

Responsible Office: Center for Clinical and Translational Science

## **HUMAN EMBRYO AND HUMAN PLURIPOTENT STEM CELL RESEARCH**

### **Rationale/Purpose of the Policy**

To ensure adherence to the basic ethical and legal principles of informed consent and protection of confidentiality, human embryonic stem cells (hESCs) may be used by UMass Chan investigators only after documentation of their provenance has been provided to and approved by the UMass Chan Stem Cell Research Oversight Committee. Documentation of provenance only needs to be provided prior to the first use of the human embryonic stem cells in research falling within the Stem Cell Research Oversight Committee's purview. Upon approval by the committee, the human embryonic stem cells will be listed on the UMass Chan hESC Registry.

### **Definitions**

#### **Chimera**

An organism composed of cells with different species origins. This includes any (non-human) animal into which human cells have been introduced. Human pluripotent stem cells (hPSCs) include human pluripotent stem cells from embryonic and non-embryonic sources.

#### **Human embryonic stem cells (hESCs)**

Cells derived from very early in development, usually the inner cell mass of a developing blastocyst. These cells are self-renewing (can replace themselves) and pluripotent (can form all cell types found in the body.)

#### **Human pluripotent stem cells (hPSCs)**

Stem cells that can become all of the cell types that are found in implanted embryo, fetus, or developed organisms. Embryonic stem cells are pluripotent stem cells.

#### **Induced pluripotent stem cells**

Stem cells that were engineered ("induced") from non-pluripotent cells to become pluripotent. In other words, a cell with a specialized function (for example, a skin cell) that has been "reprogrammed" to an unspecialized state similar to that of embryonic stem cells.

#### **Repository**

A facility designed to collect, store, and broadly distribute cells, and data or information about those cells, on an ongoing basis. It might also store and distribute DNA or other biomaterials.

### **Scope**

Applies to researchers using human embryos, human embryonic stem cells, or transplantation of human pluripotent stem cells into animals with possible central nervous system integration or germline transmission.

### **Policy**

#### **Section 1: Stem Cell Research Oversight Committee Purview**

The Stem Cell Research Oversight Committee will provide oversight for all research on campus or involving campus faculty or staff that involves any of the following:

1. The use of human embryonic stem cells or their derivatives.
2. The introduction of human pluripotent stem cells or their derivatives into nonhuman animals at any embryonic, fetal, or postnatal stage, if an expected effect is that human cells will be integrated into the central nervous system, testes, or ovaries of the animal.
3. Either:
  - I. Preimplantation stages of human development, human embryos, or embryo-derived cells; or
  - II. The production of human gametes in vitro when such gametes are tested by fertilization or used for the creation of embryos.
4. The storage or disposition of human embryos or gametes obtained for the purposes of stem cell research.
5. The storage and distribution of human embryonic stem cells through a repository (as outlined in section 5).

The Stem Cell Research Oversight Committee must review all human stem cell research regardless of the source of funding.

## Section 2: Human Embryonic Stem Cell Registries

1. [National Institutes of Health \(NIH\) hESC Registry](#)

Human embryonic stem cell lines listed on the [NIH Human Embryonic Stem Cell \(hESC\) Registry](#) are eligible for use on the UMass Chan campus with approval from the Stem Cell Research Oversight Committee. These lines do not need additional provenance review and are eligible for use with federal funding.

2. UMass Chan hESC Registry

In addition, the Stem Cell Research Oversight Committee established and maintains the UMass Chan hESC Registry. This registry includes human embryonic stem cells with provenance already approved by the committee. Lines on this registry **cannot** be used with federal funding.

Human embryonic stem cell lines not currently listed on this registry must go through review of the documentation of provenance. Once the review is completed and approval is granted, the human embryonic stem cell line will be listed on the UMass Chan hESC Registry and will be eligible for use by UMass Chan investigators.

## Section 3: Provenance Approval Process

To ensure adherence to the basic ethical and legal principles of informed consent and protection of confidentiality, human embryonic stem cells may be used by UMass Chan investigators only after documentation of their provenance has been provided to and approved by the Stem Cell Research Oversight Committee. Documentation of provenance only needs to be provided prior to the first use of the stem cells in research falling within the

committee's purview. Upon approval by the committee, the human embryonic stem cells will be listed on the UMass Chan hESC Registry

*Documentation of Provenance:* The Stem Cell Research Oversight Committee reviews documentation of the provenance of human embryonic stem cell lines before such lines may be added to the UMass Chan hESC Registry and used by university investigators. In determining which human embryonic stem cell lines may be used by university researchers, the committee will consider whether the proper consent and additional criteria have been met, but may approve human embryonic stem cell lines for inclusion on the UMass Chan's hESC Registry where procurement processes differ slightly from that specified. For a list of the criteria, please see Appendix A: Guidance for Documentation of Provenance. Consent documentation requirements are as follows:

1. *Embryos Created for Reproductive Purposes:* For human embryonic stem cell lines derived from embryos originally created for reproductive purposes, but which are now in excess of clinical need, the Stem Cell Research Oversight Committee must receive documentation that the embryo procurement process was approved by an Institutional Review Board (IRB) or appropriate institutional ethics committee and must receive a copy of the IRB-approved consent form(s) used during the embryo procurement process. If sperm or oocyte donors were used in this process, documentation of their consent to donate these excess embryos for research is not required.
2. *Embryos Created for Research Purposes:* For human embryonic stem cell lines derived from embryos created for research purposes through conventional (standard or intracytoplasmic sperm injection [ICSI] insemination) in vitro fertilization (IVF), the Stem Cell Research Oversight Committee must receive documentation that the sperm and oocyte procurement processes were approved by an IRB or appropriate institutional ethics committee and must receive a copy of the approved consent form(s) used during the sperm and oocyte procurement processes.
3. *Embryos Created by Somatic Cell Nuclear Transfer (SCNT):* For human embryonic stem cell lines derived from embryos created for research purposes through SCNT, the Stem Cell Research Oversight Committee must receive documentation that the oocyte and somatic cell procurement processes were approved by an IRB or appropriate institutional ethics committee and (1) the UMass Chan Registry should not be confused with the NIH Human Embryonic Stem Cell Registry; and (2) this conforms to NIH Guidelines. The Stem Cell Research Oversight Committee must receive a copy of the IRB-approved consent form(s) used during the oocyte and somatic cell procurement processes.

## **Section 4: Oversight for Introduction of hPSCs into Non-Human Animals (Chimeras)**

### **Definitions**

A chimera is an organism composed of cells with different species origins. This includes any (non-human) animal into which human cells have been introduced. Human pluripotent stem cells include human pluripotent stem cells from embryonic and non-embryonic sources.

### **UMass Chan Chimera Review**

This Human Embryo and Human Pluripotent Stem Cell Research policy requires the Stem Cell Research Oversight Committee to review research involving the creation of chimeras when the chimeras are created in either of two ways:

1. By introducing human embryonic stem cells, or cells derived from human embryonic stem cells, into an animal; or
2. By introducing human pluripotent stem cells obtained from non-embryonic sources, or cells derived from such human pluripotent stem cells, into an animal, when one expected effect of the introduction is that human cells will be integrated into the central nervous system, testes, or ovaries of the animal.

Particular attention should be paid to at least three factors: the extent to which the implanted cells colonize and integrate into the animal tissue; the degree of differentiation of the implanted cells; and the possible effects of the implanted cells on the function of the animal tissue.

Standard teratoma formation assays used to test whether cells are pluripotent must be reviewed by the Institutional Animal Care and Use Committee (IACUC).

### **Human Pluripotent Stem Cell Line Limitations**

The committee will not approve the introduction of any cell lines with consent limitations, or cells derived from them, into animals during their embryonic stages of development.

### **Carnegie Stages of Development and Human Pluripotent Stem Cell Limitations**

The Stem Cell Research Oversight Committee uses the definition of the embryonic stage to extend through Carnegie Stage 23. In mice, this extends through E16, in rats through E17.5, in chicks through E10, and in pigs through E32.5. (See [Carnegie Stages](#) for information about other species.)

For researchers requesting to introduce pluripotent stem cells during the embryonic stages of development, researchers must provide a rationale for introducing cells at the embryonic stage. In evaluating the application, the committee will consider the following:

- The possibility the human material could affect the cognitive abilities of the animal research subject in ways that would be morally relevant.
- The possibility that human gametes could form within animal research subjects, the breeding of which could then produce a human conceptus.

### **Prohibitions**

1. The breeding of animals into which human pluripotent stem cells have been introduced.
2. The introduction of human pluripotent stem cells, or cells derived from such human pluripotent stem cells, into non-human primate preimplantation embryos.
3. The introduction of pluripotent stem cells from any species into human preimplantation embryos.

## **Section 5: Embryo Research Oversight**

1. Research requiring comprehensive review by a stem cell research oversight process includes the following activities:
  - a. Use of IVF embryos for research.
  - b. Research that generates human gametes when such research entails performing studies of fertilization that produce human embryos.

- c. Research involving the genetic manipulation of human embryos or gametes used to make embryos in vitro.
  - d. Derivation of new pluripotent cell lines from human embryos.
    - i. The scientific rationale for the need to generate new human embryonic stem cell lines, by whatever means, must be clearly presented, and the basis for the numbers of preimplantation embryos and oocytes needed should be justified. Evidence of IRB or appropriate institutional ethics committee approval of the procurement process and a copy of the consent form used during the embryo procurement process should accompany such requests.
    - ii. Human embryos in existence at UMass Chan as of the date of the approval of this policy may be used for the derivation of new stem cell lines so long as the consent process for such use utilized a consent form approved by the IRB. Any request for the generation of new human embryonic stem cell lines from these embryos and the protocol for research using the derived lines are still subject to Stem Cell Research Oversight Committee review.
    - iii. The procurement processes for gametes or embryos used in the derivation of human embryonic stem cell lines in existence prior to the date of the approval of the original policy (July 1, 2022) are not required to fully comply with this policy. However, the provenance of pre-existing human embryonic stem cell lines must still be documented in accordance with Sections 2 and 3.
  - e. Research aimed at generating human totipotent cells that have the potential to sustain embryonic or later development.
  - f. Research involving the in vitro culture of embryos or experimental generation of embryo-like structures that might manifest human organismal potential, to ensure minimal periods of in vitro culture, as justified by compelling scientific rationale but not beyond 14 days or formation of the primitive streak, whichever occurs first.
  - g. Research in which human totipotent cells or pluripotent stem cells derived by any means are mixed with human embryos.
2. Research that is prohibited:
- a. In vitro culture of any intact human preimplantation embryo or organized embryo-like cellular structure with human organismal potential, regardless of derivation method, beyond 14 days or formation of the primitive streak, whichever occurs first.
  - b. Experiments whereby human embryos or organized cellular structures that might manifest human organismal potential are gestated in any non-human animal uterus.
  - c. Research in which human embryos produced by reprogramming of nuclei from somatic cells by nuclear transfer or comparable techniques are gestated in a human or animal uterus. Given current scientific, medical safety, and ethical concerns, attempts at human reproductive cloning are prohibited.
  - d. Research in which human embryos that have undergone modification of their nuclear genome are gestated in a human or animal uterus. Genome-modified human embryos include human embryos with engineered alterations to their nuclear DNA and/or embryos generated from a human gamete that has had its nuclear DNA modified, when such modifications will be inherited through the

- germline. Given current scientific, medical safety, and ethical concerns, attempts at germline editing are prohibited.
- e. Research in which animal chimeras incorporating human cells with the potential to form human gametes are bred to each other.

## **Section 6: Human Embryonic Stem Cell Storage and Distribution**

1. Definitions: For purposes of this policy, a repository is a facility designed to collect, store, and broadly distribute cells, and data or information about those cells, on an ongoing basis. It might also store and distribute DNA or other biomaterials.
2. When members of a laboratory store cells for their own use, or share cells derived or engineered in that laboratory with other researchers in compliance with funder policies (e.g., NIH Grants Policy Statement, Section 8.2.3) the laboratory does not become a repository for purposes of this policy. However, if a laboratory under the Stem Cell Research Oversight Committee's jurisdiction derives or obtains cells and stores them with the intent to broadly distribute them on an ongoing basis, it becomes a repository.
3. Any repository under the jurisdiction of the Stem Cell Research Oversight Committee that obtains, stores, and distributes human embryonic stem cell lines must have and follow policies and procedures to ensure that the human embryonic stem cell lines were derived ethically and in accordance with relevant laws and policies. It must have evidence-based, standardized methods and protocols in place to conduct biosafety screening; to characterize, maintain, store, and distribute cells; and to assess cell quality. It must document its activities. In particular, the repository's policies must include:
  - i. A secure system for protecting the privacy and confidentiality of donors and their medical information when materials retain codes or are accompanied by other identifiable information.
  - ii. A policy governing whether and how to return clinically significant information back to donors.
  - iii. A policy and system for disposal of cellular material, and documentation of that policy.
4. Any investigator under the jurisdiction of the Stem Cell Research Oversight Committee who derives new human embryonic stem cell lines is encouraged to deposit the lines in a repository from which they could be distributed. The deposit should occur no later than the end date of the investigator's Stem Cell Research Oversight protocol.
5. The Stem Cell Research Oversight Committee has authority to review policies and protocols for any repository under its jurisdiction.
6. The university or any repository under the jurisdiction of the Stem Cell Research Oversight Committee may refuse to accept human embryonic stem cell lines if they do not comply with this policy.

## **Section 7: Obtaining Committee Protocol Approval and Conducting Committee-Approved Research**

1. Research falling within the scope of Stem Cell Research Oversight Committee review can only be initiated after an online application has been submitted and the principal investigator has received notification of either Administrative (if appropriate) or committee approval. Applications are initiated online at (we'll need a website with the

appropriate forms). The committee will divide research proposals into three categories to determine the requisite level of oversight:

- a. Research that is permissible after expedited review. Expedited review will be conducted by one committee staff person and one committee member. Researcher provides the following to the Stem Cell Research Oversight Committee: 1) notice of the research, 2) documentation of the provenance of the cell lines, and 3) evidence of compliance with any required IRB, IACUC, IBC, or other mandated reviews.
    - i. Teratoma experiments to test pluripotency of human pluripotent stem cells
    - ii. Purely in vitro human embryonic stem cell research with NIH approved cell lines or cell lines previously approved by the Stem Cell Research Oversight Committee
  - b. Research that is permissible only after additional review and approval by the Stem Cell Research Oversight Committee:
    - i. The introduction of human pluripotent stem cells or their derivatives into non-human animals at any embryonic, fetal, or postnatal stage, if an expected effect is that human cells will be integrated into the central nervous system, testes, or ovaries of the animal. Particular attention will be paid to the probable pattern and effects of differentiation and integration of the human cells into the non-human animal tissues.
    - ii. Research in which personally identifiable information about the donors of the preimplantation embryos, gametes, or somatic cells from which the human embryonic stem cells were derived is readily ascertainable by the investigator requires IRB and Stem Cell Research Oversight Committee review and approval.
    - iii. Research that involves preimplantation stages of human development, human embryos, or embryo-derived cells or that entails the production of human gametes in vitro when such gametes are tested by fertilization or used for the creation of embryos.
  - c. Research that is not allowed (see Section 4)
2. All applicable laws, policies, and guidelines pertaining to biosafety and animal care will apply to human embryonic stem cell research, and all applications will require UMass Chan biosafety and animal care approvals where appropriate.
  3. If a university investigator collaborates with an investigator at another institution—domestic or foreign—the Stem Cell Research Oversight Committee may determine that the procedures prescribed by the other institution afford protections consistent with these guidelines and may approve the substitution of some or all of the other institution's procedures for its own.
  4. The Stem Cell Research Oversight Committee will maintain a list of UMass Chan investigators conducting human embryonic stem cell research along with a brief abstract about the type of research being performed and the human embryonic stem cell line(s) used in the research.
  5. Human embryonic stem cell research directly for clinical application will be in compliance with all applicable Food and Drug Administration (FDA) regulations. If the FDA requires that a link to the donor source be maintained, investigators and the university will document that the confidentiality of the donor is protected, that the donor is notified that a link will be maintained, and that, where applicable, federal

human subjects protections and HIPAA (Health Insurance Portability and Accountability Act of 1996) or other privacy protections are followed.

## **Section 8: Committee Structure and Composition**

1. The university establishes a Stem Cell Research Oversight Committee.
2. The committee will include at least one representative of the public and may include persons with expertise in developmental biology, embryo development, stem cell research, molecular biology, and ethical and legal issues in human pluripotent stem cell research.
3. The committee will not substitute for the appropriate IRB but will provide an additional level of review and scrutiny warranted by the complex issues raised by human pluripotent stem cell research.

## **Section 9: Principal Investigator (PI) Status**

To qualify as PI on a human embryonic stem cell research protocol reviewed by the UMass Chan Stem Cell Research Oversight (SCRO) committee, individuals must:

1. have a UMass Chan faculty appointment and be working within the scope of that appointment in performing the research, or
2. be granted an exception in writing from the UMass Chan Chief Research Officer.

## **Section 10: Amendments to Policy**

1. This policy may be amended by action of the Stem Cell Research Oversight Committee subject to the written approval of the amendment by the vice provost of clinical and translational research.
  2. First approved by vice provost of clinical and translational research on July 1, 2022.
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## Appendix A: UMass Chan Stem Cell Research Oversight Guidance for Documentation of Provenance

Researchers wishing to add lines to the UMass Chan Human Embryonic Stem Cell (hESC) Registry need to submit documentation to the SCRO Committee addressing each of the items listed below. This guidance is in addition to the consent requirements listed in UMass Chan Policy for Human Embryo and Human Pluripotent Stem Cell Research.

1. Whenever it is practicable, the attending physician responsible for the infertility treatment and the investigator deriving or proposing to use hESCs will not be the same person.
2. No cash or in-kind payments may be provided for donating preimplantation embryos in excess of clinical need for research purposes.
3. Women who undergo hormonal induction to generate oocytes specifically for research purposes (such as for nuclear transfer) may be reimbursed for direct expenses incurred as a result of the procedure, as determined by an Institutional Review Board or appropriate institutional ethics committee. Oocytes and sperm donors may be compensated at a level consistent with compensation provided for *in vitro* fertilization donors at the locale where the donation occurs. In locales where reimbursement for research participation is allowed, there must be a detailed and rigorous review to ensure that reimbursement of direct expenses or financial considerations of any kind do not constitute an undue inducement. The study protocol should also consider the long-term effects of repeated ovulation induction.<sup>1</sup>
4. Potential donors of preimplantation embryos should be informed of all available options for the disposition of their embryos, including donation to others for reproductive purposes as well as destruction. Donors who may have specified their intent to donate embryos to research prior to completion of their clinical care must provide specific informed consent for donation to stem cell research after their clinical care has been completed.
5. The consent form must address the right to withdraw. Ideally, this language should specify the right to withdraw consent until the embryos are actually used to derive embryonic stem cells or until information which could link the identity of the embryo donor(s) with the embryo is no longer retained, if applicable. Embryo donors should be told, however, that once the embryos have been transferred to a researcher, they will no longer be usable for clinical purposes.
6. In the context of donation of gametes or preimplantation embryos for hESC research, the informed consent process should ideally provide the following information, although some variation is possible:
  - a. A statement that the preimplantation embryo or gametes will be used to derive hESCs for research that may include research on human transplantation.
  - b. A statement that the donation is made without any restriction or direction regarding who may be the recipient of transplants of the cells derived, except in the case of autologous donation.

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<sup>1</sup> Based on International Society for Stem Cell Research, Guidelines for the Conduct of Human Embryonic Stem Cell Research Recommendations 11.5b(ii) and (v).

- c. A statement as to whether the identities of the donors will be readily ascertainable to those who derive or work with the resulting hESC lines.
- d. If the identities of the donors are retained (even if coded), a statement as to whether donors whose identities are retained wish to be contacted in the future to receive information obtained through studies of the cell lines.
- e. An assurance that participants in research projects will follow applicable and appropriate best practices for donation, procurement, culture, and storage of cells and tissues to ensure, in particular, the traceability of stem cells. Traceable information, however, must be secured to ensure confidentiality.
- f. A statement that derived hESCs and/or cell lines might be kept for many years.
- g. A statement that the hESCs and/or cell lines might be used in research involving genetic manipulation of the cells or the mixing of human and non-human cells in animal models subject to approval of the appropriate institutional committee.<sup>2</sup>
- h. Disclosure of the possibility that the results of study of the hESCs may have commercial potential and a statement that the donor will not receive financial or any other benefits from any future commercial development.
- i. A statement that the research is not intended to provide direct medical benefit to the donor(s) except in the case of autologous donation.
- j. A statement that embryos may be destroyed in the process of deriving hESCs.
- k. A statement that neither consenting nor refusing to donate embryos for research will affect the quality of any future care provided to potential donors.
- l. A statement of the risks to the donor.
- m. An assurance that researchers have not asked members of the infertility treatment team to generate more oocytes than necessary for the optimal chance of reproductive success.
- n. An assurance that an infertility clinic or other third party responsible for obtaining consent or collecting materials will not pay for or be paid for the material obtained (except for specifically defined cost-based reimbursements and payments for professional services.)

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<sup>2</sup> This conforms to the 2009 NIH Guidelines provision II.A.2.