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STEERING COMMITTEE FOR THE UK STEM CELL BANK AND FOR THE USE OF STEM CELL LINES

APPLICATION FORM TO IMPORT OR EXPORT HUMAN STEM CELL LINE(S) INTO OR OUT OF THE UNITED KINGDOM

Notes to Applicants

(Please read these notes before completing the application form)

- The absence of the required stem cell line(s) from the UK Stem Cell Bank catalogue should first be confirmed by checking the UK Stem Cell Bank catalogue at **http://www.ukstemcellbank.org.uk**
- It is important that this application is understandable by lay members and any abbreviations explained.

Submit your completed application form by email to the Secretary of the Stem Cell Steering Committee:

stemcellsecretary@headoffice.mrc.ac.uk

For general information contact:

The Secretary to the Steering Committee for the UK Stem Cell Bank and for the Use of Stem Cell Lines,
2nd Floor David Phillips Building
Polaris House
North Star Avenue
Swindon
Wiltshire SN2 1FL *Tel: +44 (0)20 7395 2247*

For scientific information contact:

Dr Megan Dowie: **megan.dowie@mrc.ukri.org**
or
UK Stem Cell Bank: **enquiries@ukstemcellbank.org.uk**

The following document **must** accompany **all** applications:

- A one page CV for the Principal Investigator (Applicant)

The following documents **must** accompany any applications for stem cell lines for clinical use:

- A copy of ethics committee approval (or equivalent)
- A copy of the information given to participants/patients in the clinical study/trial
- A copy of the consent form given to participants

If submitting electronically, PDF files of WORD documents are acceptable. Paper copies may be submitted to the Secretary, but must be accompanied by a completed copy of the application form.

Key to abbreviations

HESC:	Human Embryonic Stem Cell (line)	HFEA:	Human Fertilisation and Embryology Authority
MHRA:	Medicines and Healthcare products Regulatory Agency	HTA:	Human Tissue Authority
NIH:	National Institute of Health (USA)	UKSC:	UK Steering Committee

Notes to Sections

Note 1: List each cell line separately and use the cell line name designated by the originator.

Note 2: The type (embryonic, foetal, or adult), the Grade (either Research or Clinical) and the country where the cell line originated should be entered in the box provided of each stem cell line named.

Note 3: State whether each line is listed on either the US NIH (**http://stemcells.nih.gov/research/registry/**) or UKSC Register of Stem Cell Lines or neither.

Note 4: You must inform the UK Steering Committee if collaborators join the project subsequent to this application.

Note 5: The UK Steering Committee needs to satisfy itself that hESC lines are not used for trivial purposes and their uses are within the remit of HFEA regulations. The Stem Cell Steering Committee will not conduct a scientific review of experimental detail or repeat the peer review.

Note 6: The Steering Committee considers all applications on a case by case basis and appreciates that in the area of consent that there may be occasions when not all the criteria listed in Section 3 are fulfilled. The Steering Committee reserves the right to ask for original documentation if considered necessary.

Note 7: The document **The Code of Practice for the Use of Stem Cell Lines** can be found on both the UK Stem Cell Bank and the Medical Research Council websites

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APPLICATION FORM TO IMPORT/EXPORT A HUMAN STEM CELL LINE INTO OR OUT OF THE UNITED KINGDOM

SECTION 1 General Information

Complete all boxes

1.1 Name and title of Principal Applicant:

Masatsugu Ema

1.2 Title of Project (for which cell lines are requested):

Elucidation of cellular and molecular mechanism of early human development

1.3 Are you applying to: (Check only one box)

Export stem cell lines from the UK to a foreign country: ☐

Import stem cell lines from a foreign country into the UK: ☐

Import stem cell lines from the UK into a foreign country (overseas applicants)**:** ☑

1.5 Name and title of recipient *(if exporting stem cell lines from the UK)***:**

1.6 Name and title of provider *(if importing stem cell lines)***:**

Austin Smith, Professor, Director (Exeter University)

1.7 Name(s) of cell line(s) *(see Note 1)***:**	**Type of cell line(s)** *(see Note 2)***:**	**Grade** *(see Note 2)***:**	**Country of origin** *(see Note 2)***:**	**Register NIH / UKSC / none** (see Note 3)**:**
CAMe001-A (HNES1)	**embryonic**	**Research**	**UK**	**UKSC**

For HESC lines derived in the UK, please provide the HFEA licence number and HFEA centre number

Name of Cell Line:	**HFEA Licence Number** (under which cell line was derived)**:**	**HFEA Centre Number** (for the centre from which the embryo was obtained)**:**
CAMe001-A	R0178	0252

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SECTION 2A Applicant Details

2.1 Name and title of Principal Applicant: **Masatsugu Ema, Professor**	**Post held:** **2013**
Address: **520-2192, Seta, Tsukinowa-cho, Otsu, Shiga, Japan**	**Telephone: 81- 77-548-2334** **Fax: 81- 77-548-1990** **E-mail: mema@belle.shiga-med.ac.jp**

***(Complete only if different from 2.1 above)*:** **2.2 Name and title of contact person**	**Post held:**
Address:	**Telephone:** **Fax:** **E-mail:**

SECTION 2B Recipient Details

(Complete only if different from 2.1 above) **2.3 Name and title of recipient:**	**Post held:**
Address:	**Telephone:** **Fax:** **E-mail:**

SECTION 2C Provider Details

(Complete only if different from 2.1 above) **2.4 Name and title of provider of the cell lines:** **Austin Smith, professor**	**Post held:**
Address: **Living Systems Institute, University of Exeter Stocker Road, Exeter EX4 4QD, United Kingdom**	**Telephone: +44 (0) 1392 72 3042** **Fax:** **E-mail: austin.smith@exeter.ac.uk**

SECTION 2D Collaborators

Provide names and institutions of all those collaborators who will have access to the stem cell line(s) listed above as part of this application (see Note 4)

2.5 Name(s) and title(s) of collaborator(s)	**Institution(s)**
Masatsugu Ema, professor	Shiga University of Medical Science
Shoma Matsumoto, Assistant professor	Shiga University of Medical Science
Masanaga Muto, Assistant professor	Shiga University of Medical Science
Eiichi Okamura, Assistant professor	Shiga University of Medical Science

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SECTION 3A

Details of Research Project
(for which stem cell lines are being requested)

3.1 Title of Research Project:

Elucidation of cellular and molecular mechanism of early human development

3.2 Abstract of Research Project including aims and objectives. *(See note 5)*
(Approx 300 words):

Our aim is to elucidate the cellular and genetic mechanism of early human development. Although my laboratory has been studying about the early development of Cynomolgus monkey, a nonhuman primate, as an animal model to understand early human development and found that there are some primate-specific mechanisms underlying early cell lineage specification, there is still evolutionary distance between monkey and human. To understand the early human development, we are planning to generate human blastoid from HNES1, a human naïve ES cell line according to the previous reports (Yanagida et al., 2021, doi: 10.1016/j.stem.2021.04.031; Kagawa et al., 2021 doi: 10.1038/s41586-018-0051-0**) and to analyze the gene expression and epigenetic state at single cell level and observe cellular dynamics under microscope. Stem cells representing epiblast, trophectoderm and primitive endoderm are re-derived from the human blastoid. Since the generation efficiency of the blastoid is not optimal, we are improving the ES cells by modulating gene functions with genome editing, small chemicals and antibodies.**

After the blastoid are sufficiently characterized, the ES cells are subjected to co-culture with endometrial organoids to evaluate the capability of interaction with endometrial cells and initial process of placentation. Endogenous gene functions are modulated by genome editing technique, neutralizing antibody and small chemicals, and then the ES cells with modified gene function are tested for the capability to blastoid formation and the embryo-endometrial interaction.

During the above culture, we follow the 14 day rule. We observe the blastoid every days by microscopic observation and stop culturing before the sign of gastrulation. We do not transplant them into uterus of animal.

3.3 Have you previously received approval from the UK Steering Committee to use stem cells for a research project?

Yes ☐ **No** ☑

If **Yes** give UK Stem Cell Steering Committee (SCSC) number

3.4 Has the research project been subjected to peer review?

Yes ☐ **No** ☑

If **Yes** provide details (Funding body etc)

If **No** please explain why this is the case **(**e.g. generation of preliminary data), state how the research will be supported

I have submitted the application forms, but not obtained the approval yet. I also have submitted several funding. In the meanwhile, in-house funding in our University supports this study.

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SECTION 3A (continued)

3.5 Does the research project include experiments in animals, excluding teratoma assays in small mammals?

Yes ☐ No ☑

If **Yes** provide details:

3.6 Do you intend to perform experiments creating hES cell/animal embryo aggregation chimaeras?

Yes ☐ No ☑

If **Yes** provide details:

3.7 Are all experiments involving animals covered by appropriate Home Office Animal Procedures Licences (or their equivalent if the cell line is to be used outside of the UK)?

Yes ☐ No ☑

3.8 Do you intend to use the stem cell lines in clinical trials / therapy

Yes ☐ No ☑

SECTION 3B (to be completed only if Clinical Grade stem cell lines have been requested)

3.8 Has the stem cell line(s) been derived in facilities accredited / licensed by an equivalent of the UK MHRA or HTA

Yes ☐ No ☐

3.9 Do you have access to facilities accredited by the MHRA, or the HTA (or their equivalent where the application is from overseas)

Yes ☐ No ☐

If Yes provide details (e.g. regulations/directives under which the facilities are accredited)

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SECTION 4 Consent

YOU NEED ONLY COMPLETE THIS SECTION IF THE STEM CELLS IN THIS APPLICATION:

- **are somatic stem cell lines derived from foetal or adult tissue, OR are of embryonic origin and were derived outside the UK;**

AND

- **are not listed on either the Register of Steering Committee Approved Stem Cell Lines or the NIH Registry.**

Complete ALL boxes in this section *(see note 6)*.

4.1 Was the study for deriving the cell lines(s) named in this application approved by an ethics committee *(or equivalent if application is from outside the UK)***:**

Yes ☐ **No** ☐

The following criteria constitute best practice in the UK for informed consent.

4.2 Have you confirmed with the originator that at the time of consenting, the donor(s) was informed:

i about the specific research project, including any tests that may be performed as part of the licensed research project on embryos or cells derived from the embryos

Yes ☐ **No** ☐

ii that any stem cell lines created may continue indefinitely and may be used in many different research projects

Yes ☐ **No** ☐

iii that the decision whether to donate would not affect their treatment in any way

Yes ☐ **No** ☐

iv about whether the embryos/cells would be reversibly or irreversibly anonymised and the implications of this

Yes ☐ **No** ☐

v whether any information will be fed back to the donor(s)

Yes ☐ **No** ☐

vi that the donors may vary or withdraw their consent until the point the embryos/cells are used in the project

Yes ☐ **No** ☐

vii that once the embryo/cells has been used in the project, the donor(s) have no control over any use of the cells or any stem cell lines derived

Yes ☐ **No** ☐

viii that stem cell lines derived in this project will be deposited in the UK Stem Cell Bank and the implications of this including long term storage and use in other research projects and potential therapeutic applications

Yes ☐ **No** ☐

ix that stem cell lines may not be generated where the consent places a constraint on future use

Yes ☐ **No** ☐

x that cell lines may be used for commercial purposes, but that donor(s) will not benefit financially from this

Yes ☐ **No** ☐

xi that cell lines derived or discoveries made from them may be patented but donor(s) will not financially benefit

Yes ☐ **No** ☐

xii regarding how the research was funded, including any benefit which may accrue to researchers and/or their

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departments/companies

Yes ☐ **No** ☐

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SECTION 5 Declaration

By submitting this application to the secretary to the Stem Cell Steering Committee, I confirm that:

i. **The information in this form is accurate to the best of my knowledge and belief and I take full responsibility for it.**

ii. **I have read and understood the Code of Practice for the Use of Human Stem Cell Lines and agree to abide by this Code** (see Note 7).

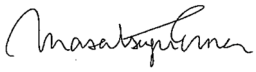
iii. **The cell line(s) will only be used for the purposes set out in this application.**

iv. **The cell lines will only be used for:**

   a. **Research that is consistent with UK legislation (as specified in the Code of Practice for the Use of Stem Cell Lines and the recipient hereby agrees to abide by this Code.**
   b. **Research which has the long term goal of helping to increase knowledge about serious diseases and their treatment.**
   c. **Basic cell research which underpins these aims.**
   d. **Development of cell based therapies for clinical trials in respect of serious human diseases.**

v. **The cell lines will only be used for research that does not contravene UK legislation such as that pertaining to reproductive cloning.**

vi. **The cells will only be used for research that is consistent with and does not contravene legislation in the country in which the recipient is working.**

Signed on behalf on Host Institution *(Person responsible e.g. Head of Department/Dean)* Date:	**Signed by Principal Applicant** *(on behalf of all principal collaborators)*  Date: February 20, 2022
	Signed by Recipient *(if the stem cell line(s)s are being exported from the UK to a foreign country)*  Date: February 20, 2022

Name and title of Signatory for Host Institution: Shinji Uemoto, President	
Post Held	**Institution** **Shiga University of Medical Science**
Postal Address: **520-2192, Seta, Tsukinowa-cho, Otsu, Shiga, Japan**	**Telephone: 81-77-548-2082** **Fax: 81-77-548-2086** **E-mail: hqsangaku@belle.shiga-med.ac.jp**

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Date application received:		
1. Principal Investigator's CV received:	**Yes** ☐ **No** ☐	
2. Recipients CV received	**Yes** ☐ **No** ☐	
3. Copy of ethics committee approval received: (clinical grade cells only)	**Yes** ☐ **No** ☐	**Not Applicable** ☐ *(if cells are Research Grade)*
4. Patient/participant information sheet received: (clinical grade cells only)	**Yes** ☐ **No** ☐	**Not Applicable** ☐ *(if cells are Research Grade)*
5. Copy of consent form received: (clinical grade cells only)	**Yes** ☐ **No** ☐ *(if No complete 5 below)*	**Not Applicable** ☐ *(if cells are Research Grade)*
6. Record details of method used to ascertain that appropriate consent would be obtained from the patients/participants.		
Print Name:	**Signature:**	
Date application considered by SC:		
Date application approved:		