

ADMINISTRATIVE POLICY

| | | |
|---|------------------------|-----------------------------------|
| Subject: Human Stem Cell Research | Page 1 of 11 | Policy # Version: 1.0 |
| Title: Use of Human Stem Cells at Northwestern University | Revision of: | Effective Date: September 1, 2020 |
| | | Removal Date: |

I. **PURPOSE**

Research using Human Stem Cells is essential to expanding fundamental scientific knowledge of cellular and developmental human biology. Such research, however, raises important scientific and ethical questions, that have resulted in restrictions on the use of federal and state funds for certain research involving such cells. In light of these concerns and to comply with applicable federal and state laws and regulations, Northwestern University has established this Policy. The goals of this Policy are to assure that:

A. Northwestern University is aware of and provides oversight and review of all research involving the procurement, derivation, gene editing, banking, distribution, and use of the following conducted at or under the auspices of Northwestern University or funded by Northwestern University:

- Human embryonic stem cells (hESC)
- Human totipotent stem cells
- Human gametes
- Human zygotes
- Human embryo ex vivo

For the purpose of this document, the above list will be collectively referred to as “Covered HuESTGZ”. This policy excludes adult multipotent and induced pluripotent human stem cells (iPSC), unless they are being used for the purpose of creating totipotent stem cells or gametes.

- B. Every person at Northwestern University working on such research is fully aware of the compliance requirements associated with such research;
- C. Northwestern University observes the federal government’s current restrictions against use of federal funds on hESC lines not included in the NIH Human Embryonic Stem Cell Registry;
- D. Northwestern University complies with any special requirements for such research imposed by research sponsors;
- E. Northwestern University is aware of and maintains a registry documenting the sources or derivation of any hESC lines planned for use or being used in research at Northwestern University; and
- F. Northwestern University establishes oversight of the Northwestern University Committee on Human Stem Cell Research (NUCHSR) NUCHSR, which is charged with reviewing and approving research protocols involving the procurement, gene editing, derivation, banking, distribution, or use of Covered HuESTGZ prior to the execution of the research. The NUCHSR’s responsibilities exclude standard of care for clinical practices.

Northwestern University’s requirements for the conduct of research with Human Stem Cells as set forth in this Policy are based in large part on and intended to comply, as applicable, with

| | | |
|---|------------------------|---------------------------------|
| Title: Use of Human Stem Cells at Northwestern University | Page 2 of 11 | Policy # Version: 1.0 |
|---|------------------------|---------------------------------|

- (i) federal requirements and limitations with respect to federally-funded human stem cell research as set forth in the “National Institutes for Health Guidelines on Human Stem Cell Research” promulgated July 6, 2009,
- (ii) state requirements and limitations with respect to state-funded research <http://www.ilga.gov/legislation/ilcs/ilcs3.asp?ActID=2938&ChapterID=35> ,
- (iii) the recommendations of the National Academies in its 2005 report (as amended in 2007, 2008 and 2010) entitled “Guidelines for Human Embryonic Stem Cell Research”, and
- (iv) the recommendations of the International Society of Stem Cell Research in its 2016 report entitled “Guidelines for the Conduct of Human Embryonic Stem Cell Research”, as each may be amended from time to time.

II. PERSONS AFFECTED

This Policy applies to all research involving the procurement, derivation, banking, distribution, or use of Covered HuESTGZ conducted at or under the auspices of Northwestern University or funded by Northwestern University, and to all other research conducted at or under the auspices of Northwestern University or funded by Northwestern University that is subject to oversight by the NUCHSR pursuant to law, regulation, or the terms of funding.

This Policy does not apply to research involving fetal tissue or stem cells derived from human adults, umbilical cord blood, placentas, or fetuses, or research involving any other type of human cells, unless the experiments are designed or expected to yield gametes or the research is otherwise subject to oversight by the NUCHSR pursuant to law, regulation, or the terms of funding.

III. POLICY STATEMENT

Northwestern University encourages investigators to engage in responsible and ethical research requiring the use and derivation of human embryonic stem cells, human totipotent cells, human gametes, and gene editing of totipotent, gametes or zygotes provided the cells are obtained and the research is conducted with appropriate oversight and in accordance with all applicable laws, rules and regulations referenced above. At the same time, certain activities relating to Human Stem Cells are expressly prohibited and others require registration with and/or review by the Northwestern University Committee on Human Stem Cell Research (NUCHSR) as provided in this Policy.

All Human Stem Cell Research conducted at or under the auspices of Northwestern University or funded by Northwestern University shall be conducted in compliance with (i) this Policy, (ii) all applicable federal, state, and local laws, regulations, and policies, (iii) the terms of any grant, contract, agreement, or other funding supporting the Human Stem Cell Research, and (iv) all other applicable Northwestern University policies, including, where applicable, the policies and procedures of the Northwestern University IRB.

| | | |
|---|------------------------|---------------------------------|
| Title: Use of Human Stem Cells at Northwestern University | Page 3 of 11 | Policy # Version: 1.0 |
|---|------------------------|---------------------------------|

IV. PROCEDURES

A. Prohibited Activities

No Northwestern University facilities, equipment or other resources, including funding, shall be used for any of the following:

1. Human Embryonic Stem Cell Research requiring or using federal funds if such research is ineligible for federal support under the NIH Stem Cell Guidelines;
2. human reproductive cloning;
3. research involving *in vitro* culture of any post-fertilization human embryos, regardless of derivation method, for longer than 14 days or until formation of the primitive streak, whichever occurs first;
4. research in which any products of research involving human totipotent or pluripotent stem cells are implanted into a human or non-human primate uterus;
5. research in which animal chimeras incorporating Human Stem Cells, including but not limited to hESCs and iPSCs, with the potential to form gametes are bred to each other; or
6. Human Stem Cell Research engaged in a manner that is contrary to any applicable federal, state or local laws, rules or regulations or the terms of the grant or other support.
7. Gene editing in human embryos after 14 days.

B. NUCHSR Review and Approval

All hESC research—regardless of the type or source of the hESCs—and certain other Human Stem Cell Research is subject to NUCHSR review and approval. Prior to use of the lines in research, investigators should submit an [application](#) to the NUCHSR. Examples of activities requiring NUCHSR review include but are not limited to:

1. Creation of a new hESC line by any means, including through use of stem cell nuclear transfer (SCNT), human zygotes, spindle transfer, or a human embryo furnished by an *in vitro* fertilization clinic or other lawful source;
2. Payment to a donor solely for the purpose of creating a human embryo to be used in hESC research;
3. Research in which personally identifiable information about the donor of the blastocysts, morulae, gametes, or somatic cells from which the hESCs or iPSCs were derived is readily ascertainable or might become known to the investigator;
4. Research using NIH ineligible hESC lines that have not been pre-approved for such use by the

| | | |
|---|------------------------|---------------------------------|
| Title: Use of Human Stem Cells at Northwestern University | Page 4 of 11 | Policy # Version: 1.0 |
|---|------------------------|---------------------------------|

NUCHSR;

5. iPSC research that includes experiments designed or expected to yield gametic cells and tissues;
6. Mixing human totipotent stem cells or iPSCs with pre-implantation human embryos. In no case shall such experiments be allowed to progress for more than 14 days of development in vitro, or past the point of primitive streak formation, whichever is first;
7. Clinical research in which cells of human totipotent or pluripotent stem cells or iPSCs are transplanted into living human subjects. In no case shall such research involve implantation of human totipotent or pluripotent stem cells into a human uterus;
8. *In vitro* culture of an intact human embryo;
9. Research that generates animal chimeras using human cells, including, but not limited to, introducing hESCs, human totipotent stem cells or iPSCs into animals other than humans or primates at any stage of embryonic, fetal, or postnatal development; and
10. Research that involves the introduction of hESCs into non-human primates at any stage of fetal or postnatal development.
11. Gene editing in human embryos or hESCs up to 14 days.

C. NUCHSR Registration

Registration is required for any covered cell types. The registry will maintain a record of all hESC lines including newly created hESC lines, kept at or under the auspices of NU. The registry will be supported and maintained within Feinberg's Office for Regulatory Affairs and will contain information on the source and provenance of the hESC lines, the location of the hESC lines, the name of the investigators responsible for the safekeeping of the hESC lines, the disposition of the hESC lines, and such other information the NUCHSR deems appropriate.

Investigators should complete the [registration form](#) to register their hESC.

The following categories of Human Stem Cell Research are subject to NUCHSR Registration only:

1. *In vitro* research using hESC lines that are listed on the NIH hESC Registry.
2. *In vitro* research using hESC lines that have been pre-approved for such use by the NUCHSR;
3. *In vitro* research using Human Stem Cells, if
 - a. Institutional Review Board (IRB) review approval has been received (i.e., the cells were obtained by a process approved by an IRB to ensure that donor(s) provided voluntary informed consent in accordance with then current federal and state law, regulations, and guidelines), and
 - b. The cell lines have been de-identified (i.e., the cell lines and any corresponding information

| | | |
|---|------------------------|---------------------------------|
| Title: Use of Human Stem Cells at Northwestern University | Page 5 of 11 | Policy # Version: 1.0 |
|---|------------------------|---------------------------------|

are anonymous or are coded in such a manner that the donor(s) cannot be identified (by the investigators or others) directly or indirectly through identifiers linked to the donor(s), pursuant to a written agreement obtained from the source of the cell lines stating that the identity of the donor(s) will not be released to the investigator under any circumstances);

4. Research involving the transplantation of non-totipotent and non-pluripotent Human Stem Cells or cells derived from non-totipotent and non-pluripotent Human Stem Cells into human subjects; and

5. Other types of Human Stem Cell Research that the Vice Dean for Research or Regulatory Affairs has made a written determination, after due consideration of the likely risks and benefits of such research, that such categories are permissible without the additional review of the NUCHSR.

D. Research and Activities That Do Not Require NUCHSR Registration.

Unless otherwise provided in the terms of the grant, contract, agreement, or other funding supporting the research and/or other activities, the following research and/or other activities are not subject to this Policy:

1. Use of non-Human Stem Cells;

2. Use of fetal tissue or stem cells derived from human adults or umbilical cord blood, placentas, or fetuses, or research involving any other type of human cells, unless the experiments are designed or expected to yield gametes;

3. Transplantation of stem cells as part of a standard of care or other recognized and accepted medical treatment for a disease or condition; Transplantation of Human Stem Cells as part of a Human Subjects Research project subject to IRB review or as part of innovative care that departs in a significant way from standard or accepted practice may require ESCRO Registration, NUCHSR review, or be prohibited;

4. The creation and *ex vivo* passage of iPSCs. NUCHSR Registration and NUCHSR review and approval are required if the iPSCs are pluripotent stem cells and are transferred into an animal or human, or are used to make an embryo; and

5. Other categories of Human Stem Cell Research or activities that the Vice Dean for Research or Regulatory Affairs has made a written determination, after due consideration of relevant legal and ethical requirements, that such research or activities are appropriate for exemption from NUCHSR Registration.

6. Derivation of human iPSCs for research purposes

E. Procurement and Transfer of Human Stem Cell Lines.

Investigators shall procure Human Stem Cell lines in a manner consistent with Northwestern University purchasing and material transfer rules and regulations. Upon procurement, the principal

| | | |
|---|------------------------|---------------------------------|
| Title: Use of Human Stem Cells at Northwestern University | Page 6 of 11 | Policy # Version: 1.0 |
|---|------------------------|---------------------------------|

investigator having authority over such newly-acquired Human Stem Cell lines shall register the Human Stem Cell (see section C).

Human Stem Cell lines shall only be transferred to other investigators, both at Northwestern University and outside Northwestern University, with the written approval of the NUCHSR and in a manner consistent with the provisions of this Policy and other applicable Northwestern University rules and regulations. This excludes iPSCs.

Transfers of Human Stem Cell lines to investigators outside Northwestern University are subject to the requirements on material transfer. As a condition to any transfer outside of Northwestern University, the recipient must submit a certification to Northwestern University that any research to be conducted with the transferred hESCs, hESC lines, iPSCs or iPSC lines will be performed in compliance with all relevant laws and other restrictions related to such hESCs, hESC lines, iPSCs or iPSC lines.

F. New hESC Lines

1. Creation of New hESC Lines

The NUCHSR and the IRB shall review and approve any proposal to procure gametes, blastocysts, morulae or somatic cells for the purpose of generating new hESC lines. Furthermore, any new hESC lines should comply with all requirements for eligibility of such stem cell lines for Human Stem Cell Research with NIH funding as set forth in the NIH Stem Cell Guidelines. Federal funding, however, must not be used in the derivation of new hESC lines.

In addition, investigators involved in the creation of hESC lines must also (i) maintain adequate records in order to enable NU and the principal investigator to demonstrate the provenance of such hESC lines and consent of gamete donors, (ii) report to the NUCHSR, IRB and any other NU safety committee with applicable jurisdiction, any adverse or unexpected outcomes that pose a threat to the health or safety of any individual or raise new ethical issues for any Human Stem Cell Research project, (iii) refrain from making any use or permitting any transfer of the new hESC lines until approval from the NUCHSR, as described in this Policy, is obtained, and (iv) transmit promptly following creation any information required by the NUCHSR to include the newly created hESC lines into the NU hESC registry described in section C.

2. Use of New hESC Lines.

Before using any hESC line that is new to Northwestern University, irrespective of source, the investigator must ascertain the provenance of the hESC line, including whether the hESC line originated from an NIH Eligible hESC line, or the provenance of the iPSC line. For these purposes, presence on the NIH hESC Registry constitutes adequate documentation of provenance.

In conducting Human Stem Cell Research involving the new hESC line, the following rules must be followed:

- a. hESC lines derived from NIH Eligible hESC lines. hESC lines created from an NIH Eligible hESC line may be used for federally funded and non-federally funded research, provided that the subsequent use is consistent with this Policy and the terms of the grant or other support provided to create the hESC line and the terms of the grant or other support

| | | |
|---|------------------------|---------------------------------|
| Title: Use of Human Stem Cells at Northwestern University | Page 7 of 11 | Policy # Version: 1.0 |
|---|------------------------|---------------------------------|

supporting the research.

- b. hESC lines derived from NIH ineligible hESC lines. Research on hESC lines created from NIH Ineligible hESC lines (including personnel and equipment) may not be charged to federal sources, even if such research is undertaken in whole or part to benefit a federally funded project. Such hESC lines may be used for non-federally funded research, provided that the subsequent use is consistent with the terms of this Policy and the grant or other support provided to create the hESC line and the terms of the grant or other support supporting the research.
- c. iPSC lines. iPSC lines may be used for federal funded and non-federally funded research, provided that the subsequent use is consistent with the terms of this Policy and the grant or other support provided to create the iPSC line and the terms of the grant or other support supporting the research.

G. Material Transfers. Incoming and outgoing transfers of Human Stem Cells, including hESCs, hESC lines, iPSCs, and other materials, shall be documented through material transfer agreements approved by Northwestern University Office of Sponsored Research, which shall be consistent with any related research funding terms.

V. ROLES AND RESPONSIBILITIES

Investigators

Investigators shall procure Covered HuESTGZ in a manner consistent with Northwestern University purchasing and material transfer rules and regulations.

In addition, investigators involved in the creation of hESC lines or iPSC lines must also maintain adequate records in order to enable NU and the investigator to demonstrate the provenance of such hESC lines or iPSC lines and consent of gamete donors.

NUCHSR

1. **Purpose.** The NUCHSR is responsible for the initial and ongoing review of all Human Stem Cell Research covered under this Policy at or under the auspices of Northwestern University. No use of Human Stem Cells in research, including the derivation of hESCs for research from any source, shall be initiated by or for Northwestern University prior to registration of the proposed research with the NUCHSR and the review and approval of the NUCHSR.

2. **Authority.** The NUCHSR shall have general authority to review, approve, conditionally approve, require modifications of, or disapprove all research proposals under this Policy. The Committee shall also require NUCHSR to have the authority to establish and enforce applicable ethical research standards pertaining to all Human Stem Cell Research at or under the auspices of Northwestern University.

3. **Composition.** The NUCHSR shall be composed of at least four (4) voting members appointed by the Vice Dean for Regulatory Affairs, who shall collectively have adequate scientific, medical and ethical training and experience, including at least one scientist with relevant expertise. A new committee member will replace an existing one every four (4) years. A new committee Chair will be

| | | |
|---|------------------------|---------------------------------|
| Title: Use of Human Stem Cells at Northwestern University | Page 8 of 11 | Policy # Version: 1.0 |
|---|------------------------|---------------------------------|

appointed every two (2) years by the joint decision of the Vice Dean for Regulatory Affairs and all four (4) members. A quorum is defined as three (3) voting members. A quorum is required for the approval of applications.

4. **Responsibilities.** The NUCHSR's review of individual Human Stem Cell Research proposals shall be specific to the scientific and ethical issues presented by such proposals. NUCHSR review and approval shall be deemed to be separate from and in addition to any other reviews or approvals otherwise required at Northwestern University for such research, including but not limited to committees or administrative offices having responsibility for review and approvals of human subjects' research, animal research, biological safety, radioactive materials, and environmental safety.

5. **Conflicts of Interest.** The members of the NUCHSR shall comply with all Northwestern University policies related to conflict of interest, including Northwestern University Policies on Conflict of Interest and Conflict of Commitment and Conflict of Interest in Research. In accordance with such policies, a member of the NUCHSR must recuse himself or herself from participating in the initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the NUCHSR.

6. **Relationship to IRB.** The duties and responsibilities of the NUCHSR shall be distinct and separate from the IRB, and to the extent practical, the subject matter of the reviews by the IRB and NUCHSR should not overlap. Notwithstanding the foregoing, each of the IRB and the NUCHSR shall provide the other with any reports of adverse or unexpected outcomes that pose a threat to the health or safety of any individual or raise new ethical issues that arise during or after the completion of any Human Stem Cell Research project.

7. **Administrative Support.** Feinberg's Office for Regulatory Affairs will provide necessary administrative support for the NUCHSR.

VI. DEFINITIONS

For purposes of this Policy, the following definitions shall apply:

A. **Adult Stem Cell** - an undifferentiated cell, found among differentiated cells in a tissue or organ, that can renew itself and can differentiate to yield primarily some or all of the specialized cell types of the tissue or organ, but the cell itself is not pluripotent or totipotent.

B. **Blastocyst** - a pre-implantation embryo of about 150 to 250 cells produced by successive rounds of cell division following fertilization. The blastocyst is a sphere made up of an outer layer of cells (the trophoblast), a fluid-filled cavity (the blastocoel), and a cluster of cells on the interior (the inner cell mass).

C. **Chimera** - an organism composed of cells derived from at least two genetically different zygotes. Theoretically, the zygote could be from separate species.

D. **Cloning** - the asexual production of a line of cells that is genetically identical to the originating cell.

E. **Embryo** - an organism in the early stages of growth and differentiation.

| | | |
|---|------------------------|---------------------------------|
| Title: Use of Human Stem Cells at Northwestern University | Page 9 of 11 | Policy # Version: 1.0 |
|---|------------------------|---------------------------------|

- F. Fetus - the unborn offspring of an animal that develops from an embryo.
- G. Gamete - a mature haploid male or female germ cell which is able to unite with another of the opposite sex in sexual reproduction to form a zygote.
- H. NUCHSR - Northwestern University's Committee on Human Stem Cell Research, (NUCHSR): This oversight committee, appointed by the Vice Dean for Regulatory Affairs, develops guidelines for the conduct of research involving the use of human stem cells.
- I. NUCHSR Registration - the registration of Human Stem Cell Research as described in section IV.
- J. hESC(s) or human embryonic stem cell(s) - one or more cells that are derived from the inner cell mass of blastocyst-stage human embryos, are capable of dividing without differentiating for a prolonged period in culture, and are known in appropriate conditions to develop into cells and tissues of the three primary germ layers (endoderm, ectoderm and mesoderm) as well as germ cells. These human embryos include those generated by fertilization, parthenogenic activation or somatic cell nuclear transfer.
- K. hESC Research - research involving the procurement, derivation, banking, distribution, or use of hESCs.
- L. Human reproductive cloning - the practice of attempting or creating a human being beyond the six somite stage.
- M. Human embryo - extending from the time of the formation of the zygote until the end of the first eight weeks of gestation. Human embryos may be derived from fertilization, parthenogenesis, cloning, or other means from one or more gametes.
- N. Human primordial germ cell(s) - cell found in the sexually bipotential human embryo or human fetus that are first identified in the extraembryonic mesoderm, that migrate to the gonadal ridge and that can develop into immature gametes.
- O. Human Stem Cell - any human embryonic stem cells, human totipotent or pluripotent cells, human neural progenitor stem cells, human gonadal progenitor stem cells, and induced pluripotent stem cells.
- P. Human Stem Cell Research - research involving the procurement, derivation, banking, distribution, or use of Human Stem Cells at or under the auspices of Northwestern University or any other research at or under the auspices of Northwestern University that is subject to oversight by the NUCHSR pursuant to law, regulation or the terms of funding.
- Q. iPSC(s) or induced pluripotent stem cell(s) - one or more human pluripotent stem cells that have been derived from non-embryonic sources somatic cell sources and are transformed into stem cells by introduction of genes that induce a pluripotent state.
- R. Intact human embryo - a human embryo that is developing in an integrated, normal fashion and continuing to progress and otherwise capable of progressing into a fully-developed human.

| | | |
|--|--------------------------------|--|
| Title: Use of Human Stem Cells at Northwestern University | Page 10 of 11 | Policy # Version: 1.0 |
|--|--------------------------------|--|

S. Morula - a solid mass of 16–32 human embryo cells that resembles a mulberry and results from the cleavage (cell division without growth) of a zygote (fertilized egg).

T. NIH Eligible hESC line - a stem cell line posted on the NIH hESC Registry or a stem cell line for which an institution has established eligibility for NIH funding under the NIH Stem Cell Guidelines.

U. NIH hESC Registry - the current list of hESC lines, as it may from time to time be revised, that are eligible for federal funding.

V. NIH Ineligible hESC line - any hESC line other than an NIH Eligible hESC line.

W. NIH Stem Cell Guidelines - the “National Institutes for Health Guidelines on Human Stem Cell Research” (2009 and subsequent updates).

X. Northwestern University - Northwestern University and its relationships with affiliated institutions (i.e., Northwestern Medicine, etc.)

Y. Pluripotent stem cell” means a stem cell having the capacity of developing cells of all germ layers (endoderm, ectoderm and mesoderm) as well as germ cells.

Z. Provenance - sufficient documentation, on the basis of usual and customary standards within the field of Human Stem Cell Research, to authenticate the history of ownership and place of origin of hESCs and/or hESC lines and/or iPSCs and/or iPSC lines.

AA. Reproductive cloning - the use of cloning for the purpose of creating one or more adult organisms that are all genetically identical to another organism.

BB. Somatic cell nuclear transfer (SCNT) - a technique that replaces the nucleus of an enucleated egg with the nucleus of a somatic cell.

CC. Spindle transfer - the process in which chromosomes from one egg are transferred into a recipient enucleated egg to make an embryo.

DD. Stem cell - a cell with the ability to divide for indefinite periods in culture and to give rise to specialized cells.

EE. Stem cell line - a mass of cells descended from and retaining at least some of the characteristics of an original stem cell.

FF. Totipotent stem cell - a stem cell having the ability to give rise to all the cell types of the body plus all of the cell types that make up the extraembryonic tissues, such as the placenta.

GG. Zygote - a cell formed by the union of male and female germ cells (sperm and egg, respectively).

HH. Human Parthenote - a chemically or otherwise activated, unfertilized human egg that develops into an early-stage embryo, but does not develop as a viable organism. ESC lines can be derived from parthenogenetic human embryos.

| | | |
|---|-------------------------|---------------------------------|
| Title: Use of Human Stem Cells at Northwestern University | Page 11 of 11 | Policy # Version: 1.0 |
|---|-------------------------|---------------------------------|

VII. POLICY UPDATE SCHEDULE:

Review changes with the NUCSHR annually.

VIII. REVISION HISTORY:

Original version: effective September 1, 2020.