

Guidance and Procedures Number: 38

Title: Stem Cell Research

Date of Last Revision: July 5, 2007

I. Introduction

When stem cell research involves human subjects,¹ the IRB collaborates with the UCLA administration, Embryonic Stem Cell Research Oversight (ESCRO) committee, other research compliance committees, and the research community to ensure that such research meets the highest scientific and ethical standards.² UCLA policy, particularly with regards to human embryonic stem cells (hESCs), is based on relevant state laws, on the recommendations of the National Bioethics Advisory Commission, the National Academies of Science-Institute of Medicine guidelines, as well as on regulations promulgated by the California Institute for Regenerative Medicine (CIRM).³

II. Definitions

- A. **Human embryonic stem cells (hESC) or “covered stem cell line”:** A covered stem cell line is a “culture derived, human pluripotent stem cell population that is capable of: 1) sustained propagation in culture; and 2) self-renewal to produce daughter cells with equivalent developmental potential. This definition includes both embryonic and non-embryonic human stem cell lines regardless of the tissue of origin. ‘Pluripotent’ means capable of differentiation into mesoderm, ectoderm, and endoderm.”⁴ Adult precursors that differentiate into cells of a single tissue type are not considered covered cells for the purposes of CIRM regulations, but may be subject to oversight by ESCRO as defined in California regulations.
- B. **Embryonic Stem Cell Research Oversight (ESCRO) Committee:** UCLA policy and California law require the creation of an ESCRO committee to oversee research involving the derivation and use of hESCs, human embryonic germ cells, and human adult stem cells, including somatic cell nuclear transplantation. The ESCRO reviews new protocols, modifications to currently approved research, and continuing research as required by State or Federal law or regulation, or by University policy.⁵

¹ See *HRPP Guidance & Procedure # 2: Determining When Research Activities Require UCLA IRB/OPRS Review* for details regarding what constitutes research involving human subjects.

² See memoranda from Vice Chancellor for Research Roberto Peccei: “Preliminary Guidance on Conducting Human Embryonic Stem Cell Research at UCLA,” August 2, 2005 (http://www.research.ucla.edu/researchpol/memos/prelim_stem_cell_guidance.htm).

“Changes in IRB Requirements for hESC Research,” January 4, 2007

³ California Code of Regulations §100010-100110. UCLA policy is that the CIRM regulations govern all hESC research at UCLA regardless of funding source.

⁴ California Code of Regulations §100020(c)

⁵ California Health & Safety Code §125119 and California Code of Regulations, §100010-100110.

- C. **Somatic Cell Nuclear Transfer (SCNT):** A scientific process in which the nucleus of an unfertilized egg (oocyte) is removed in a laboratory and replaced by, for example, a donated somatic cell, such as a skin cell (nuclear transfer). The process results in a “fertilized” egg but not in an embryo to be implanted in a woman’s womb. In hESC research, SCNT is used to isolate embryonic stem cells from eggs that have undergone nuclear transfer. The purpose is to use the hESCs to model diseases or make replacement tissue that will not be rejected by the somatic cell donor, as the resulting cells have the same genetic material.
- D. **California Institute for Regenerative Medicine (CIRM):** Established in early 2005 with the passage of Proposition 71 (the California Stem Cell Research and Cures Initiative). The initiative empowered the CIRM to promulgate regulations related to their charge as a State funding agency.

IV. **IRB Responsibility**

- A. **Review:** Consistent with federal regulations, California laws and University policies regarding the protection of human subjects in research, and regardless of funding source, IRB review is required for stem cell research that involves the following:⁶
1. clinical research in which humans are given stem cells or related products; or,
 2. research-related interventions or interactions with cell donors (including the donation of blastocysts or gametes for the purpose of creating hESCs); or,
 3. cells or lines provided to UCLA with identifiers (including direct or indirect codes) that could be used to identify the donors.
- B. **Collaboration with ESCRO:** Where IRB approval is also required, the IRB will collaborate with the ESCRO (along with other appropriate compliance committees) in order to ensure approved research meets the highest scientific and ethical standards. The collaboration includes:
1. ESCRO review will occur prior to IRB review and serve to inform the IRB review. The IRB relies on the ESCRO as a scientific review committee.
 2. ESCRO members are available to attend IRB meetings as expert consultants in order to discuss proposed research, as requested by the IRBs.
 3. The IRBs and ESCRO will freely exchange information in order to facilitate and coordinate the review of proposed stem cell research.
 4. Where IRB approval is required, the research may not be performed until full approvals by both the IRB and ESCRO are in place. Neither approval is sufficient by itself and the project cannot be performed if either committee disapproves the research. An IRB disapproval may not be overturned by any other entity. The research may also be subject to further review by University administration.

⁶ Memorandum from Vice Chancellor for Research Roberto Peccei, “Changes in IRB Requirements for hESC Research,” January 4, 2007.

C. **Research with “covered cells” that is not approvable at this time:** ⁷

1. Human reproductive cloning as defined by California law⁸ or reproductive uses of SCNT.⁹
2. Research that involves the *in vitro* culture of (i) any intact human embryo or (ii) any product of SCNT, parthenogenesis or androgenesis, after the appearance of the primitive streak or after 12 days, whichever is earlier. The 12 day prohibition does not count any time during which the embryos and/or cells have been stored frozen.
3. The introduction of stem cells from a covered stem cell line into nonhuman primate embryos.
4. The introduction of any stem cells, whether human or nonhuman, into human embryos.
5. Breeding any animal into which stem cells from a covered stem cell line have been introduced.
6. The transfer to a uterus of a genetically modified human embryo.

D. **Informed Consent:** The IRB will ensure that approved hESC research includes the applicable additional informed consent requirements as required by California laws and regulations.¹⁰

F. **Registries and banks:** Covered cells in UCLA cell registries and banks must be available for broad dissemination and comply with all relevant UCLA policies.¹¹

G. **Assisted Oocyte Production (AOP) or alternate methods of oocyte retrieval:** Prior to use of AOP or alternate methods for the purpose of procuring oocytes **for research or the development of medical therapies**, the IRB must ensure that the protections codified in California Health and Safety Code Sections 125330-125355 are in place. These protections relate to the information and care provided to subjects, documentation, employees as subjects, physician conflicts of interest, and financial incentives or other valuable consideration for subjects.

1. Please note that a “subject” as defined under state law means “any person undergoing AOP or any alternative method of ovarian retrieval for research or for the development of medical therapies” whether or not the person is considered a “human subject” under federal regulations.¹²
2. State law requires that all oocyte retrieval procedures performed in California for research or the development of medical therapies comply with these

⁷ California Code of Regulations §100030.

⁸ California Health & Safety Code §125292.10(k).

⁹ California Constitution Article XXXV, Section 3.

¹⁰ California Code of Regulations §100100(b) and California Health & Safety Code §125330 *et seq.*

¹¹ California Code of Regulations §100300.

¹² California Health & Safety Code §125330(c)

requirements, and that all oocytes procured from outside California for research taking place in California meet the same standards.¹³

3. Health & Safety Code Section 125335(b) specifies that the American Society for Reproductive Medicine *Assisted Reproductive Technology: A Guide for Patients* meets the standards for a “written summary of health and consumer issues” to be provided to subjects. This publication is available in English at <http://www.asrm.org/Patients/patientbooklets/ART.pdf> or in Spanish at <http://www.asrm.org/Patients/patientbooklets/ARTspanish.pdf>.

V. Investigator Responsibility

- A. Investigators are responsible for submitting ESCRO applications for review as required by ESCRO policies and procedures.
 1. Investigators are responsible for also submitting IRB applications for review when stem cell research involves human subjects (see Section IV above).
 2. So that the IRB and/or ESCRO can conduct a full evaluation of research, applications and related materials such as consent forms should reflect the considerations and requirements described in Section IV above.
- B. Investigators may not initiate research without ESCRO review and approval.
 1. Where IRB approval is also required, investigators may not initiate research without IRB approval in addition to ESCRO approval.
- C. Investigators are responsible for compliance with IRB and ESCRO decisions and policies as well as other compliance committee determinations and applicable laws, regulations and University policies.
- D. The investigator must ensure that clinical personnel that have a conscientious objection not be required to participate in providing donor information or securing donor consent for research use of gametes or embryos. This privilege shall not extend to the care of a donor or recipient.
- E. Provision or receipt of hESCs to or from another institution may not commence without a UCLA-approved Material Transfer Agreement (MTA).

Regulations:

45 CFR Part 46
21 CFR Parts 50, 56, and 312
California Code of Regulations, Sections 100010-100110
California Health & Safety Code 125118 *et seq.*

¹³ California Health & Safety Code §125346

References:

National Bioethics Advisory Commission, Ethical Issues in Human Stem Cell Research, 1999. <http://www.georgetown.edu/research/nrcbl/nbac/pubs.html> .

National Academies of Science-Institute of Medicine, Guidelines for Human Embryonic Stem Cell Research, National Academies Press, 2005. <http://fermat.nap.edu/books/0309096537/html/>

California Institute for Regenerative Medicine. <http://www.cirm.ca.gov/>

UCLA Stem Cell Applications and Documents.
<http://www.research.ucla.edu/researchpol/stemcelldocs.htm>