UNIVERSITY OF MICHIGAN
POLICY ON RESEARCH WITH
HUMAN PLURIPOTENT STEM CELLS
INCLUDING
HUMAN EMBRYONIC STEM CELLS AND
INDUCED PLURIPOTENT STEM CELLS

This University of Michigan policy for research involving both the derivation and use of human pluripotent stem cells is based on the principles of the "NIH Guidelines for Research Using Human Pluripotent Stem Cells" (2000, 2009), Office for Human Research Protections (OHRP) guidelines, and the recommendations of the Committee on Guidelines for Human Embryonic Stem Cell Research, National Research Council, National Academy of Sciences (2005; amendments 2007, 2008).

Human pluripotent stem cells are derived either from embryos, resulting in human embryonic stem cells (hESC), or from other sources which result in induced pluripotent stem cells (iPSC). Michigan Statute (MCLA 333.2688), effective December 19, 2008, permits the use of an embryo for non-therapeutic research and also the use of a deceased embryo with maternal consent. MCLA 333.16274 and 750.430a prohibits "human cloning" but does not prohibit other scientific research or cell-based therapies.

The University of Michigan has established the Human Pluripotent Stem Cell Research Oversight (HPSCRO) Committee to review all research at the University involving these cells. The policy below and related procedures (Addendum 1) are divided into sections applicable to human embryonic stem cell derivation and research use, and to induced pluripotent stem cell derivation and research use.

I. Human Embryonic Stem Cells

A. Derivation

When a stem cell line is to be derived from a human embryo, or when research at UM involves a stem cell line derived elsewhere from human embryos, the **UM will ensure that the following conditions apply to the derivation:**

1. Embryos may be secured only from fertility clinics and must have been freely donated when no longer suitable or no longer needed for reproductive purposes;

2. Embryos must not be purchased;

3. There must be no financial or other incentives to create embryos solely for the purposes of research or to donate embryos for research;

4. Informed consent must have been obtained for donation of the embryo;

5. Provisions to protect the donor's privacy and confidentiality must be in place before any research can take place;

6. No federally-funded salaries, equipment, space, or supplies can be used **to derive** a new stem cell line from a human embryo (Federal funds may be used **for <u>research</u>** involving human embryonic stem cell lines, according to federal policy);

7. Derivation of new human embryonic stem cell lines by somatic cell nuclear transfer is not permitted.

B. Research Use

The following research uses are not permitted:

1. Research involving in vitro culture of any intact human embryo 14 days or older;

2. Research in which human embryonic stem cells are introduced into non-human primate blastocysts or in which any embryonic stem cells are introduced into human blastocysts;

3. Research that involves breeding of any animal into which human embryonic stem cells have been introduced (at any stage of development).

II. Induced Pluripotent Stem Cells

A. Derivation

When induced pluripotent stem cells are to be derived from human tissue, or when research at UM involves induced pluripotent stem cells derived outside the University from human tissue, the **UM will ensure that the following conditions apply to the derivation**:

1. Informed consent must have been obtained from the donor for donation of the tissue unless an IRB waiver of informed consent is allowed;

2. Provisions to protect the donor's privacy and confidentiality must be in place.

B. Research Use

The following research uses are *<u>not permitted</u>*:

1. Research in which induced pluripotent stem cells are introduced into non-human primate blastocysts or introduced into human blastocysts;

2. Research that involves breeding of any animal into which human pluripotent stem cells have been introduced such that they could contribute to the germline.

A. Procedure for Obtaining Approval for Human Embryonic Stem Cell Research

1. Derivation of a Stem Cell Line at UM from an Embryo

The IRB will review the consent process for the donation of embryos from which new human embryonic stem (hES) cell lines will be derived at UM. The HPSCRO will receive notice of the submission of the application through eResearch and may provide consultation. The HPSCRO will request that the PI complete the HPSCRO application regarding the derivation and any subsequent research use of the hES cell line. When the IRB application including the derivation of a hES cell line has been approved by the IRB, and the HPSCRO Committee has all of the information it needs, the HPSCRO will place that line on an internal registry of approved hES cell lines.

The HPSCRO Committee will work with investigators as needed to apply for acceptance on the NIH Registry of hES cell lines derived at UM.

2. Obtaining Human Embryonic Stem Cell Lines Derived Outside the University

a. Material Transfer Agreements

All human embryonic stem (hES) cell lines obtained from outside the University must be accompanied by a Materials Transfer Agreement (MTA). When hES cell lines obtained through the MTA process are shared with other investigators at the University, a Memorandum of Understanding (MOU) is required.

b. NIH Registry Lines

The NIH maintains a registry of hES cell lines that have been approved by NIH through review of the provenance. NIH Registry lines can be used by an investigator at UM after approval from the HPSCRO Committee. (An expedited HPSCRO review process is available for *in vitro* research with NIH Registry lines.)

c. Lines Not on the NIH Registry

The HPSCRO Committee will review the provenance of hES cell lines that are not on the NIH Registry when a UM investigator wishes to obtain such a cell line for research. In conjunction with the HPSCRO review, the UM IRB may conduct an independent review of the consent process. The IRB may place reasonable reliance on reviews of the consent process approved by other IRBs.

When the provenance of a non-NIH Registry stem cell line derived elsewhere has been found to be acceptable by the HPSCRO Committee, the committee will place that line on an internal registry of approved hES cell lines.

3. Research Use of Human Embryonic Stem Cell Lines

Once the HPSCRO application has been completed and submitted to the HPSCRO Committee by the PI for derivation of a new human embryonic stem (hES) cell line, or for obtaining a hES cell line derived outside the university, this application is also reviewed by the HPSCRO Committee for the proposed research uses of the hES cell line. The HPSCRO Committee will issue approval of the proposed research uses.

The **research use** categories for hES cell lines are listed below. Depending upon the category of research use proposed, oversight bodies in addition to the HPSCRO Committee may also review the proposed research, as indicated:

a. *In vitro* hES cell research with pre-existing hES cell lines that are on the NIH Registry (approved by NIH for federal funding)

b. *In vitro* hES cell research with pre-existing hES cell lines that are not on the NIH Registry (not approved by NIH for federal funding*)*

c. Research involving the introduction of hES cells or their derivatives into non-human animals at any stage of embryonic, fetal, or postnatal development (UCUCA review also required)

d. Research involving the introduction of hES cells or their derivatives into humans (FDA and IRB review also required)

e. Research in which personally identifiable information about the donors of the blastocysts, gametes, or somatic cells from which the hES cells were derived is linked to the cell lines (IRB review also required)

B. Procedure for Obtaining Approval for Derivation of Induced Pluripotent Stem Cells Lines

1. Obtaining Human Tissue

a. Tissue from UM patients

The IRB will review the consent process for the donation of tissue from which induced pluripotent stem (iPS) cell lines will be derived. The HPSCRO will be notified of the review and may provide consultation. The UM IRB may place reasonable reliance on reviews of derivation protocols approved by other IRBs. The HPSCRO will review the plan for derivation of the iPS cell line.

b. Tissue from outside the University

When the tissue for derivation of an iPS cell line is to be obtained from outside the University, a Material Transfer Agreement is required. The IRB will review the consent process for the donation of tissue and may place reasonable reliance on reviews of derivation protocols approved by other IRBs. The HPSCRO will review the plan for derivation of the iPS cell line.

When the tissue procurement has been approved by the IRB, and the derivation has been reviewed by the HPSCRO, the resulting iPS cell line will be placed on an internal registry of approved iPS cell lines.

2. Obtaining an Induced Pluripotent Stem Cell Line Derived Outside the University

a. Material Transfer Agreements

Induced pluripotent stem (iPS) cell lines obtained from outside the University must be accompanied with a Materials Transfer Agreement (MTA). When iPS cell lines obtained through the MTA process are shared with other investigators at the University, a Memorandum of Understanding (MOU) is required.

b. Provenance

The HPSCRO Committee must review (with IRB consultation as needed) the adequacy of the consent process for an iPS cell line derived outside the University.

When the provenance of an iPS cell line derived elsewhere has been found to be acceptable by the HPSCRO, the committee will place that line on an internal registry of approved iPS cell lines.

3. Research Use of Induced Pluripotent Stem Cell Lines

A HPSCRO application that is completed by the PI for derivation of a new induced pluripotent stem (iPS) cell line or for obtaining an iPS cell line derived outside the University will also cover the proposed research uses of the iPS cell

line. The HPSCRO Committee will review and issue approval of the proposed research uses.

The **research use** categories for iPS cell lines are listed below. Depending upon the category of research use proposed, oversight bodies in addition to the HPSCRO Committee may also review the work, as indicated:

a. In vitro iPS cell research.

b. Research involving the introduction of iPS cells into non-human gametes or into non-human primates or other animals at any stage of embryonic, fetal, or postnatal development (UCUCA review also required)

c. Research involving the introduction of iPS cells into humans (FDA and IRB review also required)

d. Research in which personally identifiable information about the donors of the somatic cells from which the iPS cells were derived is linked to the cell lines (IRB review also required)