N A T I O N A L B I O E T H I C S C O M M I S S I O N

RECOMMENDATION

On the use of stem cells in biomedicine and clinical medicine

The National Bioethics Commission, on the invitation of its President, held meetings on June 8th, July 2nd, October 5th, November 23rd and December 21st 2001 in order to examine the ethical and social issues falling within its competence which arise from the use of stem cells in biomedicine and clinical medicine and to formulate a proposal on the matter in accordance with article 10 of the Law 2667/1998. The Commission:

- A) Taking into consideration the ever growing interest of the international scientific community for the use of human stem cells to face incurable up to date diseases, an interest that is explained by the discovery of their important therapeutic potential.
- B) Reckoning though that this use of human stem cells raises ethical problems and dilemmas, since the main source of stem cells is either human embryos deriving from in vitro fertilisation procedures or embryonic tissue following abortions.
- C) Considering that there is a need to clarify that cloning is a technique for in vitro induction of embryo development and therefore a possible way for stem cell isolation.
- D) Finally taking into account the urgent quest for an adequate legislative framework observable today in many national legal orders as well as at the level of European Union

has arrived at the following propositions, that could guide the Greek legislator to face this issue as thoroughly as possible.

Part A

1. Stem cells and developmental stages of the organism

The term *stem cells* refers to undifferentiated cells characterised by a) the capability of self multiplication and b) the potential to differentiate in cells of various tissues and organs of the organism. Stem cells are found in all stages of embryonic development. The earlier the developmental stage the higher the potential to differentiate towards various cell types.

In humans, the stem cells during the first three to four days post-fertilisation are called totipotent, since they can produce all cell types including the membranes and tissues that will support embryo development (e.g., the placenta).

Following these first days, the cells that will give rise to the supporting tissues of the embryo separate from the cells that will give rise to the embryo itself. Embryonic stem cells from this stage onwards are termed pluripotent, since they have lost their ability to differentiate to all cell types needed for a complete embryo development but they retain their potential to differentiate to any other cell type up to day 14th post-fertilisation.

During the third week of embryonic development the evolving organism consists of three different cell layers. Each cell layer is "programmed" to give rise to defined (particular) tissues and organs. Depending on the layer on which the stem cells reside, they differentiate to the predefined cell types.

As embryonic development proceeds, stem cells lose gradually part of their pluripotency. Finally in adults the stem cells that remain, and serve for the renewal of destroyed cells in the tissues, can only differentiate to cell types of the tissues where they reside.

2. *Stem cells in research*

In the field of basic research, the identification of factors that determine the process of cell differentiation during embryonic development is critical for a better understanding of the diseases that are due either to cell differentiation and cell multiplication abnormalities or to disruption of the mechanism responsible for cell renewal and replacement.

In the field of pharmacology, essays on activated pluripotent stem cells can provide a safe way for testing new drugs in a variety of cell types, substituting in many cases direct experimentation with laboratory animals or clinical trials in humans.

In the field of transplantation and replacement of destroyed cells (e.g., Parkinson, Alzheimer) the possibility of a renewable source of cells, tissues and organs derived from pluripotent stem cells, that could be used as grafts, is promising to cover the growing need of organ donation and to treat many incurable to date diseases and disabilities.

Part B

The following recommendations aim to contribute to the formation of a reliable thesis (from a scientific and deontological point of view) and to assist policy-making on the matter of stem cell use. Currently these recommendations could be proved useful for an active participation of Greek representatives in decision-making meetings that take or will take place on the international level. In the future these recommendations could be used in the case of elaboration of specialized relative legislation.

The following points concern the three possible sources for stem cell derivation: points 1 to 3 refer to stem cell removal from embryonic tissue following elective abortion, points 4 to 7 refer to removal

from embryos produced in vitro, points 8 and 9 refer to removal from an adult person. The last two points deal with stem cell use in general (10) and the funding of relevant research projects (11).

1. *Stem cell removal and abortion*

The Commission points out the connection that exists between stem cell removal and the approval of abortion. In both cases the question is whether the worth of the embryo is equivalent to that of a "person". Most members of the Commission recognize that, although abortion naturally raises certain ethical considerations, it is entrenched in the framework of contemporary law. Consequently, to the degree that removal of stem cells following abortion does not raise ethical dilemmas of a different nature, there is no reason to be prohibited in advance.

From the point of view though of a member of the Commission (D. Roupakias), the worth of "person" (as unity of body and soul) exists from the moment of fertilization. Therefore, not only stem cell removal cannot be accepted but also abortion itself is morally questionable. According to this view the only probable acceptable source are somatic stem cells derived from an adult or a minor (if there are intended for his own therapy), in condition that there is firm prohibition for their use in reproductive cloning or embryogenesis (embryo induction for therapeutic purposes) and after setting the technical specifications for approved research laboratories and the terms for conducting such research.

2. *Removal from embryonic tissue*

In accordance with the above mentioned, most members of the Commission consider that stem cell removal from embryonic tissue after abortion is legitimate, on condition that the donors of the gametes have given their consent following appropriate information about the specific use.

3. *Prohibition of agreements*

The Commission considers that antecedent or posterior to conception agreements resorting to abortion and stem cell derivation should be prohibited since they might conceal embryo commercialization and women exploitation that offend her human worth. The relevant penalties should be more severe in cases where such agreements comprise financial compensations.

4. *Research on embryos in vitro*

Most members of the Commission agree with the general principal of article 18, of the Convention on Human Rights and Biomedicine by the Council of Europe, that generally allows research under specified conditions on embryos in vitro. They consider though that further clarification is needed concerning the conditions for embryo research and stem cells derivation.

5. Conditions for stem cell removal from embryo in vitro

Most members of the Commission consider that authentic and informed consent from the donors of the gametes is required in order to derive stem cells from an embryo in vitro. Furthermore the donors of the gametes should be given certified assurance that refusal of consent will not affect any future medical assistance to them.

In order to protect the donors from exploitation by third parties, the possibility of agreements, which comprise financial compensation for stem cell removal, should be precluded.

6. Agreements which comprise financial compensation

Many members of the Commission consider that financial agreements for stem cell derivation from embryos in vitro should be precluded in order to prevent donors' exploitation from third parties. However, other members of the Commission consider that absolute prohibition of such agreements does not guarantee lack of exploitation, since it incites to illegal trade, and functions as an impediment to research progress. According to this point of view, financial agreements could be allowed in the form of either gamete sale or participation of donors to future economic benefits coming from research applications.

7. Embryo production for therapeutic purposes (therapeutic cloning)

Most members of Commission consider that embryo production for therapeutic purposes via cloning and derivation of stem cells from such embryos should not be precluded, in condition that there is no alternative cure.

It is noted that article 18 of the Convention on Human Rights and Biomedicine of the Council of Europe prohibits generally embryo production for research purposes. However, since therapeutic intervention cannot be applied –even on an experimental phase- without research being carried out previously, it seems that article 18 prohibits embryo production for therapeutic purposes as well.

It is however stressed in the Additional Protocol to this Convention (where explicitly it is prohibited embryo production via cloning for reproduction purposes) that "some cloning techniques themselves may contribute to scientific knowledge and its medical application". Based on this, the Commission (by majority) reckons that therapeutic cloning is exempted from the general prohibition of article 18.

8. Removal from a person

The Commission holds the view that removal of somatic stem cells from an adult presupposes his/her authentic consent, under the same guarantees as previously mentioned. It should be appropriate to preclude removal of somatic stem cells from a minor for research purposes but it could be allowed for

his/her own therapy, given that similar to transplants principles for minors' protection personhood are adhered.

9. Anonymity of the donor

In order to avoid unfair reliance and to protect the personhood of the donor and the recipient of the stem cells, it should be apt to observe the rule of donor anonymity, as is the case for transplant donation, in the exception of therapeutic use on him/herself.

10. Use of stem cells on humans

The recipient of stem cells – or tissue and graft that might be derived in the future from stem cells- should be protected against the odds of becoming a research "means". The Commission notes that the Convention on Human Rights and Biomedicine includes the fundamental principles that guarantee the protection of a person from such a threat.

11. Funding research projects

The Commission, given the great importance of research on this field, reckons that the State should elaborate a funding policy of research projects based, among others, on the above-mentioned deontological principles. In order to facilitate the observation of such principles it is recommended that all research projects should be accompanied by a report of ethical adequacy. Research ethics committees that would function in the frame of the funding and research institutions should assess the project based on the report. According to a member of the Commission (D. Roupakias) funding according to the above-mentioned conditions should be restricted exclusively to research on somatic stem cells derived from an adult person.