

## Sources of human embryos for stem cell research: ethical problems and their possible solutions

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**Key words:** embryonic stem cells, therapeutic cloning, embryonic research, medical ethics.

**Summary.** Using different sources of human embryonic stem cells for research raises different ethical problems. Experimenting on embryos created for *in vitro* fertilization but left unused, or embryos, created specially for research raise ethical questions. In the first case – whether using “spare” human embryos for research means a lack of respect for the beginning of human life, and in the second – whether creation of embryos for research is morally worse than experimentation on already created, but unused human embryos. The possibility of therapeutic cloning also raises a question whether it is ethical to create human embryos for therapeutic purposes. When balancing the possible benefit of embryonic stem cell research inventing new therapies, and the ethical problems, raised by this research, a question is posed whether there are any equally effective alternatives to research on viable human embryos that could avoid or at least decrease these problems.

The aim of this literature review is to present the main arguments for and against using different sources of human embryonic stem cells and to acquaint with possible alternatives to human embryo research.

**Methods.** The literature review of the last five years.

**Conclusions.** The currently used sources of human embryonic stem cells and research methods raise ethical objections in certain sectors of society, based on the arguments for the need of respect for the human embryo. However, there already theoretical possibilities of embryonic stem cell research exist, the application of which could decrease the ethical objections to such research. This should be taken into consideration when making decisions on the regulation of embryonic stem cell research. But so far there is no consensus on these questions, and the article presents both favorable and unfavorable opinions regarding this research.

### Introduction

The discovery of human embryonic stem cells has been one of the most exciting developments in the biological sciences in the past decade. The medical community has become very interested in the potential applications of stem cells in regenerative medicine. These potential applications may involve tissue engineering, genetic engineering, and other techniques to repair, replace, or regenerate failing tissues and organs. There is little controversy regarding the application of human adult stem cells, but human embryonic stem cells have raised a number of ethical controversies. The extent of these controversies is partly dependent on the source of embryonic stem cells (1). There are three currently used sources of embryonic stem cells:

1. Already existing embryonic stem cell lines;

2. Embryos that are left unused after *in vitro* fertilization procedures (the so-called “spare” embryos);
3. Embryos created by means of somatic cell nuclear transfer technique (the same technique that was used when Dolly was created) for the purpose of conducting research.

Deriving embryonic stem cells from already existing embryonic stem cell lines is a less controversial practice than deriving them from “spare” embryos left from *in vitro* fertilization procedures. Stem cells derived from embryos created for research by somatic cell nuclear transfer technique raise major ethical objections from certain parts of society, arguing from religious and other moral perspectives (1).

However, even those opposing embryonic stem cell research generally agree that the first source of embryonic stem cells (already created embryonic stem

cell lines) is an acceptable one. They base this opinion on the argument that stem cell lines have already been created and it is impossible to save the lives of former embryos from which they were created, even if harvesting of embryos itself may have been a morally wrong action. Therefore, they allow using these lines on the condition that further creation of embryonic stem cell lines should not be encouraged (2).

The other two sources of embryos raise serious ethical questions, namely, whether using “spare” human embryos for research means a lack of respect for the embryos and whether using embryos created for research purposes is morally worse than using existing “spare” embryos for research. The application of the technique of the somatic cell nuclear transfer, in its turn, raises a question on what ethical problems relate to creating human embryos by means of this technique. For example, the polls in the United States show that there is quite a big public controversy over human embryonic stem cell research and therapeutic cloning. The polls also show that the public remains in the dark about the scientific issues related to embryonic stem cell research. The public appears to have limited knowledge about the specifics of the issue and to have strong reservations about research that destroys embryos (3). Such opposition from some sectors of the society might slow down the progress of stem cell research and, therefore, deprive patients of possible benefits of stem cell-based therapies. Therefore, the ethical conflicts raised by embryonic stem cell research pose a question whether there are some alternatives to embryo research in order to avoid or minimize those conflicts and thus not to slow down the research. There is no unanimous position among the scientists, ethicists and politicians on the above-mentioned ethical issues. The article presents different positions (listing both arguments and counter-arguments) regarding these issues as well as presents possible alternatives to research on viable human embryos.

#### **Does using “spare” human embryos for research mean a lack of respect for the embryos?**

*Argument.* There are a couple of reasons why using spare embryos for research would mean treating them without respect.

- If stem cell therapies became routine treatments, human embryos would become a source of therapeutic materials, and using them as merely means to achieve the ends may decrease the respect for human life (4). There is also a danger that such devaluation of human

embryos at the very beginning of their life would encourage a policy of sacrificing the vulnerable for the benefit of others (5, 6). This is the so-called “slippery slope” argument, meaning that if we accept a certain action, such acceptance takes us to further toleration of other presently unacceptable actions. For example, an instrumental use of embryos may increase the social toleration of the loss of life, which may make it easier for society to accede to currently more controversial practices involving the ending of life. In its turn, that could ultimately put at risk persons with disabilities and the aged (5, 6). If we consider a human pre-embryo as a human being, utilitarian arguments stressing the benefit of embryonic stem cell research cannot justify an unethical act and transform it into ethical one (7). Even if we regard research on embryos as not wrong, it may still open the way to a “slippery slope” of dehumanizing practices, such as embryo farms, cloned babies, the use of fetuses for spare parts, and the commodification of human life (8).

- According to some moral philosophers, there is a moral difference between acts and omissions, between actively killing something, and passively failing to intervene to stop its destruction from other causes (when one could have intervened). Even though the outcome is the same in each case, it can be argued that it is worse to actively bring about the destruction oneself (5).

*Counter-argument.* There are also several reasons why using spare embryos for research would not mean the treatment of human embryos without respect.

- There is no reason to believe that destruction of embryos will undermine the respect for human life in society. The destruction of embryos in connection with *in vitro* fertilization treatment as well as abortion have been practiced for some time, and no special change in the way we view the value of human life has been observed. Destruction of spare embryos during *in vitro* fertilization (in the cases when they are neither implanted nor donated to other couples) could thus be considered more problematic than the destruction of spare embryos resulting from *in vitro* fertilization to produce stem cells for research with therapeutic aims (9).

- If we consider that it is immoral to sacrifice embryos for the sake of curing or treating devastating diseases, we should also consider that it is immoral to sacrifice them for the sake of treating infertility. To regard an embryo as a mere thing, open to any desired use, does not respect its significance as potential human life. It remains a question whether embryos

can be used for all the purposes or only for certain. For example, few would favor the destruction or use of embryos for the purpose of developing a new line of cosmetics (8). Currently the accepted position is that human embryos should be used only for research purposes with therapeutic aims to tackle serious human diseases.

- Whether the spare embryos are donated for research or left to perish after being defrosted, they are actively destroyed anyway – either after they have served as the subjects of research or after the time limit for keeping them in the freezer has expired. If the result of the embryo research can help to cure so far incurable diseases, the interest of those who are suffering from these diseases should be considered (10, 11) and spare embryos should better be used for research than wasted after their freezing time has expired.

**Is using embryos created for research purposes morally worse than using existing “spare” embryos for research?**

*Argument.* There is a moral difference between *different intentions*, although the final result is the same. In the case of “spare” embryos, the initial reason for creating them was to use them for fertility treatment and thus to give them the chance of becoming human beings. Therefore, research on “spare” embryos left over from fertility treatment is morally more acceptable, according to some writers, than research on embryos created specifically for research purposes, knowing that they will have to be destroyed in the course of conducting research (12).

*Counter-argument.* We must bear in mind, however, that in both cases the destruction of the embryos, either “spare” or created for research, is inevitable, since there is an international consensus that embryos used for research must not be inserted in the womb of a woman. We must also take into consideration that in fact there is nothing unnatural about creation of “spare” embryos, at least in the case of *in vitro* fertilization treatments, since “spare” embryos are produced in almost every natural pregnancy as well. Most of these spare embryos have to die enabling a sibling embryo to come to birth. The loss of embryos is an inevitable consequence of many pregnancies. The production of spare embryos, created only to perish, is not unique to assisted reproduction techniques. Therefore, in normal *in vitro* fertilization as in normal sexual reproduction, the creation and “sacrifice” of embryos in pursuit of a live child is accepted as natural and necessary (13). It can further

be argued that if it is normal to create “spare” embryos for *in vitro* fertilization purposes, knowing that they are created to perish, it should be normal to create embryos for research purposes. Anyone who renounces the production of embryos for research purposes simultaneously renounces a wide range of research possibilities and, therefore, therapeutic possibilities. Stem cells harvested from surplus embryos, for example, do not necessarily match well with the needs of patients. If one produces embryos for research purposes, one has a better chance that they will match the needs of future patients, since stem cell lines created from embryos produced by means of therapeutic cloning would be immunologically compatible to patients (see the following chapter) (2).

**What are the ethical problems related to therapeutic cloning?**

Somatic cell nuclear transfer or, in other words, cloning is the technique used when Dolly was created. It involves transferring the adult nucleus from a somatic cell into an egg without a nucleus. The term “therapeutic cloning” refers to the procedure of deriving an embryonic stem cell line from an embryo created by means of this technique, using the nucleus from the patient’s somatic cell. If such an egg containing the nucleus of the patient’s somatic cell was stimulated for example with electricity to develop to the blastocyst stage, pluripotent stem cells could be derived from the blastocyst to form cells genetically identical to the patient (14). In 2004 South Koreans proved that therapeutic cloning is possible. They have created a human stem cell line using nuclear transfer technique. This success in research confirms potential of therapeutic cloning, although clinically useful results are still a long way off (15). The term “therapeutic cloning” is somewhat misleading, since the procedure itself is therapeutic neither for the created embryo nor for the patient – it is the application of the derived stem cells for treatment that can be therapeutic. Concern has also been expressed that this not yet completely tested technique is too early labeled as “therapeutic” and that such “misnomer” distracts attention from significant practical and ethical implications of its use and raises unrealistic expectations (16). Also, the same term has been used by Professor Antinori, but meaning a completely different thing – he was proposing to use reproductive cloning to provide progeny for incurably sterile patients (personal communication with Prof. A. McLaren). Besides, the difficulties with the terminology, there is also no consensus regarding the ethical aspects of the so-called

“therapeutic cloning”.

*Argument.* There are several reasons why therapeutic cloning should be pursued:

- Embryo experimentation (including therapeutic cloning) is not sufficiently wrong to outweigh the benefits of embryo research. Although clinical benefits are still in the future, they could be numerous. For example, in the area of transplantation, therapeutic cloning could allow the extraction of pluripotent embryonic stem cells and offer a potentially limitless source of cells for tissue engineering applications (17–19). Therapeutic cloning could also help in the novel treatments of diabetes mellitus. Stem cells could offer the potential for use as renewable sources of glucose-responsive, insulin-secreting cells. Somatic cell nuclear transfer avoids many of the problems associated with heterologous transplantation (14, 20). A concern has been expressed that the so-called precautionary principle when regulating stem cell research would harm patients by slowing the development of new therapies. Instead it has been suggested to reject the precautionary principle and “rely on conscientious trial and error as a superior way to approach implementing new biomedical technologies ethically” (21).
- Even if destruction of human embryos as a result of conducting research is viewed as “killing”, it can be argued that the moral obligation not to kill, although very strong, is not one that can never be overridden. There may be some circumstances where very great harms can be avoided by actively ending someone’s life. For example, assassinating Hitler might have saved 6 million Jewish people. Similarly, sacrificing human embryos for research might lead to finding cure for millions of suffering patients (5).
- There could be a great benefit for research from cloning for stem cells, since embryonic stem cell lines could be created from embryos containing the nucleus of somatic cells of patients suffering from very rare genetic diseases or even common diseases but with a complex genetic or environmental basis. Such stem cell lines would be very beneficial for researchers since otherwise it may be very difficult to get enough of such tissues for biochemical and physiological analysis, as such cases are rare. Once such stem cell lines have been created, they could be studied by many researchers and possibly contribute to future therapy (personal communication with Prof. A. McLaren).
- We do not know if embryos produced by somatic cell nuclear transfer technique have the same potential as “normal” early embryos to develop into viable human beings (2). If it is discovered that they do not have the same potential, this could be one more

argument in favor of therapeutic cloning.

*Counter-argument.* There are also several ethical arguments against therapeutic cloning:

- If cloned human embryos were created, it would be much easier for someone misguided to go to the next step and allow them to be implanted, or for someone rich enough to seek a clandestine “off-shore” treatment of infertility by means of reproductive cloning (11). Thus it can be argued that allowing research on embryos created by somatic cell nuclear transfer would be a step towards human reproductive cloning and its acceptance by society (4, 6). If all the technical problems in the first steps of cell nuclear replacement techniques are solved successfully then it would become both easier and more tempting (because certain risks have been reduced) to try to use nuclear replacement techniques for reproductive cloning (22). However, there is a counter-argument to this line of thinking. As the worldwide prohibition of certain technologically possible experiments with human beings shows, legislation is able to restrict the use of certain technologies worldwide (such as non-somatic gene therapy). Therefore, legislation could prohibit reproductive cloning even if the use of somatic cell nuclear transfer technology to produce embryos for the harvesting of embryonic stem cells may be a decisive step in the development of the technology of cloning (2). However, it is important to outlaw human reproductive cloning worldwide if therapeutic cloning is allowed (11).
- There is also a danger of *commercial pressures* driving to conduct more research on embryos and a danger of decrease of respect for the intrinsic value of human life and its *reduction to an asset for researchers*. This danger especially becomes an issue with the pressure from the scientific and medical communities to go ahead, in order not to delay therapies or to lose opportunities to other countries (11). The danger of commercialization of human embryos poses a danger irrespective of religious beliefs on the moral status of the embryo. It does not require religious beliefs to recognize that we belong to a wider society that has embedded traditions about how we reproduce. Therefore, the way we treat the beginning of human life, particularly if we commercialize them, has wider implications. By commercialization we would risk to turn those embedded social traditions into instrumental matter open to economic speculation. If this happens, what cost would we pay (23)?
- There is also a danger of exploitation of women. If stem cells are to be produced from embryos that are not “spare” after *in vitro* fertilization, the ova for

this production must come from women (22). Therapeutic cloning would require large numbers of oocytes and this demand could result in putting *pressure on women to donate eggs*. There is a danger that in this way their acts of altruistic donation may be demeaned (5, 6). In the initial research phase the number of needed ova can be relatively small, but if routine stem cell-based therapy becomes available, this number may become very large (22, 23). With a therapy based on somatic cell nuclear replacement from the intended recipient in order to ensure perfect immunological compatibility, at least one ovum would be needed for each patient. It is, therefore, unclear how this new practice of procuring ova for non-reproduction purposes would influence the status of women in society (22). There is a risk that embryonic stem cell technology and therapeutic cloning have the potential to alter the social meaning of both human conception and human mortality (23). Women may become at risk of being alienated from their reproductive labor, and their ova could become at *risk of becoming the means to achieve the aims* (5). We should also ask ourselves a question on who would be most likely to “donate” their eggs and why? Most likely, it would be poor women, quite possibly from countries with less stringent (or no) legal prohibition against such exploitation (such as developing countries). Therapeutic cloning could lead to the commercialization and exploitation of such women to provide the raw materials for the treatment of developed world diseases. In the worst case, it could even lead to a global trade in human eggs (23). There is a concern that it would be mostly the women from the Southern countries that would possibly be exploited as ovum donors, since many of those countries have no national ethics committees or guidelines (24).

However, there is a possible solution to the problem of the shortage of human oocytes. They could be derived from embryonic stem cells. This has already been proved possible on mouse models in 2003 (25). If the derivation of oocytes from human embryonic stem cells becomes possible then there will be no need to harvest female oocytes (2). Another possible source of oocytes for nuclear transfer research could be the oocytes that have failed to fertilize during in vitro fertilization treatments. Such oocytes could prove to be adequate to support the development of embryos created by means of nuclear transfer. Yet another option to obtain unfertilized eggs would be to use primordial oocytes (there are many thousands of them in the ovaries of aborted female fetuses) matured in vitro, if such technique became possible (personal communication with Prof. A. McLaren).

- It is unclear whose lives would be made better by stem cell-based therapies. The patients in the poorer sections of the developed world and the vast majority of patients in the developing world would be unlikely to have access to any of this technology, even if it becomes a routine therapy. Looking at the history of pharmaceutical conglomerates withholding generic therapies in the quest for profit and dumping unsafe drugs on developing world markets there are reasons to fear that stem cell-based therapies would be accessible only to small numbers of patients (23). It would probably prove to be a time-consuming and very expensive method for treating disease. Thus, it is questionable whom the new technique would benefit and at what cost, if ever developed (26).

#### **What could be the alternatives to embryo research in order to avoid or minimize ethical conflicts?**

Whether embryonic stem cell research involving the destruction of embryos is the right thing to do or not, will partly depend on what the alternatives are, and how their particular benefits and drawbacks balance out. To date, eight possible alternatives to conducting research on viable human embryos have been identified.

*Alternative 1.* Stem cells have been identified in adult tissues including skin, intestine, liver, brain and bone marrow (the latter stem cells have been studied most thoroughly) (27). Therefore, those who are against embryo research argue that adult stem cells could be used instead of embryonic stem cells. According to the current scientific understanding, however, it cannot be presumed that adult stem cells would be universally productive in the same way as the embryonic stem cells (11). There are several reasons that make adult stem cells less attractive than embryonic stem cells as sources for research and therapeutic application:

1. It is difficult to isolate stem cells from adult tissues;
2. The cells are few in number;
3. It is difficult to keep adult stem cells proliferating in culture;
4. To date, it appears that cultured adult stem cells give rise to only a limited number of cell types – they cannot be pluripotent<sup>1</sup> like embryonic stem cells;
5. They are adult cells and have been exposed to a lifetime of environmental toxins and have also accumulated a lifetime of genetic mutations (27).

<sup>1</sup> Able to differentiate into all the possible types of cells that can be found in human body. Embryonic stem cells can be pluripotent and have such a capacity.

For all the above-mentioned reasons and according to presently existing knowledge it would not be possible to use adult stem cells as effectively as embryonic ones. In order to avoid the use of embryos, it has been suggested that priority should be put on *nuclear transfer research* by direct programming from one adult body tissue type to another (11). In this way, adult stem cells could be used to attain the same goals as would be sought with embryonic stem cells.

The problem with this alternative is, however, that this would probably be impossible without some human embryo research to work out the method. Thus it would raise another ethical problem: whether a limited and fixed number of experiments should be allowed to obtain the data necessary to avoid any such use of embryos in the future (11). Most researchers believe, however, that both adult and embryonic stem cells will be required because both have certain limitations, and different diseases may require different routes for producing the relevant replacement cells. To find out which cells are going to be suitable for new therapies more research needs to be done with adult, fetal and embryonic stem cells as well as cells from cord blood, and it is premature to decide which cell source should be prioritized (28, 29).

*Alternative 2.* A possible way to avoid destroying viable human embryos in the course of conducting embryonic stem cell research would be to produce non-viable human embryos by taking a human cell and performing a nuclear transfer into a de-nucleated egg of other suitable species (11). Harvesting stem cells from blastocysts created by trans-species somatic cell nuclear transfer is an acceptable procedure if there is no possibility of creating viable hybrid creatures and if such research is done for therapeutic purposes (2). The problem with this technique, however, is that it is unknown yet whether the use of ova from other species is technically possible and whether the stem cells produced in this way would be functionally and immunologically equivalent to those produced using human ova (22). Another problem is that even though this technique avoids the creation of viable human embryos, the mixing of human and animal genetic material might raise an ethical objection in society (11). Although it can be argued that ethical problems might be less than in the case when human ova are used, because the moral status of these "less than human" embryos could be seen as less important, this technique is very controversial (22). Like in the case of xenotransplantation, there are serious concerns about using ova from other species due to the risk of retrovirus. The crucial question here is not the moral

status of such semi-human blastocysts, but rather whether it is permissible to transgress the natural border between species (2). In 1984, the Warnock Report in the United Kingdom recommended that trans-species fertilization could be used for the assessment or diagnosis of subfertility with a condition that the development of any resultant hybrid should be terminated at the two-cell stage (30). If one follows the same line of thought, then the decisive factor in the aim of this kind of stem cell research is the therapeutic purpose, just like the therapeutic purposes mentioned in the Warnock Report. The blastocyst created in the course of such research would be destroyed after harvesting the stem cells even though there is no possibility that the blastocyst created could develop into a fetus (2).

*Alternative 3.* Embryonic stem cells used for transplantation may be immunologically incompatible with the recipient if they are not obtained by means of therapeutic cloning. To solve this problem of immunological incompatibility a "tissue bank" with a sufficiently large number of different embryonic stem cell types could be established. Such a tissue bank could serve to generate tissues that can be immunologically matched with different recipients. However, to establish such a tissue bank would require a huge number of human embryonic stem cell lines. The drawback of such an embryonic stem cell bank is that it would be technically difficult and expensive to generate (5).

*Alternative 4.* Instead of creating new embryos and embryonic stem cell lines, the scientists could use embryonic stem cells, and the differentiated cells obtained from them, which are supplied by other researchers (from other countries where embryonic stem cell research is allowed) or are commercially available. However, this alternative would hardly be acceptable to those who regard therapeutic cloning or using spare embryos for research as an immoral act (31).

*Alternative 5.* A new possibility has recently been discovered to grow cells from embryos at an earlier stage than it has been done before. The scientists managed to *grow stem cells from four-day-old human embryo called morula* (32). Previously, stem cells were grown only from blastocyst-stage embryos, which are a day or two older and have more specialized tissues. The new method is advantageous because it avoids culturing embryos until they grow into blastocysts, a period when perhaps half of them stop growing or die. It also cuts out a laborious step from the currently applied technique, in which the outer shell of the blastocyst is destroyed to gain access to the pre-

cious 20–30 stem cells inside. In the new method, the entire morula of around 60–70 cells is grown in culture (33). It can be argued that since this new method of research requires only very early human embryos, such research could perhaps be considered more ethical than the conventionally used method. However, the opponents of embryonic research would still point to the fact that a human embryo, even if at an earlier stage, is still destroyed to create stem cell lines.

*Alternative 6.* There is a theoretical possibility to avoid the destruction of the embryo after embryonic stem cell line is derived from its cells. Researchers want to test the radical concept of growing stem cells from a single cell plucked from a morula-stage embryo without damaging the rest of it. In this way, the single cell could be used to derive the stem cell line, and the rest of the cells of the morula would continue to develop as a human embryo. That would enable the couples undergoing *in vitro* fertilization treatment to have one of their embryo's cells removed before the embryo is implanted in the womb. The removed cell could be grown into a stem-cell line and stored in case the child should need it for disease therapy in the future. In this way the child would have an immunologically compatible stem cell line for future therapeutic purposes, if needed. Researchers might also use the new method to grow stem cells from morula-stage embryos that have ceased to develop and are therefore incapable to grow into babies. These techniques would avoid the destruction of the entire embryo and could, therefore, remove a big obstacle from an ethical standpoint (33).

*Alternative 7.* If embryonic stem cell research were mainly prohibited in order to preserve the uniqueness of each embryo from being destroyed, a possible solution would be to split the embryo. One could be saved in order to preserve the unique genetic code and the other could be destroyed to harvest embryonic stem cells. It could also be possible to use somatic cell nuclear transfer technique by which no new unique genetic code is produced, if the egg and the somatic cell are from the same person (2).

*Alternative 8.* If it became possible to genetically modify the oocytes derived from embryonic stem cells in some way guaranteeing that they would never have the potential to develop into a viable human being, this option could possibly be a solution to the ethical problem. For example, blastocysts produced by somatic cell nuclear transfer into enucleated oocytes created from human stem cells and genetically modified would lack the potential to develop into viable

human beings. The moral status of such blastocysts would be the same as the moral status of non-human beings as far as the protection of their lives is concerned. Following this method of research, no human embryos with a potential to develop into viable human beings would be destroyed. In addition, there would be no need for female oocytes. Furthermore, the procedure of somatic cell nuclear transfer could never develop into reproductive cloning because of the missing potential to develop into a viable human being. Therapeutically, this option would also be beneficial: the stem cells harvested from this type of blastocyst would be compatible with the donor of the somatic cell. There would be no immunological reaction. And there would be a never-ending source of stem cells available for the researchers. However, this option is still only a hopeful thought (2).

### Conclusions

All the currently acknowledged methods of embryonic stem cell research and sources of embryos for such research raise numerous ethical questions and ethical objections based on the respect for the moral status of the early human embryo, or, in other words, the moral status of the fertilized human egg. There are, however, theoretical possibilities of embryonic stem cell research methodology that could contribute to solving some of the ethical problems related to embryonic stem cell research. The new research possibilities could possibly tackle the ethical problems related to the moral status of the early human embryo as well as the sources of human oocytes needed for research and therapeutic purposes. When discussing the ethics of embryonic stem cell research, these new theoretical possibilities of embryonic stem cell research methodology should be taken into consideration. Even though some of them have only been tested on animal models and others still remain theoretical possibilities, they might be able to change the ethical arguments regarding embryonic stem cell research if they start to be widely applied in research. When taking regulative decisions today regarding embryonic stem cell research these theoretical possibilities as well as the interests of the patients who could possibly be helped by applying stem cell-based therapies should be carefully weighed against current ethical concerns regarding the moral status of the early embryo.

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## Žmogaus embrionų šaltiniai kamieninių ląstelių tyrimams Etinės problemos ir galimi jų sprendimai

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**Raktažodžiai:** embrioninės kamieninės ląstelės, terapinis klonavimas, embrionų tyrimai, medicinos etika.

**Santrauka.** Skirtingų žmogaus embrioninių kamieninių ląstelių šaltinių panaudojimas šių ląstelių tyrimams yra susijęs su skirtingomis etinėmis problemomis. Ar eksperimentuojama su embrionais, sukurtais dirbtiniam apvaisinimui (bet tam nepanaudotais), ar embrionais, sukurtais specialiai tyrimams – abiem atvejais kyla etinių problemų. Pirmasis atvejis: ar nepanaudotų žmogaus embrionų atidavimas tyrimams reiškia nepagarbą užsimezgasiai žmogaus gyvybei? Antrasis atvejis: ar embrionų kūrimas specialiai tyrimams yra mažiau moralus nei kitais tikslais sukurtų ir nepanaudotų embrionų panaudojimas tyrimams? Terapinio klonavimo galimybė taip pat kelia klausimą, ar etiška kurti embrionus terapiniais tikslais. Įvertinus galimą embrioninių kamieninių ląstelių tyrimų naudą, kuriant naujus terapijos būdus, ir etines problemas, kurių randasi dėl šių tyrimų, galima iškelti klausimą, ar nėra efektyvių alternatyvų tyrimams su gyvybingais žmogaus embrionais, kurių pritaikymas leistų išvengti šių problemų ar bent jas sumažinti.

Šios literatūros apžvalgos tikslas – apžvelgti pagrindinius argumentus už ir prieš, skirtingų kamieninių ląstelių šaltinių panaudojimą bei supažindinti su galimomis embrionų tyrimų alternatyvomis.

*Metodai.* Paskutinių penkerių metų literatūros apžvalga.

*Išvados.* Dabar tyrimams naudojami embrioninių kamieninių ląstelių šaltiniai ir šių ląstelių tyrimų metodai tam tikrai visuomenės daliai sukelia etinių prieštaravimų, grindžiamų nepagarba žmogaus embrionui. Beje, jau yra teorinių embrioninių kamieninių ląstelių tyrimų galimybių, kurių pritaikymas galėtų sumažinti etinius prieštaravimus. Į tai reikėtų atsižvelgti priimant embrioninių kamieninių ląstelių tyrimų reguliavimo sprendimus. Deja, kol kas nėra sutarimo šiais klausimais. Literatūros apžvalgoje pateikiamos tiek palankios, tiek nepalankios nuomonės apie tokį tyrimą.

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### References

1. Daar AS, Bhatt A, Court E, Singer PA. Stem cell research and transplantation: science leading ethics. *Transplant Proceed* 2004;36:2504-6.
2. Knoepffler N. Stem cell research: an ethical evaluation of policy options. *Kennedy Institute Ethics J* 2004;14:55-74.
3. Nisbet MC. The polls-trends: public opinion about stem cell research and human cloning. *Pub Opin Quart* 2004;68:131-54.
4. Campbell AV. Ethical issues in therapeutic cloning. Round table “Ethical aspects of human stem cells research and uses”, Brussels, 26 June 2000 [cited 2005 Jan 10]. Available from: URL: [http://europa.eu.int/comm/european\\_group\\_ethics/docs/dp15rev.pdf](http://europa.eu.int/comm/european_group_ethics/docs/dp15rev.pdf)
5. Rickard M. Current issues brief No. 5, 2002-03: Key ethical issues in embryonic stem cell research. Department of the Parliamentary Library, Australia, 2002 [cited 2005 Jan 12]. Available from: URL: <http://www.aph.gov.au/library/pubs/CIB/2002-03/03cib05.pdf>
6. Nippert I. The pros and cons of human therapeutic cloning in the public debate. *J Biotechnol* 2002;98:53-60.
7. Chu G. Embryonic stem-cell research and the moral status of embryos. *Internal Med J* 2003;33:530-1.
8. Sandel MJ. Embryo ethics – the moral logic of stem-cell research. *New Eng J Med* 2004;351:207-9.
9. Welin S. Ethical issues in human embryonic stem cell research. *Acta Obstetrica et Gynecologica Scandinavica* 2002;81:377-82.
10. Pennings G, Van Steirteghem A. The subsidiarity principle in the context of embryonic stem cell research. *Human Reproduct* 2004;19:1060-4.
11. Bruce D. Church and Society Commission of the Conference of European Churches. “Therapeutic uses of cloning and embryonic stem cells”. A Discussion Document of the Bioethics Working Group of the Church and Society Commission. Conference of European Churches. Society, Religion and Technology Project, Church of Scotland, 5 September 2000 [cited 2005 Jan 10]. Available from: URL: <http://www.srtp.org.uk/clonin50.htm>
12. Muscati SA. Embryonic stem cell research and the law – a Canadian and international perspective, 2002 [cited 2005 Jan 12]. Available from: URL: [http://www.innovationlaw.org/lawforum/pages/Stem\\_cell\\_paper2.doc](http://www.innovationlaw.org/lawforum/pages/Stem_cell_paper2.doc)
13. Harris J. Stem cells, sex, and procreation. *Cambridge Quarterly Healthcare Ethics* 2003;12:353-71.
14. European Group on Ethics in Science and New Technologies. Group of Advisers on the Ethical Implications of Biotechnology to the European Commission. Opinion No. 15 14/11/2000 Ethical aspects of human stem cell research and use [cited 2005 May 7]. Available from: URL: <http://europa.eu.int/>

- [comm/european\\_group\\_ethics/index\\_en.htm](http://comm/european_group_ethics/index_en.htm)
15. Tamkins T. South Koreans create human stem cell line using nuclear transfer – Research confirms potential of therapeutic cloning, but clinically useful results are still a long way off. *Lancet* 2004;363:623.
  16. Shanner L. Stem cell terminology: practical, theological and ethical implications. *Health Law Rev* 2002;11:62-6.
  17. Hipp J, Atala A. Tissue engineering, stem cells, cloning, and parthenogenesis: new paradigms for therapy. *J Experiment Clin Assist Reproduct* 2004;1:3.
  18. Koh CJ, Atala A. Therapeutic cloning applications for organ transplantation. *Transplant Immunol* 2004;12:193-201.
  19. Shufaro Y, Reubinoff BE. Therapeutic applications of embryonic stem cells. *Clin Obstet Gynaecol* 2004;18:909-27.
  20. Ben-Yehudah A, Witchel SF, Hyun SH, Chaillet JR, Schatten G. Can diabetes be cured by therapeutic cloning? *Pediatric Diabetes* 2004;5:79-87.
  21. Bailey R. Deciding about your health care: the ethicist as policy-maker. *Health Care Analysis* 2001;9:265-81.
  22. Holm S. Going to the roots of the stem cell controversy. *Bioethics* 2002;16:493-507.
  23. Cregan K. Ethical and social issues of embryonic stem cell technology. *Intern Med J* 2005;35:126-7.
  24. Dickenson D. Commodification of human tissue: implications for feminist and development ethics. *Develop World Bioethics* 2002;2:55-63.
  25. Hübner K, Fuhrmann G, Christenson LK, Kehler J, Reinbold R, De La Fuente R et al. Derivation of oocytes from mouse embryonic stem cells. *Science* 2003;300:1251-6.
  26. Borge OJ, Evers K. Aspects on properties, use and ethical considerations of embryonic stem cells – A short review. *Cytotechnology* 2003;41:59-68.
  27. Fishbach GD, Fischbach RL. Stem cells: science, policy and ethics. *J Clin Invest* 2004;114:1364-70.
  28. Orive G, Hernandez RM, Gascon AR, Igartua M, Pedraz JL. Controversies over stem cell research. *Trends Biotechnol* 2003;21:109-12.
  29. Vats A, Tolley NS, Polak JM, Buttery LDK. Stem cells: sources and applications. *Clin Otolaryngology* 2002;27:227-32.
  30. Warnock M. The Warnock report. *Br Med J* 1985;291:187-90.
  31. Dios Vial Correa J. Declaration and the scientific and therapeutic use of human embryonic stem cells. Pontifical Academy for Life, Vatican City, 25 August 2000 [cited 2005 Jan 12]. Available from: URL: <http://www.cin.org/docs/stem-cell-research.html>
  32. Reproductive BioMedicine Online [cited 2005 May 10]. Available from: URL: <http://80-www.rbmonline.com.ludwig.lub.lu.se/Article/1558>
  33. Pearson H. Early embryos fuel hopes for shortcut to stem-cell creation. *Nature* 2004;432:4.

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Unlabelled: Using different sources of human embryonic stem cells for research raises different ethical problems. When balancing the possible benefit of embryonic stem cell research inventing new therapies, and the ethical problems, raised by this research, a question is posed whether there are any equally effective alternatives to research on viable human embryos that could avoid or at least decrease these problems. Stem cells derived from embryos created for research by somatic cell nuclear transfer technique raise major ethical objections and constraints from certain parts of society, arguing from religious and other moral perspectives [47,331].

- 2 Scientific Background of Human Embryonic Stem Cell Research.
- 3 Addressing Ethical and Scientific Concerns Through Oversight.
- 4 Current Regulation of Human Embryonic Stem Cell Research.
- 5 Recruiting Donors and Banking hES Cells.

Great possibilities for improvements in human health are offered by research using human stem cells, both adult and embryonic. Like many scientific advances, these technologies raise questions about balancing the evident promise against the potential for inappropriate application. In the case of embryonic stem cell research, there are differing opinions within our society about the relative merits and risks of various approaches and there are philosophical differences about what is or is not appropriate. Using different sources of human embryonic stem cells for research raises different ethical problems. Experimenting on embryos created for in vitro fertilization but left unused, or embryos, created specially for research raise ethical questions. In the first case--whether using "spare" human embryos for research means a lack of respect for the beginning of human life, and in the second--whether creation of embryos for research is morally worse than experimentation on already created, but unused human embryos. The possibility of therapeutic cloning also raises a question whether it is ethical to create human embryos for therapeutic purposes. Research involving human embryonic stem cells and human non-embryonic stem cells has the potential to lead to better understanding and treatment of many disabling diseases and conditions. Here, he expresses his position on the field and its future. Advances over the past decade in this promising scientific field have been encouraging, leading to broad agreement in the scientific community that the research should be supported by Federal funds. For the past 8 years, the authority of the Department of Health and Human Services, including the National Institutes of Health (NIH), to fund and conduct human embryonic stem cell research has been limited by Presidential actions. Stem cell research creates ethical and policy concerns associated with every advance in biomedical research, including concerns relating to the ethical conduct of basic and clinical research, justice and resource allocation, equal access to health-care, intellectual and other property rights, and public accountability. Adult stem cell research falls under the heading of research with human subjects, for which adequate regulation and protection exists in most countries. Because of their unique capacity to give rise to virtually any cell type in the body (their pluripotency), and their ability to expand indefinitely in the

10 One suggested solution to the problem of "killing" embryos in stem cell research is simply to opt for less controversial ways of obtaining stem cells.