBRA NSW 2035 IVF Australia Southern Sydney Level 3 St George Private Hospital South St KOGARAH NSW 2217

Persons authorised to use excess ART embryos

Condition number	*Condition*
9301	The Principal Supervisor is authorised by the licence to participate in the use of excess ART embryos. The Principal Supervisor is that person identified in Section A Part 2 of the application dated 1 October 2003 (2003/59734, f. 18) and lodged in accordance with s.20 of the *Research Involving Human Embryos Act 2002*, or as subsequently notified to and authorised by the Licensing Committee. The Principal Supervisor is responsible for supervision of the use of excess ART embryos as authorised by the licence.

9302	Other personnel authorised by the licence to participate in the use of excess ART embryos are those identified in the attachments received on 16 December 2003 (2003/59734, f. 77) and 25 May 2004 (2004/30104, f. 15) to the application dated 1 October 2003, and lodged in accordance with s.20 of the *Research Involving Human Embryos Act 2002*, or as subsequently notified to and authorised by the Licensing Committee.

Reporting

9401	The licence holder must report progress on establishing embryonic stem cell lines in writing to the NHMRC Licensing Committee when 40 of the 100 excess ART embryos authorised in condition 9101 have been used.
9402	The licence holder must report immediately in writing to the Licensing Committee when each or either of the following situations arises: (a) the combined total of: (i) the number of established embryonic stem cell lines, being fewer than 6; and (ii) the number of potential embryonic stem cell lines under investigation exceeds 6; and (b) the number of established embryonic stem cell lines equals or exceeds 6.
9403	In the event that any potential lines under evaluation referred to in condition 9402 above, result in the establishment of one or more embryonic stem cell lines so that the total number of embryonic stem cell lines exceeds the authorised limit of 6 as provided in condition 9104, then the licence holder must immediately report that fact in writing to the Licensing Committee.

MATERIAL TRANSFER AGREEMENT

South Eastern Sydney and Illawarra Area Health Service
ABN 670 629 86109

and

The University of New South Wales
ABN 57 195 873 179

19

MATERIAL TRANSFER AGREEMENT

Date	15 December 2009
Parties	**South Eastern Sydney and Illawarra Area Health Service** (ABN 78 390 886 131) of Lawson House, Wollongong Hospital, Level 4, Loftus Street, WOLLONGONG NSW 2500 **(SESIAHS)**, through the Diabetes Transplant Unit (DTU) SESIAHS Contact: Professor Margaret Rose Area Director Research Governance - SESIAHS G6, Level 2, Clinical Sciences Bld., Prince of Wales Hospital Barker Street. Randwick. NSW. 2031 Phone: +61 2 9382 3908 or 4253 4800 Fax: +61 2 9382 4049 **THE UNIVERSITY OF NEW SOUTH WALES** (ABN 57 195 873 179), a body corporate established pursuant to the *University of New South Wales Act 1989* (NSW) of UNSW SYDNEY NSW 2052, through the Faculty of Medicine and School of Psychiatry **(Recipient)**. General Contact: A/Prof Kuldip Sidhu, Head, Stem Cell Lab Phone: 02 9385 3938 Fax: 02 9385 1483 Legal Contact: Janice Besch Director, UNSW Grants Management Office The University of New South Wales UNSW SYDNEY NSW 2052 Phone: 02 9385 7230 Fax: 02 9385 7238
Original Material	Endeavour-2 (E2) cell line
Transport	Frozen vials will be picked up by Recipient from the DTU
Location	Stem Cell Laboratory (SCL) of the Faculty of Medicine and School of Psychiatry, located at R-406 of Wallace Worth Building of University of New South Wales (UNSW)
Research	The cell lines/materials will be used solely for teaching and research purposes exclusively for the research projects with ethics approval (if applicable) detailed in Appendix 1 of this Agreement, as supplemented by written agreement of the parties; entitled NIH and SCL
Research Director	A/Prof Kuldip Sidhu, Phone: +61 2 9385 2002 (Lab) /9385 3839 (Off). Email: k.sidhu@unsw.edu.au
Commencement Date	The date when this Agreement has been executed by both Parties.
Completion Date	As specified for each research project in Appendix 1 of this Agreement.
Fees & Payment	A$400 per vial (ex GST)
Owner of Research IP	Jointly owned as tenants in common in equal shares by SESIAHS and Recipient
Special Conditions	Prof Sidhu may liaise with third parties and commercial entities in his capacity as an inventor of the Materials and Research IP, only on the conditions that Prof Sidhu notifies the SESIAHS Contact (above) in writing of such liaisons within twenty-four hours of commencing the liaison and that the SESIAHS Contact approves ongoing liaisons between Prof Sidhu and the commercial entities within 36 hours of commencing the liaison; however, Prof Sidhu must make it clear to all third parties at the commencement of their liaison that his liaisons are non-binding and negotiations must be carried out between those parties and SESIAHS directly.

Agreement

SESIAHS and Recipient agree that SESIAHS will supply the Original Material to Recipient for the Research in accordance with the Details and the attached Terms and Conditions and Attachments (which together form this Agreement).

Signed for and on behalf of
South Eastern Sydney and Illawarra Area Health Service

Signature of Authorised Officer

Print Name

Position

Date

Prof. Margaret Rose
Area Director
Research Governance

December 10, 2009.

Signed for and on behalf of
The University of New South Wales

Signature of Authorised Officer

Daniel Owens
Print Name Acting Director

Position

Date 15/12/09

UNSW GRANTS MANAGEMENT OFFICE
University of New South Wales
UNSW SYDNEY NSW 2052

TERMS AND CONDITIONS

1.Definitions

Confidential Information means all information of SESIAHS of a confidential nature, including information relating to:

a) the Materials and any technical information and documentation relating to the Materials;

b) SESIAHS's IPR; and

c) the business and operations of SESIAHS,

whether disclosed verbally, in writing, in electronic form or by any other means, but excluding information which:

d) Recipient can prove by written records it knew or possessed before the Confidential Information was disclosed;

e) is or becomes available to the public otherwise than by a breach by Recipient of this Agreement;

f) is lawfully acquired by Recipient from a third Party without restrictions as to its use or disclosure.

Details means the matters set out in the table on the front page of this Agreement.

GST means the tax imposed by A New Tax System (Goods and Services Tax) Act 1999 (Cth).

IPR means all statutory and other proprietary rights (including rights to require information be kept confidential) in respect of know-how, trade secrets, copyright, trade marks, designs, patents, plant breeder's rights, circuit layouts and all other rights as defined by Article 2 of the Convention establishing the World Intellectual Property Organisation of July 1967 and all rights to apply for same.

Materials means the Original Material and includes any Progeny and Unmodified Derivatives of the Original Material.

Modification means substances created by the Recipient including modified derivatives of the Original Material, but not including Materials.

Progeny means an unmodified descendant from the Original Material, such as virus from virus, cell from cell or organism from organism.

Research IP means all IPR in the Results.

Results means outcomes of the Research, including but not limited to all data, Modifications, discoveries and ideas, but not including Materials. The Results include any substances created through the use of the Materials or Modifications but which are not Progeny or Unmodified Derivatives.

Terms and Conditions means these terms and conditions.

Unmodified Derivative means a substance which constitutes an unmodified functional unit or product expressed by the Original Material, including without limitation, subclones of unmodified cell lines, purified or fractionated subsets of the Original Material, proteins expressed by DNA/RNA supplied by SESIAHS, DNA/RNA supplied by SESIAHS, or polyclonal and/or monoclonal antibodies secreted by a hybridoma cell line or sub-sets of the Original Material such as novel plasmids or vectors.

UNSW means the University of New South Wales (ABN 57 195 873 179).

2. Interpretation

a) All capitalised terms not defined in these Terms and Conditions have the meaning specified in the Details.

b) If the Details specify special conditions, they override the Terms and Conditions to the extent of any inconsistency.

c) The singular includes the plural and vice versa, and words importing one gender include any other gender.

d) A reference to a Party includes that Party's successors and permitted assigns.

e) A reference to a person includes a company, other corporations, or a body of persons (corporate or incorporate).

f) "including" and similar expressions are not words of limitation.

g) Headings are used for convenience only and do not affect the interpretation of this Agreement.

h) A reference to a thing (including a right) includes a reference to a part of that thing.

i) Where words or expressions are defined, other parts of speech and grammatical forms of that word or expression have corresponding meanings.

3. Materials

a) SESIAHS will supply the Original Material or arrange for the Original Material to be supplied to Recipient in accordance with the Details. All risk in the Original Material transfers to Recipient upon dispatch.

b) Recipient may use the Materials solely at the Location for the conduct of the Research under the direction of the Research Director (if named in the Details) and may not supply or transfer the Materials to any other location without the prior written permission of SESIAHS from SESIAHS Contact.

c) Recipient must store, transport and use the Materials in accordance with all applicable laws, regulations and guidelines. The Materials must not be used in or in relation to humans without the prior written permission of SESIAHS from SESIAHS Contact.

d) Recipient acknowledges that the Materials are experimental in nature with not all of their characteristics known and shall be used with prudence and appropriate caution.

e) Recipient's right to use the Materials under this Agreement is non-exclusive.

f) Recipient acknowledges that the Materials are proprietary to SESIAHS and are of considerable value, both in terms of research use and in terms of potential commercial applications.

4. Payment of Fees

Recipient will pay SESIAHS the Fees (if any). Invoices are payable within 14 days of issue.

5. Results and IPR

a) Each Party retains its rights in its background IPR. In particular, SESIAHS retains IPR ownership of the Materials, including any Materials contained or incorporated in Modifications.

b) Upon completion of the Research or termination or expiry of this Agreement Recipient must within 60 days provide to SESIAHS a written report of the progress of the Research, including copies of samples of the Results and details of any Research IP.

c) The Research IP will be owned by the Parties specified in the Details.

d) The Results of the Research into the cell lines/material supplied by SESIAHS shall be the property of the Parties specified in the Details. Disclosure of those Results will be as per the terms under clause 8.

e) Nothing in this Agreement gives Recipient any licence of or other interest in any IPR of SESIAHS other than as expressly set out in this Agreement.

f) Where IPR is vested in a Party by this clause 5, the other Party must do all things and sign all documents (including formal assignment documents) as may be necessary to vest, confirm, perfect and record ownership by that Party in accordance with this clause.

6. Commercialisation

Except where this Agreement is terminated by SESIAHS under clause 12(b) in which event no such right is granted, if Recipient wishes to commercialise any Results or Research IP or use for a commercial purpose any Materials or Modifications, the Parties will negotiate in good faith an agreement for this purpose on terms acceptable to both Parties.

7. Obligation of confidentiality

Recipient must (except as may be required by law or with SESIAHS' prior written consent) maintain the confidentiality of the Confidential Information, only use it for the purposes of the Research and return or destroy it upon request.

8. Publications

A Party (including in the case of SESIAHS) may present or publish material relating to the Research or the Research IP subject to the prior written consent of the other Party, such consent not to be unreasonably withheld. To seek such consent:

a) the party must submit a written request to the other party at least 30 days before the intended submission for publication or presentation;

b) the other party must consider the request within 21 days of receipt and notify the first party of its decision in writing. If the other party fails to notify the first party in writing of its decision within 30 days the first party is deemed to be given consent;

c) the other party must not unreasonably withhold its consent provided that it may withhold consent if it reasonably believes the publication or presentation will adversely affect Confidential Information or the protection or commercialisation of the Research IP; and

d) the party so presenting or publishing must make appropriate citation of authorship or acknowledgment of the other party's contribution to the Research.

9. Non-excludable liability

a) Subject to any terms which by law may not be excluded, restricted or modified, all representations, warranties and conditions not stated in this Agreement are excluded, including warranties as to fitness for purpose, merchantability and no infringement of IPR.

b) To the extent permitted by law, all liability of SESIAHS for a claim arising from a breach of any non-excludable term or condition implied by statute is limited, at its option, to resupply of the Materials or paying the cost of resupply.

10. Exclusion of liability

To the extent permitted by law, SESIAHS will have no liability to Recipient for any direct or indirect loss, damage or expense (including loss of profits, loss of business opportunity and liabilities in respect of third Parties) arising out of or in connection with the supply of the Materials or this Agreement, whether arising under common law, statute, tort (including negligence) or otherwise.

11. Warranties and Indemnities

a) Recipient releases and indemnifies SESIAHS, their officers, employees, contractors and agents from and against all claims, damages, costs and other remedies actual, contingent or otherwise, arising directly or indirectly in connection with the supply of the Materials to, or use of the Materials by or on behalf of, Recipient.

b) SESIAHS warrants that:

(i) it is the sole owner of IPR in the Materials, with good legal and beneficial title to the IPR free and clear of all charges, encumbrances, liens and interests whatsoever; and

(ii) it has documentary evidence, which it will promptly provide to the Recipient upon request, of a) informed (anonymised) donor consent and b) approval from a local research ethics committee as proof that any cell line Materials were derived in accordance with national ethical and regulatory requirements.

12. Termination

a) This Agreement will commence on the Commencement Date and terminate on the Completion Date unless it is terminated earlier in accordance with its terms.

b) Either Party may terminate this Agreement by written notice if at any time: the other Party commits a material breach of this Agreement which it fails to correct within 30 days of notice from the first Party; or the other Party becomes insolvent, enters into liquidation, receivership, becomes subject to any form of external administration, makes a composition or arrangement with its creditors generally, or takes advantage of any statute for relief of insolvent debtors.

c) Upon termination or expiry of this Agreement for any reason Recipient must return to SESIAHS or destroy, at SESIAHS' option, all remaining Materials in its possession or control.

d) Clauses 5 to 11 and 12(c) survive expiry or termination of this Agreement for any reason.

13. General

a) This Agreement contains the entire agreement between the Parties as to its subject matter and is not capable of variation except in writing signed by both Parties. Notices must be given to the Parties' addresses in the Details or as otherwise notified by the Parties in writing.

b) Recipient must not assign its rights or obligations under this Agreement without SESIAHS' prior written consent.

c) Nothing in this Agreement may be construed as creating a relationship of employment, partnership, joint venture or principal/ agent.

d) No part of this Agreement is to be construed to the disadvantage of a Party because that Party was responsible for its preparation.

e) No delay or indulgence by a Party in enforcing this Agreement will prejudice or restrict the rights of that Party, nor will a waiver of those rights operate as a waiver of a subsequent breach.

f) If taxes are payable on any supply made under this Agreement (including GST), Recipient must pay an additional amount equivalent to the taxes. SESIAHS will provide a tax invoice.

g) A Party, at the request of the other Party, must do all things necessary to give effect to this Agreement or to assist the other Party to protect the Research IP. Recipient shall not seek protection of Research IP without the express written consent of SESIAHS.

TERMS AND CONDITIONS

h) If any provision of this Agreement offends any law or is invalid or unenforceable then where the provision can be read down so as to be valid and enforceable, it must be read down to that extent, or otherwise will be deemed severed from the other provisions.

i) The signatories to this Agreement warrant that they have the authority to bind to this Agreement the Party they are stated to represent.

j) This Agreement is governed by the laws of New South Wales, Australia and the Parties submit to the non-exclusive jurisdiction of the courts of that State.

TERMS AND CONDITIONS

APPENDIX 1 - Approved Projects

1. [Insert details of Project] See below the email communication from NIH USA

   Ethics Approval: [not applicable]

   Completion Date: [Lines submitted to NIH will remain on its website for their continuous use for research by workers]

From: Cole, Laura (NIH/NIDCD) [E] [mailto:colel@nidcd.nih.gov]
Sent: Tuesday, 17 November 2009 3:08 AM
To: 'k.sidhu@unsw.edu.au'
Subject: Do You Have Human Embryonic Stem Cell Lines for NIH Review?

Dear Human Embryonic Stem Cell Scientist,

On March 9, 2009, President Obama lifted the restrictions on human embryonic stem cell research that had previously been in effect.
Subsequently, on July 7, 2009, the U.S. National Institutes of Health (NIH) issued new Guidelines describing the conditions under which the embryo donations must have been made in order for the derived embryonic stem lines to be eligible for NIH funding (http://stemcells.nih.gov/policy/2009guidelines.htm). Cell lines that are determined to be eligible through an NIH Review process will then be listed on an NIH Registry (http://grants.nih.gov/stem_cells/registry/current.htm <http://grants.nih.gov/stem_cells/registry/current.htm>).

If you have human embryonic stem cell lines that you think meet the requirements of the Guidelines, we encourage you to submit your documentation for consideration by NIH. To facilitate this process, NIH has set up an easy-to-use, transparent, on-line submission process that has already been used by a number of investigators and institutions at http://hescregapp.od.nih.gov/NIH_Form_2890_Login.htm. Please note that the embryonic stem cell line may only be submitted by the person or entity having the authority and/or rights (e.g., the owner, deriver or licensee or have written permission of the same to submit).

As explained in the Guidelines, cell lines that meet the specific requirements of Section IIA of the Guidelines (regardless of when or where the embryos were donated, i.e., before or after July 7th in the US or abroad) may be approved under an administrative review (ADM) process at NIH. Cell lines that were generated from embryos donated in the U.S. or abroad prior to July 7, 2009 that do not meet the specific requirements of Section IIA may be considered by a Working Group of the Advisory Committee to the Director (ACD). Also, cell lines that were generated from embryos donated outside of the U.S. on or after July 7, 2009, which do not meet the specific requirements of Section IIA, may be considered by the ACD Working Group.

To make the review process operate more efficiently, we recently made one minor adjustment to the review process. Because administrative review at NIH is expected to take less time than review by the ACD, you can submit a line to NIH for administrative review if you believe that it meets the Section IIA requirements. If NIH determines that the line is not approvable under Section IIA, NIH will forward the submission to the ACD for review.

If you have questions, please send an e-mail to hescregistry@mail.nih.gov <mailto:hescregistry@mail.nih.gov> and we will respond by e-mail or phone.

TERMS AND CONDITIONS

Thank you for your consideration of this request. NIH is committed to full and expeditious implementation of the Executive Order so that we can expand the opportunities for NIH funded human embryonic stem cell research.

Sincerely,

Story C. Landis, Ph.D.

Chair, Stem Cell Task Force

U.S. National Institutes of Health

From: kuldip sidhu [mailto:k.sidhu@unsw.edu.au]
Sent: Tuesday, 17 November 2009 11:54 AM
To: 'l.issa@unsw.edu.au'
Cc: 'Perminder Sachdev'; 'Margaret Rose'
Subject: FW: Do You Have Human Embryonic Stem Cell Lines for NIH Review?
Dear Laura,

I am the co-inventor of the human embryonic stem cell line Endeavour-2 from Australia and am keen to submit the same to NIH for review to be included in future for their wider distribution for research and development worldwide as outlined in the email below. Endeavour-2 is the property of the South Eastern Sydney and Illawarra Area Health Service and have access to Endeavour-2 under a Material Transfer Agreement.

There are specific guidelines for institutions to submit lines for review as outlined in the email below. Please advise how to proceed further quickly without loosing this opportunity to launch this line through NIH.

Thanks,

A/Prof Kuldip Sidhu

Director, Stem Cell Lab

Chair, Stem Cell Biology,

Faculty of Medicine,

14B Samuels Building(BABS)

UNSW, NSW 2052

Australia

In Vitro Cell.Dev.Biol.—Animal
DOI 10.1007/s11626-010-9280-8

Derivation of a new human embryonic stem cell line, Endeavour-2, and its characterization

Kuldip S. Sidhu · John P. Ryan · Justin G. Lees · Bernard E. Tuch

Received: 24 March 2009 / Accepted: 14 January 2010 / Editor: J. Denry Sato

Abstract Here, we describe the derivation of a novel human embryonic stem cell (hESC) line, Endeavour-2 (E-2), propagated on human fetal fibroblasts (HFF) in a serum-replacement media. The inner cell mass (ICM) was manually dissected from the blastocyst without using immunodissection and, therefore, antibodies from animal sources. A total of 20 embryos were thawed and cultured, eight embryos were hatched, and five ICMs were obtained. They were transferred onto HFF used as feeder layer, and one colony representing the initial cell proliferation of a new hESC line, E-2, was obtained. The newly emerged hESC colony was passaged first by physical dissection and subsequently by enzymatic dissociation. E-2 has been in culture for over 6 months and has been shown to possess typical features of a pluripotent hESC line including expression of stem cell surface markers (SSEA4, TRA-160, and integrin alpha-6), intracellular alkaline phosphatase, and pluripotency gene markers, OCT4 and NANOG. This hESC line shows lineage-specific differentiation into various representative cell types expressing markers characteristic of the three somatic germ layers under both in vitro and in vivo conditions. E-2 line shows a normal karyotype (46 XX) and has been successfully cryopreserved and thawed several times using slow-freezing procedures. E-2 adds to the repertoire of existing hESC lines for research and development purposes in the field of regenerative medicine.

Keywords Pluripotency · Teratomas · Blastocyst · Differentiation

K. S. Sidhu · J. G. Lees · B. E. Tuch
Diabetes Transplant Unit,
Prince of Wales Hospital & University of New South Wales,
Sydney, NSW, Australia

K. S. Sidhu (✉)
Stem Cell Lab, School of Biotechnology and Biomolecular Sciences and School of Psychiatry, Faculty of Medicine,
University of New South Wales,
408 Wallace Wurth Building,
Sydney, NSW, Australia
e-mail: k.sidhu@unsw.edu.au

J. P. Ryan
IVF Australia,
Sydney, NSW, Australia

Introduction

Ten years after the first successful derivation of hESC lines by Thomson et al. (1998), many more new hESC lines have been created (Cowan et al. 2004; Stojkovic et al. 2004, 2005; Sidhu et al. 2008a, b). It is estimated that more than 1,071 hESC lines have been produced worldwide (Loser et al. 2009; Sidhu 2009). More than 179 of these lines are characterized to some extent and available for research. Many of these hESC lines have been derived on different feeder layers (mouse embryonic fibroblasts, fetal muscle, skin, and foreskin, adult fallopian tube epithelial cells) and under different culture conditions including serum- and/or feeder-free (Sidhu et al. 2008a, b); hence, comparison of these lines is very difficult (Carpenter et al. 2004; Rosler et al. 2004; Sato et al. 2004; Beattie et al. 2005; Xu et al. 2005). Several studies indicate that there are substantial differences between hESC lines in terms of gene expression and differentiation profiles (Richards et al. 2003; Inzunza et al. 2004; Pekkanen-Mattila et al. 2009). Recently, some attempts have been made to derive new hESC lines under more defined conditions such as serum-, feeder-, and/or xeno-free (Heins et al. 2004; Genbacev et al. 2005; Wang et

Published online: 23 February 2010

al. 2005; Ellerstrom et al. 2006; Ludwig et al. 2006; Chavez et al. 2008). Previously, we described the derivation of a novel hESC line, Endeavour-1, under defined conditions (Sidhu et al. 2008a). Here, we describe the derivation of another novel hESC line called Endeavour-2 (E-2), in culture conditions largely devoid of animal products, using serum replacement medium and a human fetal fibroblast (HFF) feeder layer.

Materials and Methods

All reagents were obtained from Gibco/Invitrogen (Carlsbad, CA, http://www.invitrogen.com) unless specified otherwise.

Human embryonic stem cell culture and ethics approvals. This study to work on hESC and HFF lines including derivation of new hESC lines was approved by the Institutional Human Research Ethics Committee (HREC 02247/02267). Human embryos were obtained from donors undergoing infertility treatment at IVF Australia clinic after informed consent. Derivation of new hESC lines was carried out at the Diabetes Transplant Unit (DTU), Prince of Wales Hospital (Sydney, Australia) after obtaining a license #309708 from the National Health and Medical Research Council Licensing Committee (Australia) issued to IVF Australia Clinic for donation of human embryos to DTU.

Derivation of HFFs as feeder layer. HFFs were derived from human fetal skin after therapeutic termination of pregnancies and with maternal consent as described previously (Sidhu et al. 2008a), with some modifications. Briefly, $2\times3\text{-mm}^2$ pieces of skin were washed twice with PBS containing 25 U/ml penicillin and 25 μg/ml streptomycin and finely chopped into small pieces with a pair of fine scissors. Single-cell suspensions were prepared by treating for 15 min at 37°C with 0.25% trypsin. After washing, the HFFs were cultured in HFF media (Sidhu and Tuch 2006) containing 20% FBS in T75 tissue culture flasks. The primary cultures of HFFs were cryopreserved by a standard slow-freezing procedure in serum-containing media prepared with 10% DMSO.

Derivation of new hESC line, Endeavour-2. A total of 20 embryos (days3–5) were thawed at IVF Australia, Sydney. Eight embryos survived and were cultured in Quinns Advantage Cleavage and Blastocyst medium supplemented with 5% human serum albumin (SAGE Biopharma, Bedminster, NJ). Seven of the embryos hatched following laser breaching of the zonae pellucidae and were transferred to HFF feeder layers in six-well plates, where they were cultured in serum-replacer medium (SR medium) consisting of Dulbecco knockout (KO-DMEM) high glucose, supplemented with 20% knockout serum replacer (Gibco), 2 mM L-glutamine, 0.1 mM nonessential amino acids, 0.01 mM 2-mercaptoethanol, 1× insulin–transferrin–selenium, basic fibroblast growth factor (bFGF), 4 ng/ml, 25 U/ml penicillin, and 25 μg/ml streptomycin for a further 2 to 3 d as described previously (Sidhu et al. 2008a, b). The attached ICMs (five) were dissected manually, transferred into fresh feeder layer plates, and then transported to the DTU in a portable 5% CO_2 incubator. The appearance of a single hESC colony was observed after 2 wk in culture. The newly emerged hESC colony was initially passage two to three times by physical dissection before using enzymatic dissection as describe previously (Sidhu et al. 2008a, b). E-2 was cryopreserved at various passages (<p10) using slow-freezing techniques described previously (Reubinoff et al. 2001; Sidhu and Tuch 2006).

Maintenance of new hESC line, Endeavour-2. Cryopreserved colonies of the hESC line E-2 were thawed and maintained in six-well culture plates (Becton Dickinson, Franklin Lakes, NJ; http://www.bdbiosciences.com) coated with gelatin and on gamma-irradiated (45 Gy) HFF (passage 6–9) feeder layers (1.5×10^6 cells/ml). The incubations were carried out in SR media at 37°C in 5% CO_2. Colonies were passaged using enzyme dissociation techniques as described previously (Sidhu and Tuch 2006).

Characterization of Endeavour-2. Fluorescence-activated cell sorting (FACS): Using primary antibodies (1:40) against the surface markers SSEA-4 (MAB4304), TRA-160 (MAB4360), and integrin alpha-6 (MAB1982) (Millipore, Sydney, Australia; http://www.millipore.com), single-cell suspensions of E-2 hESCs were assessed by FACS. Epitope binding of the primary antibodies was detected using appropriate fluorophore-conjugated secondary antibodies as per suppliers instructions (Millipore) and as described previously (Sidhu and Tuch 2006).

Alkaline phosphatase staining: The pluripotent intracellular marker, alkaline phosphatase was assessed by using a commercially available fusion chromogen substrate kit (Sigma–Aldrich, St. Louis, MO; http://www.sigmaaldrich.com/) following the manufacturer's instructions.

Quantitative PCR: Total RNA was prepared from hESC colonies by using a GE spin column kit according to the manufacturer's instructions (GE healthcare, Sydney, Australia; http://www.gehealthcare.com). DNA contamination was removed by treating RNA samples with on-column RNase-free DNaseI. cDNA was prepared by using approximately 100 ng of RNA. Standard reverse transcription was performed using SuperScript III First-Strand Synthesis System and Oligo (dT) primers according to manufacturer's instructions. Quantitative PCR (Q-PCR) was carried out

using ABsoluteTM Blue Q-PCR SYBR Green Master Mix (Thermo Scientific, Waltham, MA). Each Q-PCR reaction consisted of 10 µl of SYBR Green PCR master Mix, 0.15 µl of 10 µM forward and reverse primers, 7.7 µl of nuclease-free water, and 2 µl of diluted template cDNA in a total volume of 20 µl. Q-PCR was performed using the Mx3000P1 (Stratagene, Cedar Creek, TX). Initial enzyme activation was performed at 95°C for 15 min, followed by 40 cycles of denaturation at 95°C for 15 s, and primer annealing/extension at 60°C for 1 min. Melting curve analysis was performed at 95°C for 1 min, 60°C for 30 s, and 95°C for 30 s. Relative gene expression was determined by applying a mathematical model (Pfaffl 2001) that is based on the Q-PCR efficiencies of individual primers and where quantified values were normalized against the input determined by the housekeeping gene, GAPDH. After normalization, each sample was plotted relative to genes expression measured for a standard cDNA super mix which is known to contain a substantial quantity of cDNA for all genes assessed. Primers used for gene expression analysis were GAPDH (forward—GTCAGTGGTGGACCTGAC CT; reverse—CCCTGTTGCTGTAGCCAAAT), NANOG (forward—AGAAGGCCTCAGCACCTAC; reverse—GGCCTGATTGTTCCAGGATT), OCT4 (forward—TGGG CTCGAGAAGGATGTG; reverse—GCATAGTCGCTG CTTGATCG), NESTIN (forward—GGCAGCGTTGGAAC AGAGGTTG; reverse—CTCTAAACTGGAGTGGTC AGGGCT), VIMENTIN (forward—GGCTCAGATTC AGGAACAGC; reverse—GCAGGCTCAGATTCAGG AAC), and SOX17 (forward—GGCGCAGCAGAATC CAGA; reverse—CCACGACTTGCCCAGCAT).

Karyotyping: A standard G-banding analysis was used for analysis of E-2 karyotype. For each sample, 20 metaphases were analyzed for modal determination.

Analysis of pluripotency in vitro: Pluripotent colonies growing within a six-well plate were differentiated by exposing colonies to FDMEM consisting of DMEM, FBS, L-glutamine, and Pen/Strep (Sidhu and Tuch 2006) for several d which induced spontaneous differentiation. The cells were then passaged into 12-well plates and differentiated for a further 2 wk in FDMEM. RNA was then extracted using the GE spin column kit. The expression of lineage markers in hESC cultures representing ectoderm, mesoderm, and endoderm were evaluated by quantitative PCR as described above.

Analysis of pluripotency in vivo: To assess in vivo pluripotency, approximately 1×10^6 E-2 cells were injected under the kidney capsule of NOD-SCID mice. The animals were euthanized 4–8 wk later and after hematoxylin and eosin (H&E) staining of paraffin sections as described previously (Sidhu and Tuch 2006), grafts were examined by a hospital pathologist for assessment of histological characteristics.

Results

We have demonstrated that the efficiency of deriving a new hESC line, E-2, from eight hatched blastocycsts (and five ICMs) in our hands is about 20%. E-2 has similar morphology to a typical hESC line with clear boundaries and as compact mass of cells that have a high nuclear–cytoplasmic ratio. E-2 maintained an undifferentiated morphology when proliferated on HFF. The hESC line displayed a normal 46 XX karyotype when tested (Fig. 1*A–D*).

E-2 hESC colonies propagated under the conditions described here showed robust expression of the pluripotency marker alkaline phosphatase and quantitative PCR analysis demonstrated a high expression of pluripotent markers, OCT4 and NANOG (Fig. 2*A–C*). Characteristic stem-cell-specific surface markers were present on a large proportion of E-2 cells tested as determined by FACS analysis SSEA4 (~96%), TRA-160 (~72%), and integrin alpha-6 (~99%) (Fig. 2*D–F*). E-2 has been passaged up to 10 times and has been cultured over a period of more than 6 mo without any apparent deterioration in pluripotency characteristics. The E-2 hESC line has been cryopreserved repeatedly and recovered after each thawing.

Differentiation potential of E-2. The potential of the E-2 hESC line to differentiate into representative cell types, characteristic of the three somatic germ lineages, was tested under both in vitro and in vivo conditions. Spontaneous differentiation of E-2 for >14 d in serum-containing medium (FDMEM) produced a disorganized expansive heterogeneous mixture of cell types within the culture dish. Quantitative PCR showed that representative genes from all three somatic germ layers; NESTIN (ectoderm), SOX17 (endoderm), and VIMENTIN (mesoderm), were expressed by cells within the heterogeneous mixture (Fig. 3*A–D*). Following the injection of E-2 hESCs under the kidney capsule of NOD SCID mice, large cellular outgrowths (both solid and cystic) were observed (Fig. 3*E*). Histological examination of grafts retrieved after at least 4 wk in vivo differentiation revealed the presence of tissues derived from the three somatic germ layers including neural ectoderm-like structures (ectoderm), primitive gut-like structure (endoderm), and cartilage-like structure (mesoderm; Fig. 3*F–H*). These results confirmed the potential of the E-2 cell line to form teratomas.

In summary, E-2 is a characterized hESC line, propagated under the defined conditions demonstrating a stable karyotype. With its ability to form cell types derived from the three somatic germ layers under both in vitro and in vivo conditions, E-2 is demonstrated to be pluripotent.

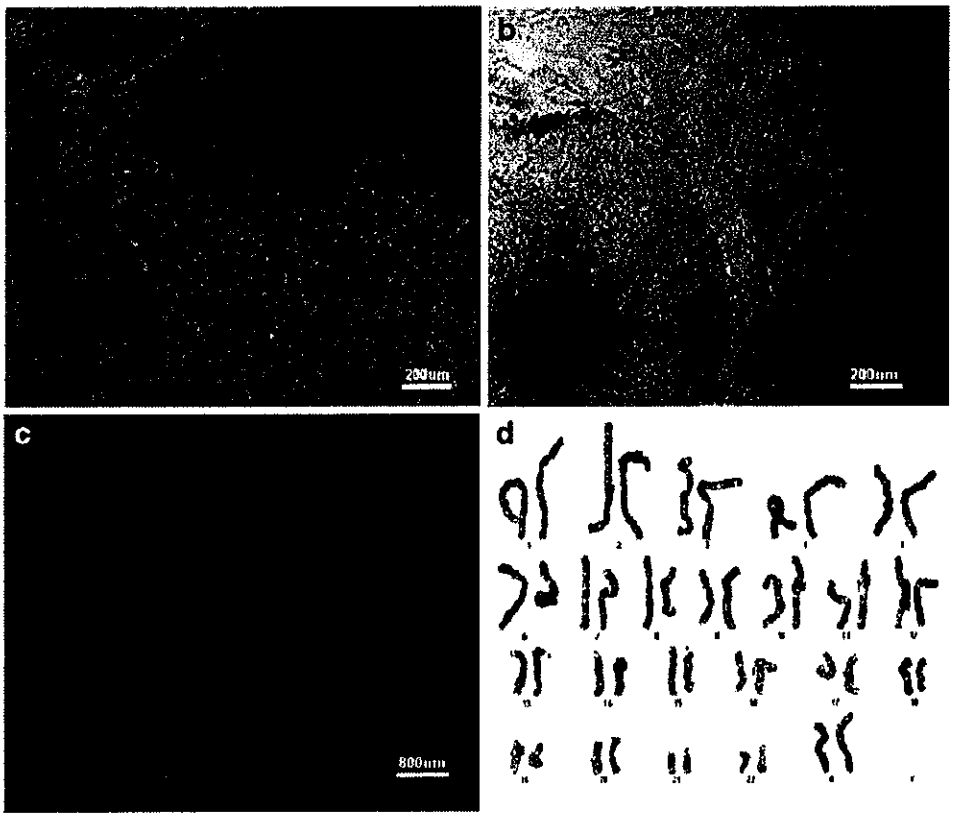

Figure 1. Derivation of E-2. *A*, emergence of new hESC colony from ICM (inner cell mass); *B*, E-2 p1; *C*, E-2 p10; *D* E-2 p9 normal karyotype 46XX.

Discussion

The majority of earlier hESC lines was derived and propagated using MFF as feeder layer and media containing FBS (Thomson et al. 1998; Reubinoff et al. 2000). These animal-derived products run the risk of contaminating these hESC lines with animal retroviruses and other nonhuman pathogens that may be transmitted to donors if used for transplantation purposes. It has been demonstrated that such culture procedures are liable to introduce nonhuman sialoproteins, which could be immunogenic in humans (Martin et al. 2005). Thus, eliminating nonhuman pathogens that might be found in animal sera and feeder layers during the derivation of new hESC lines, so that these lines might be used for potential therapeutic purposes, has been the hall mark of some recent investigations (reviewed by Mallon et al. 2006; Stacey et al. 2006). Here, in this study, we addressed some of these issues and defined conditions that are serum-free and largely xeno-free and derived a new hESC line, E-2. The ICM was removed from blastocysts by a laser dissection and grown on in-house produced HFF in serum-free medium. E-2 has been in culture for more than 6 months. It possesses all the characteristic features of a pluripotent hESC line that renews itself in culture as shown by gene expression, FACS analysis, and the production of teratomas after transplantation under the kidney capsule of NOD SCID mice indicating pluripotency.

Earlier attempts to replace mouse feeder fibroblasts with human feeder fibroblasts as feeder layer for hESC derivation (Hovatta et al. 2003; Richards et al. 2003; Miyamoto et al. 2004; Park et al. 2004; Stojkovic et al. 2005; Wang et al. 2005) used heterologous sera (FBS, KSR) and immunosurgery to remove ICM and, hence, were not xeno-free systems. Similarly, feeder-free culture systems employed for a similar purpose used complex extracellular matrices such as matrigel, fibronectin, or laminin mostly derived from animal sources and, hence, were not xeno-free (Xu et al. 2001; Brimble et al. 2004; Rosler et al. 2004; Beattie et al. 2005). In these feeder-free studies, either conditioned medium from mouse fibroblasts or growth factors (bFGF, TGFb, activin A, Nodal, Noggin, LIF, PDGF) were used, and some degree of differentiation were observed in hESC colonies in culture including chromosomal abnormalities (Draper et al. 2004; Inzunza et al. 2004, 2005; Klimanskaya et al. 2005).

Ludwig et al. (2006) not only used defined feeder-free conditions for derivation of two new hESC lines but also used immunosurgery for isolation of ICM from blastocysts using antibodies derived from animal sources and karyotypically; both these new hESC lines turned unstable under

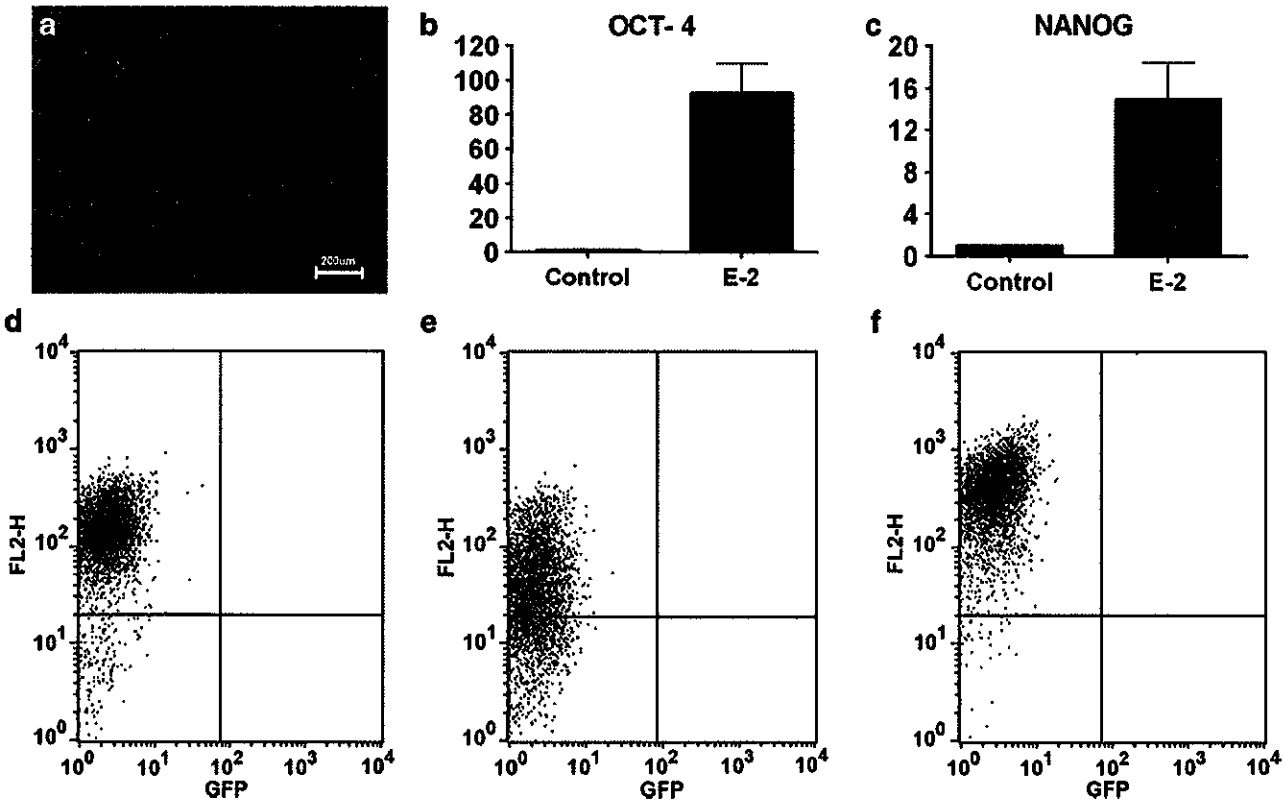

Figure 2. Characterization of E-2 pluripotency. *A*, Alkaline phosphatase-stained colonies of E-2; *B*, *C*, relative fold change in the expression of OCT4 and NANOG in E-2 cells compared to a cDNA supermix (control) containing significant quantities of both genes (n=2); FACS analysis of E-2 showing the gating of *D*, SSEA4 (~96%), *E*, TRA-160 (~72%), and *F*, integrin alpha-6 (~99%) positive E-2 cells.

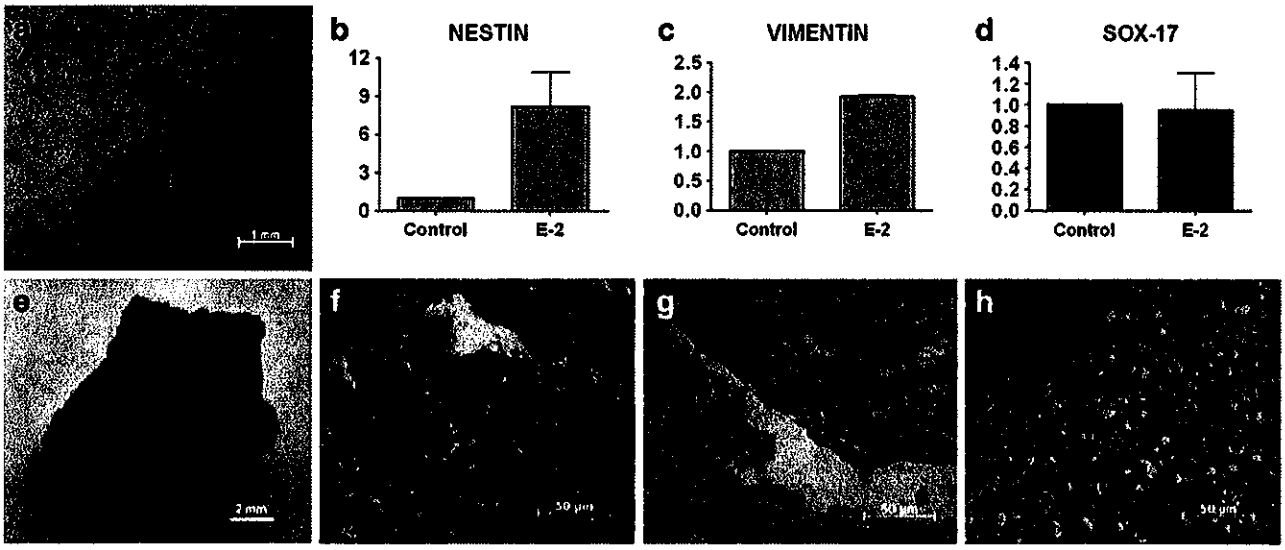

Figure 3. Characterization of E-2 differentiation potential. *A*, spontaneously differentiated E-2 cells in monolayer culture; *B–D*, relative fold change in the expression of NESTIN, VIMENTIN, and SOX17 by E-2 cells compared to a cDNA super mix (control) containing significant quantities of these genes (n=2); *E*, image of teratoma after transplantation into the kidney capsule of NOD SCID mouse and retrieved after 4.5 wk; *F–H*, H&E staining shows examples of neuronal clusters, primitive endoderm-derived epithelium and connective tissue.

propagation in feeder-free conditions. Thus, feeder-free systems may not be a suitable procedure to derive transplantable hESC lines until the molecular mechanism of self renewal is fully understood.

In summary, we have described the creation of a stable hESC line using serum replacement and largely xeno-free conditions. To meet future clinical requirements, hESC lines will also need to be derived under GMP conditions.

Acknowledgments This study was supported by the Sydney Foundation for Medical Research, Diabetes Australia Research Trust and the Australian Foundation for Diabetes Research. We thank Bo Yuan and Jaemin Kim for their help in tissue culture, Leonie Gaudry for assistance with FACS (SEALS, Prince of Wales Hospital), and Pauline Dalzell Pauline Dalzell, (Cytogenetics Laboratory, SEALS Prince of Wales Hospital) for assistance with karyotyping and Emeritus Professor Doug Saunders from IVF Australia for organizing egg donations.

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From: Kuldip Sidhu
To: Gadbois, Ellen (NIH/OD) [E]
Cc: Daniel Owens
Subject: FW: IVF Australia
Date: Sunday, March 21, 2010 7:47:48 PM
Attachments: Clinical ART Consent.pdf
Donation to Research Consent.pdf
Research Study Consent.pdf
Heads of Agreement.pdf

Dear Ellen,

Below is a copy of the email along with all the documents (attached) from our collaborating IVF Australia Clinic addressing all the issues raised in dot points 3rd-6th below in your email.

* Institutional Relationships

Re Dot point 1st. It is to certify that the Prince of Wales Hospital is one of the affiliated institutions of the University of New South Wales. A general summary of the institutions involved in the IVF clinical treatment and stem cell research as well as the nature of the relationships between these institutions is explained in the attached document (heads of agreement)

Dot point 2nd. This information is contained in the documents supplied earlier.

Hope all these documents help to make decision at your level.

Regards,

A/Prof Kuldip Sidhu
Director, Stem Cell Lab
Chair, Stem Cell Biology,
Faculty of Medicine,
402-408 Wallace Wurth Building
UNSW, NSW 2052
Australia

Tel: + 61 2 9385 3938 (Off)
+61 2 9385 2002(Lab)
Fax: + 61 2 9385 3938
http://psych.med.unsw.edu.au/psychweb.nsf/page/SCL

-----Original Message-----
From: John Ryan [mailto:jryan@ivf.com.au]
Sent: Friday, 19 March 2010 4:42 PM
To: Kuldip Sidhu
Subject: IVF Australia

Hi Kuldip,

Please find attached de-identified copies of the consents for the patients donating the embryo from which Endeavour 2 stem cell line was created.

1. Clinical ART Consent
2. Donation to Research Consent
3. Research Study Consent

Please note that the research study consent includes a statement which confirms the Patient

Information document was read by the donating couple.

The doctor responsible for managing the patient throughout their clinical treatment was not involved in the subsequent consenting process or the establishment of the hESC line.

I hope this is what you were after.

Cheer

John Ryan
Director, Embryology Lab
IVF Australia

Hi Ellen,

The information asked for in your email will be forthcoming soon as I am waiting for the same from IVF clinic.

Thanks,

A/Prof Kuldip Sidhu
Director, Stem Cell Lab
Chair, Stem Cell Biology,
Faculty of Medicine,
402-408 Wallace Wurth Building
UNSW, NSW 2052
Australia

Tel: + 61 2 9385 3938 (Off)
+61 2 9385 2002(Lab)
Fax: + 61 2 9385 3938
http://psych.med.unsw.edu.au/psychweb.nsf/page/SCL

From: Gadbois, Ellen (NIH/OD) [E] [mailto:gadboisel@od.nih.gov]
Sent: Saturday, 27 February 2010 3:50 AM
To: Daniel Owens; Kuldip Sidhu
Cc: HESCREGISTRY (NIH/NIDCD)
Subject: RE: New hESC Registry Application Request #2010-ADM-002

Thank you again for your submission to NIH. The NIH Administrative Review Team has conducted an initial review of your submission and has several questions. Could you please provide the following documentation:

- A general summary of the institutions involved in the IVF clinical treatment and stem cell research as well as the nature of the relationships is between those institutions. Please also clarify if the Prince of Wales Hospital is part of the University of New South Wales.
- A general explanation of the documentation provided to NIH.
- A copy of the clinical consent form for IVF treatment that was signed by the donors of the embryo from which the cell line was derived (please redact any information identifying the donors).
- A copy of the research consent form to donate the embryo from which the cell line was derived (please redact any information identifying the donors).
- Please confirm whether the donors of the embryo from which the cell line was derived received

EXTERNAL HEADS OF AGREEMENT

The Parties

1. The Australian Foundation for Diabetes Research Ltd (AFDR) is a tax exempt charitable entity that provides support to the goal of overcoming the need for insulin injections in people with diabetes.

2. IVF Australia Ltd s a private organization assisting infertile couples to have children.

3. South Eastern Sydney Area Health Service (SESAHS) administers public hospitals in Sydney's south east for the treatment of patients, teaching of students and carrying out medical research. The Diabetes Transplant Unit is a non-legal entity within the SESAHS.

The Plan

The aim of this Agreement is to facilitate the creation of human embryonic stem (hES) cell lines in Sydney from spare fertilized eggs available.

Contributions

1. AFDR:
   - [redacted]
     (a) to allow the employment of a senior scientist, such as Dr Kuldip Sidhu, to make hES cell lines.

     (b) to assist in the purchase of materials required to make and propagate hES cell lines

   - has provided the initiative to create a relationship among all parties to this Agreement

2. IVF Australia:
   - will obtain a licence from the National Health and Medical Research Council to allow the creation of hES cells and at all times comply with the requirements of that license
   - will advise the Diabetes Transplant Unit in writing of any legislative requirements or changes to the licence as they arise.
   - will provide spare frozen fertilized eggs, which the donors have agreed may be used to make hES cell lines
   - will allow one its senior scientists, Dr John Ryan, to spend up to 10% of his time to assist Dr Sidhu, or another senior scientist of similar expertise, in creating hES cell lines.

3. SESAHS
   - will allow the Diabetes Transplant Unit to use its laboratory space to allow the creation and propagation of hES cell lines

- will allow the personnel in the Diabetes Transplant Unit to provide their expertise in creating and propagating hES cell lines
- will allow the use of maintenance funds of the Diabetes Transplant Unit to be used to purchase materials required to make and propagate hES cell lines
- will at all times comply to the license requirements granted by the NHMRC and as communicated by IVF Australia. These may be subject to change as a result of the audit process IVFAustralia is required to undergo as part of the granting of the licence.

Outcomes

1. It is expected that a number of hES cell lines will be produced pursuant to this Agreement.
2. Members of the Parties, including the Diabetes Transplant Unit, may use these hES cell lines for research and or therapeutic purposes
3. The hES cell lines may be distributed to other researchers provided those researchers obtain approval for the use of the lines from Human Ethics Committees constituted as per the national guidelines of the country in which the researchers reside.
4. When the hES cell lines are provided to 3rd parties for research purposes, as per point 3 above), a charge will be levied to offset the cost of the production and propagation of the hES cell lines. .

[redacted]

6. [redacted]

Good faith agreement

1. This is a Heads of Agreement entered into in good faith by all parties.
2. If it appears likely that commercialization of hES cell lines created or products from these cell lines will occur, it will be necessary to create a more formal document among the parties. It is agreed that if this occurs, all parties will continue to act in good faith and follow the principles set out in this Heads of Agreement.

Signatures

.....

Professor Bernie Tuch
Director
Australian Foundation for Diabetes Research Limited

_____
Date

.....

Sue Channon
Chief Executive Officer
IVF Australia Ltd

_____
Date

.....

Barry Shepherd
Acting Chief Executive Officer
South Eastern Sydney Area Health Service

_____
Date

From: Kuldip Sidhu
To: HESCREGISTRY (NIH/NIDCD); Daniel Owens
Subject: RE: New hESC Registry Application Request #2010-ADM-002
Date: Saturday, April 03, 2010 7:04:13 AM
Attachments: Chapter 36.pdf

Dear Ellen Gadbois,

PI see below my response highlighted in blue re your queries # 1-3:

1) Please confirm that no payments were offered for the donated embryos.

   It is to certify that no payments were offered for donated embryos

2) Can you assure that the following element was satisfied and provide any relevant documentation: "Policies and/or procedures were in place at the health care facility where the embryos were donated that neither consenting nor refusing to donate embryos for research would affect the quality of care provided to potential donor(s)."

3) Can you assure that the following element was satisfied and provide any relevant documentation: "During the consent process, the donor(s) were informed of the following:...that the donation was made without any restriction or direction regarding the individual(s) who may receive medical benefit from the use of the hESCs, such as who may be the recipients of cell transplants."

   It is to clarify that issuance of licence by NHMRC for derivation of stem cells (E-2) from human embryos was contingent upon satisfying all the ethics requirements and that were met re # 2,3 as detailed under National Statement on Ethical Conduct in Human Research. Attached is a pdf file with excerpts (highlighted) and that may satisfy the points raised in # 2 & 3 above. Below is website re National Statement for reference:

   http://www.nhmrc.gov.au/_files_nhmrc/file/publications/synopses/e72-jul09.pdf

   Thanks,

A/Prof Kuldip Sidhu
Director, Stem Cell Lab
Chair, Stem Cell Biology,
Faculty of Medicine,
402-408 Wallace Wurth Building
UNSW, NSW 2052
Australia

Tel: + 61 2 9385 3938 (Off)
+61 2 9385 2002(Lab)
Fax: + 61 2 9385 3938
http://psych.med.unsw.edu.au/psychweb.nsf/page/SCL

From: HESCREGISTRY (NIH/NIDCD) [mailto:hescregistry@mail.nih.gov]
Sent: Saturday, 3 April 2010 1:09 AM
To: Daniel Owens; Kuldip Sidhu
Cc: HESCREGISTRY (NIH/NIDCD)
Subject: RE: New hESC Registry Application Request #2010-ADM-002

Chapter 36: human stem cells national statement on ethical conduct in human research |

Beneficence

3.6.5 Those conducting research involving stem cells derived from a human embryo or foetus should have no involvement in the clinical care of the woman from whom an ovum, embryo or foetus was obtained. Such research should be conducted in a location that maintains a separation of the woman's clinical care from research (see paragraph 4.1.11, page 53, and the ART guidelines, clause 15.5).

Respect

3.6.6 In addition to the information described in paragraph 2.2.2 (page 19), those who are considering donating embryos or tissue for the derivation of stem cells for research should also be given: (a) an explanation of the research for which the stem cells are to be used and, where extended or unspecified consent is sought, sufficient information to meet the requirements of paragraphs 2.2.1 (page 19) and 2.2.16 (page 21); (b) an explanation of the implication of removing identifiers (see paragraphs 3.6.3 and 3.6.4) from stem cells, including loss of a say in the use of the stem cells and, potentially, loss of their use for treatment for the participant or his or her blood relatives; (c) an assurance that they are free to decline to participate in research and entitled to withdraw from research at any time before identifiers are removed and a cell line is created; (d) an explanation that the research could result in the production of a stem cell line that could be maintained for many years, distributed to other parts of the world, and used for various research purposes; and (e) an explanation that the research participants will not benefit financially from any future commercialisation of cell lines, and that the donor will not have any authority over any cell lines created once their identifiers have been removed. Conscientious objection

Comment [k1]: Re # 3

3.6.7 Those who conscientiously object to being involved in conducting research with embryos, foetuses or embryonic or foetal tissue should not be obliged to participate, nor should they be put at a disadvantage because of their objection.

Conscientious objection

3.6.7 Those who conscientiously object to being involved in conducting research with embryos, foetuses or embryonic or foetal tissue should not be obliged to participate, nor should they be put at a disadvantage because of their objection.

Comment [k2]: Re # 2