Guidance for Research Involving Human Embryonic Stem Cells, Germ Cells, and Cells Obtained from Cord Blood

Ministry of Public Health
Department of Research

Guidance Regarding Research Involving Human Embryonic Stem Cells, Germ Cells, And Cells Obtained From Cord Blood

Introduction:

Human stem cell research touches on many ethical, legal, scientific, and policy issues. Therefore, Guidelines are needed to make explicit how research involving human stem cells, germ cells, and cell-derived test articles can be pursued most responsibly. Hence, this document presents Guidelines to assist researchers primarily in the State of Qatar, but they may be applicable for international collaboration as well.

Stem cell research is one of the most significant medical applications that has great promise but also has led to great controversy. For example, studies of human embryonic stem cells may yield information about the complex events that occur during human development. Some of the most serious medical conditions, such as cancer and birth defects, are due to abnormal cell division and differentiation. A better understanding of the genetic and molecular controls of these processes could provide information about how such diseases arise and suggest new strategies for therapy. Human embryonic stem cells may also be used to test new drugs.

Perhaps the most important potential use of human stem cells (particularly embryonic stem cells) is the generation of cells and tissues that could be used for cell-based therapies. Recent reports show that donated tissues and organs are often used successfully to replace ailing or destroyed tissue, but the need for transplantable tissues and organs far outweighs the available supply. Stem cells, directed to differentiate into specific cell types, offer the possibility of a renewable source of replacement cells and tissues to treat diseases and conditions, including Parkinson's disease, amyotrophic lateral sclerosis, spinal cord injury, burns, heart disease, diabetes, and arthritis.

On the other hand, stem cell research, also has led to great controversy. The controversy centers on the ethics of conducting research involving the generation, usage and destruction of human embryonic stem cells. However, it should be noted that new approaches and innovative strategies have yielded embryonic stem cells without destruction of embryos. In any case, despite the fact that the therapeutic potential of stem cell technology is needed to be investigated through more in depth clinical-based research, researchers should not cross ethical, religious, cultural and moral boundaries.

The purpose of this document is to provide guidance and procedures under which proposed research in this area, **conducted in Qatar publicly or privately funded,** is ethically responsible, scientifically worthy, and conducted in accordance with applicable laws. These Guidelines describe the conditions and informed consent procedures required for the utilization of human stem cells in biomedical research. **These Guidelines will be up-dated whenever new scientific insights emerge.**

The Qatar Health Research Ethics Committee has unanimously approved this document. A law to legally enforce this document is in process.

In developing these Guidelines, the Ministry of Public Health consulted the thoughtful Guidelines developed by other national and international committees of scientists, physicians, bioethicists, religious scholars and stakeholders in addition to publications from various organizations including the U.S. National Academy of Sciences, the U.S. National Institutes of Health, the International Society for Stem Cell Research, and others.

Summary

In this appendix, human embryonic stem cells are defined as “cells that are derived from the inner mass of blastocyst stage of human embryos, are capable of dividing without differentiating for a prolonged period in culture, and are known to develop into cells and tissues of the three primary germ layers”.

Qatar allows human stem cell research using adult stem cells and induced pluripotent stem cells. Research involving human embryonic stem cells is allowed using cells obtained only from samples (if available) that were intended for use in reproductive purposes and are no longer needed for that purpose, the age of the fertilized egg is not more than **six days** and that it is not allowed to develop to further embryonic stages.

Research using human embryonic stem cells derived from other sources, including somatic cell nuclear transfer, parthenogenesis, and/or In Vitro Fertilization (IVF) embryos generated for research purposes, is not allowed under the current policies and Guidelines in Qatar. Further, the derivation of stem cells from human embryos, other than spontaneous miscarriage, is prohibited in Qatar. In addition, there are some uses of human embryonic stem cells and human induced pluripotent stem cells that, although those cells may come from allowable sources, are nevertheless not allowed in Qatar. For example, it is not allowed to introduce human embryonic or pluripotent stem cells into non-human blastocysts. Also, it is prohibited to perform research on breeding animals with possible human contribution to the germline.

Qatar Ministry of Public Health's “Guidelines, Rules and Policies for Research Involving Human Subjects” establishes safeguards for individuals who participate in clinical research either as research subjects or are the source of tissues, including non-embryonic human adult stem cells and human induced pluripotent stem cells. When research involving human adult stem cells or induced pluripotent stem cells constitutes human subject research, Institutional Review Board (IRB) review is required and informed consent must be obtained per the requirements detailed in the basic policy published by the Qatar Ministry of Public Health.

It should be reiterated that human subjects' research is clinical research that involves interactions with living individuals. This would include the introduction into humans of cells or test articles, drugs, devices, or biological products, and therefore is subjected to the requirements outlined in the basic policy "The Guidelines, Rules and Policies for Research Involving Human Subjects". IRB review and approval is required for such research.

Research that involves neither interactions nor interventions with living individuals or obtaining identifiable private information is not considered human subjects research. Accordingly, [with certain exceptions (e.g. point III A below)] *in vitro* research and research on animals using already derived and established human cell lines, from which the identity of the donor(s) cannot readily be ascertained by the investigator, are not considered human subject research. The institution's IRB could determine whether an IRB review is needed.

In addition, *In vitro* research or research in animals using a human cell line that retains a link to identifying information ordinarily would not be considered human subjects research if: (1) the investigator and research institution do not have access to identifiable private information related to the cell line; and (2) a written agreement is obtained from the provider of the cell line certifying that the identifiable private information related to the cell line will not be released to the investigator under any circumstances. In this case, the research may be considered to not involve human subjects because the identity of the donor(s) could not be "readily ascertained" by the investigator or associated with the cell line. Under such circumstances, an institution or an IRB could determine that IRB review of the research using the cell line is not needed.

In brief:

What is **allowed**?

• Human adult stem cells,
• Human embryonic stem cells using cells obtained only from samples (if available) that were intended for use in reproductive purposes and are not suitable, or no longer needed for that purpose, are less than 6 days old, and not implanted into the womb,
• Human induced pluripotent stem cells,
• Cells from Cord Blood and placenta,
• Cells from miscarriage fetuses (caused by clinical reasons or naturally)
• In Vitro research and research in animals using already existing and established human cell lines, from which the identity of the donor cannot readily be ascertained by the investigator.

What is **not allowed**?

• Research using human embryonic stem cells derived from somatic cell nuclear transfer, parthenogenesis, and/or IVF embryos created specifically for research purposes.
• Derivation of stem cells from human embryos.
• Introduction of human embryonic or pluripotent stem cells into non-human blastocysts.
• Breeding animals with possible human contribution to the germline.
• Research using imported cells from sources in other countries that generate these cells either by derivation of stem cells from human embryos or from somatic cell nuclear transfer, parthenogenesis, and/or IVF embryos.
• Harvesting stem cells from human embryos where the embryo is destroyed.

It is recommended that research institutions should be sensitive to the rights of the laboratory personnel who wish to opt out, for personal beliefs, from participating in research with embryonic stem cells without jeopardizing their jobs.

GUIDELINES FOR HUMAN STEM CELL RESEARCH

All proposed human stem cell research reviewed and approved by Institutional Review Boards (IRBs) must obtain approval by the Qatar Ministry of Public Health's Recombinant DNA Advisory Committee prior to receiving funding and initiation of the studies.

I. Scope of Guidelines

This Appendix to the Qatar Ministry of Public Health's "Guidelines, Rules and Policies for Research Involving Human Subjects" describes the circumstances under which human embryonic stem cells are allowed for use in research. It also includes a section on uses of human embryonic stem cells or human induced Pluripotent stem cells that are not approved for research in Qatar. Research using stem cells obtained from cord blood or placenta is also addressed. For the purpose of these Guidelines, "human embryonic stem cells" are defined as cells that are derived from the inner mass of blastocyst stage of human embryos, are capable of dividing without differentiating for a prolonged period in culture, and are known to develop into cells and tissues of the three primary germ layers".

II. Guidelines for Eligibility of Human Stem Cells for Use in Research

The Qatar Ministry of Public Health supports the conduct of responsible, scientifically worthy human stem cell research, including human embryonic stem cell research, to the extent permitted by this guidance document and meets the required consents and documents listed below.

Adult stem cells, induced pluripotent stem cells and cells obtained from cord blood and placenta are allowed to be used in biomedical and therapeutic research.

Human embryonic stem cells may be used in research if the cells were:

- Obtained from samples intended for reproductive purposes (if available) and were not suitable, or no longer needed for that purpose.
- The samples were donated voluntarily by individuals who sought reproduction treatment.
- The age of the fertilized egg is not more than **six days** and that it is not allowed to develop to further embryonic stages. Freezing and storing of the fertilized egg in its current state is permissible, so is its future usage.
- The egg is not implanted into another woman's uterus.
- The eggs are not used for business, commercial use or profit.
- Cells from miscarriage fetuses (naturally or for medical reasons).
- Voluntary written consent for research purposes was given by the donor.
- Documentation for all of the following must be assured:
  1. All options pertaining to use of samples no longer needed for reproductive purposes were
  2. No inducements were offered for the donation.
  3. A policy was in place at the health care facility where the samples were donated that neither consenting nor refusing to donate samples for research would affect the quality of care provided to potential donor(s).
  4. Those conducting research involving stem cells should have no involvement in the clinical care of the donors. Such research should be conducted in a location that maintains a separation of the clinical care from research.
  5. There was a clear separation between the prospective donors' decision to produce embryos for reproductive purposes and the prospective donors' decision to donate the samples for research purposes.
  6. At the time of donation, consent for that donation was obtained from the individuals who had sought reproductive services. Decision to donate was made free from the influence of researchers. Donors were informed that they retained the right to withdraw consent until the samples were actually used for research.
  7. The following information, which is pertinent to making the decision of whether or not to donate samples for research purposes, was in the written consent form for donation and discussed with potential donors in the informed consent process:

     - A statement that donors understood that the samples would be used to generate stem cells for research; that the cells may survive in a laboratory environment for extended period of time and may be used in multiple research projects; that donors was provided with information about what would happen to the samples in the process of generating stem cells for research and alternative options pertaining to use of the samples;

     - A statement that donation of the samples for research was voluntary and that the donation was made without any restriction or direction regarding the individuals who may receive medical benefit from the use of the stem cells; and that the research was not intended to provide direct medical benefit to the donors;

- An explanation of the research for which the stem cells are to be used, that the results of research using the stem cells may have commercial potential, and that the donors would not receive financial or any other benefits from any such commercial development;

- A statement as to whether or not information that could identify the donors would be retained prior to the use of the stem cells and the implication of removing identifiers from stem cells, including loss of a say in the use of the stem cells and, potentially, loss of their use for treatment for the participant or his or her blood relatives; and

- A statement that the individual donor may remain identifiable even if his or her genome is only partly represented in those stem cells. This is particularly so if analysis of the stem cells is combined with other sources of information such as genealogical, phenotypic (including medical record) or genetic data.

Prior to initiating the research project: The investigators must ensure that: (1) the stem cells were derived consistent with these Guidelines; and (2) the research institution maintains appropriate documentation demonstrating such consistency. The responsible grantee institutional official must provide assurances with respect to (1) and (2) when endorsing applications and progress reports submitted to the funding entity for projects that utilize these cells.

III. Research Using Human Embryonic Stem Cells And/Or Human Induced Pluripotent Stem Cells That, Although The Cells May Come From Allowable Sources, Is Nevertheless Not allowed In Qatar

Human embryonic stem cells and human induced Pluripotent stem cells are defined as human cells that are capable of dividing without differentiating for a prolonged period in culture, and are known to develop into cells and tissues of the three primary germ layers. There are some uses of these cells that, although they may come from allowable sources, are nevertheless not allowed in Qatar, as follows:

A. Research in which human embryonic stem cells or human induced Pluripotent stem cells are introduced into non-human blastocysts.
B. Research involving the breeding of animals where the introduction of human embryonic stem cells or human induced Pluripotent stem cells may have contributed to the germ line.

IV. Other Non-Allowable Research

A. The derivation of stem cells from viable human embryos.
B. Research using human embryonic stem cells derived from other sources, including somatic cell nuclear transfer, parthenogenesis, and/or In Vitro Fertilized embryos created specifically for research purposes.
C. Research using imported cells from sources in other countries that generate these cells as described in A or B.
D. Research using human embryonic stem cells obtained by harvesting stem cells from human embryos where the embryo is destroyed.

Stem Cells Obtained from Cord Blood

Cord-blood is an important source for stem cells and has been considered as a specific potential therapy in certain diseases. Because it is a relatively new therapy, our practical knowledge for its utility is limited and its use requires extensive research. Thus, cord blood banks have been created to collect, process, test and store cord blood that could be used for research or donated for use by children and adults faced with a life-threatening illness who need a "stem cell" transplant from a related or unrelated donor.

Despite its current official status as an experimental stem cell source, cord blood is used as an alternative to bone marrow as a source of stem cells for human transplant therapy and/or research.

Cord blood is a "biological" product and is currently considered an experimental source of stem cells. Research or patients who are given cord blood transplants, therefore, are considered "human research subjects" and are entitled to protection under Qatar's "Guidelines, Regulations and Policies for Research Involving Human Subjects". Under those rules, each research or clinical center must obtain approval from its own Institutional Review Board (IRB), must use cord blood under research protocols and is responsible for obtaining consent from the patients who will receive cord blood transplants and thereby become research subjects. Hence, the transplant or treating medical centers must report the outcome of each transplant.

From the regulatory perspective, the donors of cord blood (the mothers who donate their newborn's cord blood) also are "human research subjects" and come under the same rules. For this reason, cord blood must be collected following protocols, policies and procedures formally accepted by the IRB of the treating hospital as well as the IRBs of each of the collaborating collection centers.