Roche Position[1] on Human Stem Cells

Background

Stem cells and treating diseases. Stem cells and their applications offer an enormous potential for the treatment and even the cure of diseases, along with enhancing and extending quality of life. Roche is highly interested in scientific developments in stem cell research and its related applications – both as a discovery tool and as a potential therapeutic modality. Roche is also fully aware of the important societal and ethical questions raised with regard to human stem cell research and its potential applications.

As in all our activities, we follow applicable law and we are open to dialogue with all stakeholders surrounding stem cell research.

About stem cells. Stem cells are particular cells that have the unique capability to renew themselves and to give rise to specialized cell types such as heart cells or blood cells. Stem cells are classified as follows:

- **Adult stem cells** are isolated from tissues including bone marrow, blood, and fat. They are already successfully used for the treatment of patients with leukemia. The treatment of further diseases with adult stem cells is currently under evaluation. Because adult stem cells only develop into a limited number of cell types, the need remains for research with embryonic stem cells.
- **Fetal stem cells** are isolated from placental tissue, amniotic fluid, and umbilical cord blood. They can also be isolated from fetal organs and bone marrow following spontaneous or induced pregnancy termination, or after a stillbirth.
- **Embryonic stem cells** are isolated from donated, leftover IVF embryos or existing embryonic cell lines. These cells are pluripotent, which means that they can develop into any fetal or adult cell type (e.g., blood, heart, brain cells), but they cannot develop into a complete organism.
- **Induced pluripotent stem cells (iPSC)** are derived from adult cells, such as skin cells, and are re-programmed to a pluripotent stage. Once re-programmed, they exhibit similar properties as embryonic stem cells. If iPS cell technology develops as expected, it may eventually replace the need to derive stem cells from embryos.

- **Organoids** are tiny, self-organised three-dimensional tissue cultures that are derived from stem cells. Such cultures can be crafted to replicate much of the architectural and functional complexity of a human organ, or to express selected aspects of it, like producing only certain types of cells. Researchers have been able to produce organoids that resemble the brain, kidney, lung, intestine, stomach, and liver, and many more are on the way. Organoids are useful tools for the study of disease mechanisms.

Stakeholders' Concerns and Expectations

Expectations and hopes that stem cell research will produce transformational medical products are high. Stem cells and their applications may eventually enable researchers to find successful treatments for severe diseases for which there are currently few, if any, effective therapies. Diseases or indications often mentioned in this context include Alzheimer's disease, multiple sclerosis, paraplegia, diabetes, Parkinson's disease, eye disease, heart failure, as well as pediatric rare diseases.

Ethical considerations regarding the use of stem cells vary widely and depend on the type of stem cell, the nature of the research and intended application, as well as personal cultural and religious backgrounds.

In general, stakeholder concerns are derived from the following topics:

- The destruction of blastocysts to derive stem cells. (A blastocyst is a human embryo in a very early, pre-implantation stage of development from which embryonic stem cells can be isolated).

- Whether human embryonic stem cells should be used for research and/or as potential treatments for disease.

- Stem cells sourced from deceased fetuses.

- Whether and how society should accommodate diverse views in regulating the use of stem cells, with due consideration of adherence to robust regulations, the freedom to pursue ethical research, and the goal of patient benefit.

- The creation of embryoids/synthetic embryos/gastruloids using pluripotent stem cells to model early human development and congenital diseases, exploring teratogenicity and organogenesis, and producing highly functional specialized cell types such as beta cells and blood stem cells.

- The creation of human-animal chimera or mixed species embryos.

Roche's Position

Stem cell research is necessary. Worldwide progress in stem cell research over the past years has shown that scientific developments in pluripotent stem cell biology (i.e., the reprogramming of adult stem cells or somatic cells into pluripotent ones) provides a promising opportunity for the future. Roche is engaged in research using these technologies; however, the scientific understanding of these technologies is still at an early stage. Parallel research using both adult and embryonic stem cells, as well as iPSCs, is necessary to increase the understanding of diseases and develop treatments.

Roche is aware of the ethical concerns related to stem cell research. Roche conducts such research in-house as well as in cooperation with external partners, to become technically-enabled in this area. We believe that the vast potential and hope that stem cells might bring to patients to treat, prevent or diagnose a disease justifies this research, provided it is done responsibly, in compliance with laws and regulations, and in dialogue with stakeholders. Ultimately, we aim to develop treatment strategies for incurable or inadequately treated severe diseases.

Principles for using Human Stem Cells in research. Roche is committed to a responsible and transparent approach to stem cell research. For this reason, Roche has developed clear principles for the Use of Human Stem Cells in research. The following principles apply to all Roche research projects involving human stem cells. They include:

- projects using stem cell research as a discovery tool
- projects investigating potential therapeutic modalities.

All Roche employees involved in human stem cell research are subject to these principles that are designed to be applicable worldwide, subject to national laws and regulations.

General Principles for Human Stem Cells for Research

Principles 1-7 apply to research on all human stem cells.

1) The ultimate aim of Roche's research using stem cells is to increase the understanding of serious diseases and to develop effective diagnostic tools and

treatments.

2) Each research project must have clear scientific objectives and design, in particular in accordance with Good Clinical Practice.

3) Prior written, voluntary informed consent of the donor[2] of the genetic material[3] must be obtained before human stem cell research is carried out.

4) Roche will not offer any inducements, financial or otherwise, to donors.

5) Roche will comply with all applicable national laws and regulations on stem cell research, which may differ from country to country.

6) Roche is committed to an open dialogue with stakeholders in this area of research.

7) All external contractors and known collaborators who perform stem cell research for Roche must abide by the same principles, and conduct their research with the same high standards as Roche.

In addition to principles 1-7, principles 8-11 apply to research involving human embryonic stem cells and fetal stem cells.

8) Roche intends to move increasingly toward using technologies such as induced Pluripotent Stem Cells (iPSCs) that could one day replace the need to derive stem cells from embryos. Until such technologies are fully developed, parallel research using both embryonic stem cells and iPSCs will remain necessary.

9) In the case of stem cell lines derived from embryos, Roche uses only embryos that have been created through *in vitro* fertilisation for reproductive purposes, that are no longer needed for those purposes, and that have been donated for research (with voluntary, informed consent).

10) Roche will not engage in human reproductive cloning or the creation of human-animal chimera.

11) Employees with moral distress about working with embryonic or fetal stem cells/tissue should discuss this with their Line Manager and should be permitted to abstain from working with these materials without reprisal.

Outlook

The Roche Science and Ethics Advisory Group (SEAG) offers advice and counsel on a broad range of ethical matters. It is a panel made up of independent, international external experts in bioethics and philosophy, and provides consultative feedback on ethical approaches to biomedical and clinical research, in particular on topics that are perceived as particularly sensitive or controversial by the public at large, in order to take into account as many perspectives as possible. SEAG has provided feedback to this Position Statement, including its revision.

Notes

1. Pertains to Sustainable Development Goals 3 and 16
2. The term donor is generally understood as an individual who donates biological material, and, in the case of human embryo donation (in jurisdictions where applicable), the individual or couple for whose reproductive use embryos were created.
3. Examples of genetic material: tissue, gametes (eggs or sperm), embryos.

This updated position paper was proposed by the Corporate Sustainability Committee and adopted by the Corporate Executive Committee on 13 May, 2013 and entered into force the same day. It was reviewed and revised in February 2023.