

Roche Position on Human Stem Cells and Cloning

Background

Stem cells and their applications offer an enormous potential for the relief of chronic pain, the treatment and even the cure of disease, along with enhancing and extending the quality of life. Roche has a high level of interest 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 stem cell research and its potential applications.

Roche has adopted a policy not to pursue human cloning for reproductive purpose; however, we caution that efforts to codify restrictions on reproductive cloning should not inadvertently impede other important avenues of human health research.

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

Stakeholders' Concerns and Expectations

Expectations and hopes within this area of research are high: stem cells and their applications may eventually enable researchers to find successful treatments for severe diseases for which we can offer few, if any, effective therapies today. Diseases or indications often mentioned in this context include Alzheimer's, multiple sclerosis, paraplegia, diabetes, Parkinson's and heart failure.

In this debate, opinions vary widely, and to some extent, may depend on an individual's cultural and religious background. The discussion centers around the following topics:

- The use (?) of blastocysts (a blastocyst is a human embryo in a very early, preimplantation 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 various diseases.
- Whether and how society should regulate stem cell activities with regard to these diverse views considering how such regulation affects the freedom of research and the benefit for patients.

Roche's Position

Roche is keenly aware of the tremendous potential of this resource for basic science and future health care applications and has therefore recently entered into this field through several institutional and industrial collaborations. These collaborations (see Appendix) involve providing our external partners with compounds from our drug library for toxicological and safety tests and screening in various human stem cell lines in an effort to improve drug development whilst reducing animal testing and potential Serious Adverse Events in human trials.

In addition to these ongoing activities with external partners, Roche has commenced stem cell research in-house, including use of human embryonic stem cells both as a discovery tool and as a potential therapeutic modality. Roche is developing expertise to become technically enabled in this research area and to conduct research on human stem cells and their use in drug discovery. The aim is to develop treatment strategies for incurable or inadequately treated severe diseases, for example, Central Nervous System disorders. Roche has already started research and pre-clinical feasibility projects on the use of adult stem cells also in other devastating diseases like lung fibrosis and evaluates similar indications with high unmet medical need like renal failure or type 1 diabetes.

We comply with existing laws and regulations and engage in dialogue with various stakeholders as we believe that responsible research on human stem cells should be carried out as long as it is aimed at advancing the knowledge required to develop new and more effective therapies for diseases that can currently not, or only partly, be treated.

Worldwide progress in stem cell research within the last several years has shown that scientific developments in pluripotent stem cell biology (e.g. reprogramming adult stem cells or somatic cells) provides a promising opportunity for the future. Roche is closely following these developments as we move toward using these technologies. However, the scientific understanding of these technologies is still at an early stage, therefore parallel research using adult as well as embryonic stem cells is necessary to increase the understanding of diseases and develop promising treatments benefiting patient lives.

Current engagement, initiatives and guidelines

Examples of Roche's current engagement, initiatives and guidelines can be found in the Appendix.

Outlook

The Roche Science and Ethics Advisory Group (SEAG), a body of external experts from the fields of ethics, law, and social science, as well as lay members of the community such as patient advocates, advise Roche on a regular basis on issues associated with innovative developments in biomedicine, with particular emphasis on their ethical impact, including stem cell research. The SEAG has also reviewed this Position Paper and the Roche Principles for Use on Human Stem Cells.

This position paper was proposed by the Corporate Sustainability Committee and adopted by the Corporate Executive Committee on May 12, 2009 and entered into force the same day. It was updated and approved by the Corporate Sustainability Committee on April 28, 2011.

Appendix 1

To Roche Position on Human Stem Cells and Cloning

Current engagement, initiatives and guidelines

Roche Principles for Use on Human Stem Cells

In 2011, Roche adopted principles governing the use of human stem cells for research, which have been developed in consultation with the Roche SEAG. They apply to all research projects involving human stem cells that Roche or its contractors undertake (see Appendix 2).

Collaboration with Massachusetts General Hospital (Boston, USA) and Harvard University (Cambridge, USA)

In the first quarter 2010, Roche commenced a three-to-five year joint research collaboration with Massachusetts General Hospital (Boston, USA) and Harvard University (Cambridge, USA). In this collaboration stem cell technologies are used to advance drug discovery in areas of high unmet medical need with an initial focus on metabolic disorders and cardiovascular disease.

The aim is to develop cellular models of diseases based on human stem cell lines and to investigate the potential efficacy, safety and toxicology profile of new drug candidates from Roche's compound library. Cell lines will be derived from the tissues of healthy volunteers and from patients with various diseases.

Collaboration with I-STEM, Paris, France

In June 2009, Roche signed an agreement with I-STEM, the Institute for Stem cell Therapy and Exploration of Monogenic Diseases, to use I-STEM's technologies in discovering novel therapies for devastating neurodegenerative and psychiatric disorders such as Alzheimer's, schizophrenia, and depression.

In this two-year collaboration, neuronal stem cell proliferation techniques are used to screen Roche's compound libraries and to identify molecules that could potentially be useful in treating neurodegenerative diseases. Scientists from Roche are closely

collaborating with I-STEM researchers in Evry (Paris), as well as carrying out parallel research programs at Roche's headquarters in Basel, Switzerland.

Collaboration with Cellular Dynamics International Inc.

Cellular Dynamics International Inc. (CDI) entered into an agreement with Roche in March 2008 to supply purified cardiomyocytes created from either human embryonic stem cells or induced pluripotent cells. In July 2009, CDI and Roche announced a significant expansion of their existing agreement to test drug development candidates for their potential to cause cardiotoxicity, or damage to heart tissue. Currently, more than 30 percent of all drug failures are a direct result of cardio-toxicological problems. The two-year collaboration aims to enhance drug safety testing to bring promising therapies to patients faster. The two companies collaborate to perform various cell characterisation, toxicological and electrophysiological tests. In March 2011, the collaboration has been completed and transitioned into a standard supply agreement of induced pluripotent stem cell-derived cardiomyocytes as a predictive tool for assessing the potential cardiotoxic effects of developing drug candidates.

Collaboration with UK Stem Cell Consortium (SC4SM -Stem Cells 4 Safer Medicines)

The objective of this consortium is to create a repository of stem cells suitable for toxicology testing in high-throughput platforms. The initiative is divided into two phases, a one-year pilot phase, from 2008-2009, followed by a four-year main phase, in which Roche is participating. The initiative is mainly supported by the UK government (72 percent of costs) with Roche and two other pharmaceutical companies contributing. Activities are coordinated by a Board of Directors and a Scientific Advisory Board. Roche is represented on the steering bodies of this initiative and funded this initiative for the pilot phase.

Appendix 2

Roche Principles for use of Human Stem Cells

Background

Stem cells and their applications offer enormous potential for new treatments, and for extending and enhancing the quality of a patient's life. Roche is keenly aware of the promise of stem cells both as a tool for discovery and as a possible future treatment.

In the discovery phase, stem cells help us better understand how the human body works, and they might help uncover the underlying causes of serious diseases. In a laboratory setting, differentiated cell lines derived from human stem cells might also enable researchers to predict drug metabolism and thus the safety of medicines more accurately than existing techniques, including animal research¹.

The future benefits that stem cells might bring to patients account for the high level of interest Roche has in exploring and developing the technology. Roche currently applies stem cells as research tools as well as tools to investigate potential future treatments.

Stem cells are particular cells that have the unique capacity 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 derived from tissues like bone marrow or cord blood. These cells are already successfully used for the treatment of patients with leukemia. The treatment of further diseases with adult stem cells is currently under evaluation. However, those cells give rise only to limited number of cell types. Hence the need for concomitant research on embryonic stem cells for certain applications is still remaining.
- **Embryonic stem cells**, as their name suggests, are isolated from embryos. These cells are pluripotent, which means that they can develop into any fetal or adult cell type (blood, heart, brain cells, etc.), but they can't develop into a complete organism.

¹ See also Roche's Position on Animal Research:

http://www.roche.com/corporate_responsibility/principles/policies_guidelines_and_positions.htm

- **Induced pluripotent stem cells (iPS)** are derived from cells, such as skin cells, and are being 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.

Research on stem cells raises certain ethical questions. Roche is aware of these ethical concerns. However, we believe that the vast potential and hope that stem cells might bring to patients to treat, prevent or diagnose a disease justifies stem cell research, provided this research is done in a responsible manner, in compliance with laws and regulations, and in dialogue with stakeholders.

Roche is committed to a responsible and transparent approach to stem cell research. For this reason, clear principles for conducting such research have been developed in consultation with Roche's independent Science and Ethics Advisory Group (SEAG)².

SEAG consists of external experts in the fields of ethics, law and social science, as well as lay members of the community such as patient advocates. SEAG advises Roche, on a regular basis, regarding issues associated with innovative developments in biomedicine, including human stem cell research with particular emphasis on their ethical impact.

Scope

The following principles apply to all research projects involving human stem cells that Roche undertakes. These include:

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

All Roche employees involved in human stem cell research are subject to these principles. These principles 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 treatments.

² http://www.roche.com/en/ethics_advisory_group.pdf

- 2) Each research project must have clear scientific objectives and design, in particular in accordance with good clinical practice.
- 3) Prior written, informed consent of the donor³ of the genetic material⁴ must be obtained before human stem cell research is carried out. Such consent is voluntary and can be withdrawn by the donor at any time if and as long as the material is not anonymised⁵.
- 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 open dialogue with stakeholders in this area of research.
- 7) Roche will require that all its external contractors, who perform stem cell research for Roche, follow the same principles and conduct their research with the same high standards as Roche.

Principles for Human Embryonic Stem Cells for Research

In addition to principles 1-7, principles 8-10 apply to research on human embryonic stem cells.

- 8) Roche intends to move toward using technologies such as Induced Pluripotent Stem Cells 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 iPS is 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 and informed consent).
- 10) Roche will not engage in human reproductive cloning⁶.

³ 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.

⁴ Examples of genetic material: tissue, gametes (=eggs or sperm), embryos.

⁵ As anonymised samples and associated data are not traceable back to the human subject, it is not possible to undertake actions such as sample withdrawal, or the return of individual results, even at the human subject's request.

⁶ See also [Roche's Position on Human Stem Cells and Cloning](#)