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What Can We Say About Embryonic Stem Cell Researches from Ethical Point of View?

Embriyonik Kök Hücre Araştırmaları Hakkında Etik Açıdan Ne Söyleyebiliriz?

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ABSTRACT Stem cell researches are among the primary areas in which the humanity has experienced exciting developments since the end of the 20th century. The discovery of the potential of stem cells in the regeneration of devastated cells has been a source of hope for many incurable diseases. Another type of stem cell is embryonic stem cells. Embryonic stem cells are obtained from the cells in the embryo (which consists of only 50-150 cells a few days after fertilization) that have just begun to develop. These cells can transform into any cell of more than two hundred species found in the human body. Human embryonic stem cells are not debated not only by the biologists by whom they were discovered but also by the medical profession, media, ethicists, teologian, governments and politicians. It is an inevitable fact that there might also be inevitable ethical and legal problems in stem cell practices, which comprise a new and very dynamic area. In this context, embryonic stem cell research from ethical point of view; have a particular importance. In the light of the relevant literature, this article emphasizes basic ethical topics such as the usage opportunities of human embryonic stem cell, regulations developed by various countries regarding the application of these techniques and violation of patient rights, informed consent, accessibility to treatment due to expensiveness, and making it trading.

Keywords: Embriyonic stem cell; medical law; patient rights; informed consent; research ethics

ÖZET Kök hücre araştırmaları, insanlığın 20. yüzyılın sonlarından bu yana heyecan verici gelişmeler yaşadığı başlıca alanlar arasındadır. Kök hücrelerin harap olmuş hücrelerin yenilenmesindeki potansiyelinin keşfedilmesi tedavi edilmesi olanaklı olmayan pek çok hastalık için umut kaynağı olmuştur. Bir başka kök hücre çeşidi ise embriyonik kök hücrelerdir. Embriyonik kök hücreler henüz yeni gelişmeye başlamış (döllenmeden birkaç gün sonraki, sadece 50-150 hücreden oluşan) embriyonun içindeki hücrelerden elde edilir. Bu hücreler başkalaşarak insan vücudunda bulunan iki yüzden fazla türdeki herhangi bir hücreye dönüşebilir. İnsan embriyonik kök hücreleri, sadece keşfedildikleri biyologlar tarafından değil, tıp mesleği, medya, etik uzmanları, teolog, hükümetler ve politikacılar tarafından da tartışılmaktadır. Yeni ve çok dinamik bir alan oluşturan embriyonik kök hücre araştırmalarında üstesinden gelinemez etik ve yasal sorunların olabileceği kaçınılmaz bir gerçektir. Bu bağlamda, embriyonik kök hücre araştırmaları etik açıdan tartışılması özel bir öneme sahiptir. Bu makale; akademik yazın doğrultusunda insan embriyonik kök hücresinin kullanım olanakları, ilişkin çeşitli ülkeler tarafından geliştirilen düzenlemeler ve bu ülkelerin uygulamaları, hasta haklarının ihlali, bilgilendirilmiş onam, tedaviye erişim ve ticarileşme olasılığı gibi temel etik konuları vurgulamaktadır.

Anahtar Kelimeler: Embriyonik kök hücre; tıp hukuku; hasta hakları; aydınlatılmış onam; araştırma etiği

Today, stem cell (SC) researches are starting to constitute a large part of studies in the biomedical field. The fact that SCs and particularly embryonic stem cells represent an efficient model allowing for the examination of the embryonic development phases in detail is an important factor. On the other hand, their potential healing capabilities such as cell and tissue renewal make them a treatment means in the treatment of "incurable" diseases in regenerative medicine.[1,2] Being the only resource where the SC researches and human embryonic stem cell (hESC) researches, which is a large part of the former, are used even in countries of the world with the scientifically competent and sufficient medical technological in-

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frastructure, the "embryo" causes a series of ethical problems such as the position of embryo as an ethical subject and cloning (cloning the human).[3-8] From this point of view, the current situation on hESC research primarily requires ethical discussions and then establishment of legal foundations on this basis.

THE USAGE OF EMBRYONIC STEM CELL

SC's are structures which proliferate by cell division, forming differentiated cells as they proliferate. They can be successfully used in a broad group of diseases including Parkinson's disease, Alzheimer's disease, multiple sclerosis, paralyses caused by accidents, diseases associated with the destruction of nerve cells, heart failure associated with heart attack, orthopedic conditions such as osteoarthritis and bone-cartilage loss, leukemia, group of diseases associated with immunodeficiency such as cancer, diabetes, spinal cord injury as well as burns.[9-11] On the other hand, inadequacy in providing suitable donors and several factors associated with the recipient in some diseases where organ and tissue transplantation is the last and only choice make treatment impossible.

The preference to use SCs for the treatment of organs and tissues, which have a low self-renewal capability, is one of the important advances in medicine world. The prediction that hESC obtained from human embryo would improve healing at the cellular level in the group of diseases for which they are preferred is dominant. The most important reason for preferring hESCs is their capability to differentiate to form the whole body, tissues and organs. hESCs are obtained from the embryo sac, which is called a blastocyst approximately 5-6 days after the fertilization of the fertilized female egg cell, and comprises of approximately 100 cells that are differentiated to form placenta in which it would be located.[12-20]

In the historical development process of hESCs, it is accepted that a scientific breakthrough was made when J.A. Thomson et al. obtained hESC "cell lines" which produce uniform cells from humans under laboratory conditions for the first time in 1998 .[20,21] This milestone gave rise to new studies aiming to obtain types of these cells that are differentiated enough to be applied in humans at centers in many countries of the world. These studies use hESCs formed by two different technologies (while the first one is attained from waste embryos that are developed with invitro fertilization (IVF), the other one is attained from pregnancies that are terminated voluntarily).

In studies performed with hESCs, many positive results proving that diseases could be successfully treated were obtained. However, there is a requirement for a greater number of such studies and access to the results of different disease groups that are treated efficiently. In addition to all these developments that are significant from the medical aspect, one of the most remarkable developments in the past decade is that Hwang et al. attained a pluripotent hESC line (SC that has the capability of multi-directional differentiation and enables the formation of many tissues in the organism) from cloned human embryonic sacs through the transfer of a somatic cell nuclear (attainment of an artificial embryo from a new cell on which the transfer of a body cell nuclear will be performed to an egg cell without nucleus. This study represents a milestone since it enabled the production of human hESCs by attaining from body cells of living individuals for the first time and using the method of nuclear transfer of body cell.[3]

Different methods regarding waste embryos in IVF units and fetal tissues, which are residues of voluntarily terminated pregnancies, were used to obtain hESC. The main reason for the problems in the use of hESCs is the acquisition method. The status of embryo in obtaining hESCs gives rise to multi-dimensional ethical discussions.[12,15,16,21,22]

Since the method of nuclear transfer enables the hESCs development of the nucleus that is compatible with the donor, it represents a positive treatment option by preventing the immune system responses (such as rejection of cell, tissue and organ) of patients who are in need of cell, tissue and organ. However, the requirement for egg cells from many female donors and several other reasons including financial dimensions restrict the use of hESCs.[2,22,23]

HOW DO WE THINK ABOUT THE REGULATORY REGIME IN THE WORLD IN GENERAL DEALS WITH EMERGING STEM CELL RESEARCH TECHNIQUES?

In almost every country of the world, it is commonly agreed to prohibit cloning for reproduction in human beings, but permit the attainment of hESCs by using the cloning methods for research and treatment within the scope of hESC research. In addition, technological developments and opportunities encountered every passing day make it necessary to increase the researches on such cells and make evaluations regarding the efficiency of the SC treatment in some severe diseases and injuries.[24-27]

In researches conducted on hESCs and a global evaluation about the use of such cells for treatment; it is observed that legal regulations do not show a homogeneous distribution. It is also remarkable that practical guides used and legal regulations considerably vary from country to country and along with countries with a comprehensive legislation in terms of content, there are also countries without any regulation. It could be asserted that these regulations either regulate such researches and studies, or prohibit and legalize them, which decriminalizes them.[1,22,24,28-34]

We see that there are no related regulations in Ireland aimed at hESCs research; however, in all countries, including those that prohibit the hESC production, it is allowable to obtain human embryo through the method of nuclear transfer in order to conduct researches. On the other hand, it is prohibited to attain embryo through the method of nucleus transfer in Brazil, Canada, France, Germany and Italy even for the purpose of research. hESC is produced legally from "waste" embryos that are not used in the IVF units in all countries except for Germany and Italy.[35] Reflections about religious beliefs are effective on the legal regulations of countries in question. It is assessed that theological factors have a strong influence on the precise prohibition of the attainment of hESC from human in Germany and Italy. According to the assessment report that was prepared by the Australian Stem Cell Center in 2011, either the hESCs import or the use of hESClines are allowed in all countries except for Ireland.[35]

The hESC (human embryonic stem cells) researches that were restricted during the Bush period (2001) in the United States of America (USA) acquired a different dimension when the monetary restriction was abolished by the President Obama. Policy of the Obama government regarding hESC prevents the destruction of human life for researches and some abuses. Practical guides of USA regarding the hESC researches include the use of blastocysts, which are attained in IVF clinics of institutes, universities and private sector for reproduction, for researches afterwards, as well as the attainment of blastocysts in IVF clinics especially for reproduction and nuclear cell transfer to oocysts.[22,28,29] The guide on hESC that prevents conducting researches on an embryo older than 14 days and prohibits conducting the hESCsoperation with animal cells allows the attainment of hESC lines from blastocysts donated from fertilized oocysts in IVF units or blastocysts that are attained through the nuclear transfer. SC researches are very recent in Mexico and they have no formal regulations. In Brazil, it is possible to work with frozen "waste" embryos not older than 3 years by means of the regulation that was made in 2005. [29]

Examining the regulations of EU countries regarding the hESC research; there is no national law, which prohibits reproductive cloning, in Belgium, Cyprus (Greek), Czech Republic, Greece, Ireland, Poland and Turkey. There have been regulations anticipating the SC researches in Finland, France (only allowing somatic SC), Hungary, Italy, Holland, Slovenia, and England. The regulations allow researches on embryos only until the age of 14 days in Slovenia, 14 days in Sweden, 14 days in Swiss and England and the regulations in Finland and Holland only allow researches on waste embryos and human embryos. Finland, France, Italy, Holland, Norway, Slovakia, Slovenia, Spain, Sweden and England have regulations that allow researches on fetal tissues. In almost all EU countries, SC researches are controlled by ministries of health of countries and different ministries in some countries cooperate in the matter of cellular treatments.[22,29] England has the oldest and most fundamental regulations in terms of SC researches. It is possible to conduct embryonic researches just for research and put the knowledge into

practice in severe diseases. Thus, England nearly ranks first with its SC centers, in terms of hESCresearch.[29]

Evaluating the positions of Far East countries in terms of hESC researches; South Korean Hwang Woo-suk who asserts that he is the first biomedical scientist cloning the hESC in 2006 attracts attention. Researches that mainly conduct cloning for treatment are continuing in South Korea today.[22,29] According to the practical guides regarding hESC in Malaysia, it is allowed to conduct adult SC researches and SC researches, which are attained from tissues of pregnancies terminated legally with the fetal SC, and SC researches that cannot be attained from human beings and the use of hESCs lines for research. It is allowed to conduct researches with hESCs that are attained from "waste" embryos. It is prohibited to produce embryos with the SCNT or ART method without restriction even only for researches. It is not allowed to conduct invitro studies on human embryos older than 14 days. Singapore is considered as the SC center of Asia and there are more than 40 SC research groups there. It is allowed to use embryos not older than two weeks for therapeutic purpose. We see that regulations in China have attained flexibility. The practical guide that was prepared in 2003 supports the use of embryos in IVF units, fetal tissues in inferior materials, blastocysts formed with the nuclear transfer and cell lines in SC research on condition that they are donated voluntarily. This practice, on the other hand, has been shaped with the thought "human life begins with birth" according to the belief system in China.

Iran was among the first 10 countries of the world, producing hESC, in 2003. The content of the guide of researches on gamete and embryo in Iran is as follows: respect for human honor and human rights, voluntary and informed participation, respect for privacy and confidentiality, and consideration of benefits-harms especially in researches involving clinical treatment. It is possible to prohibit the production of hybrid embryos from human beings and animals, prevent the formation of pure race, prohibit the production of embryos for researches, and use only the waste embryos younger than 14 days that are destroyed for researches in IVF units. Even though there is no legal regulation directly concerning the SC applications in Turkey, the rules in the "Guide for Non-embryonic Stem Cell Researches" of Ministry of Health are applied.[1,21,22,36] Furthermore, the Ministry involves the "Stem Cell Transplantations Advisory Board", which consists of academicians. Lack of legal grounds aimed at these research hinders the acceleration of research.

HOW MUCH EMPHASIS HAVE THE POTENTIAL ECONOMIC BENEFITS OF STEM CELL RESEARCH RECEIVED IN THE PUBLIC IN GENERAL?

Considering the effect of the gradual increase of the interest and curiosity of researchers towards the subject, expectations from positive outcomes of hESCs in the disease group are high in researches conducted. As well as treating the disease, the hESCs have introduced a new economic market as a biomedical field.[22,23] In addition to the economic dimension of the hESC production, the cost of sustaining processes such as keeping, storing these cells under proper conditions is very high. The method through which the hESCs will be attained is a determining parameter for the cost. In this context, it is important to develop the SC banking and efficient storage facilities. Selection of economic, durable and long-life technical materials to be used in cellular production might decrease the cost. Supporting the researches financially plays the primary role in enabling the access to treatment. Individuals have a limited number of opportunities of having a practice in IVF clinics, which is a very expensive treatment option. Funds to be established for such practices might be a way of overcoming economic problems.

Apart from the aforementioned economic problems, the disputes about different problems in Western countries that have prepared their technological infrastructures have restricted and prevented the hESC research and enabled the research to direct towards countries with a convenient background like South Korea.[21,22,29] Medicolegal conditions in these countries support these research, as well. Thus, it is observed that a broader natural research field with a narrowed restriction has been formed.

RESULT AND CONCLUSION

There have been still hopes about hESCs, which rank first in today's science-technology agenda. It is required to prove the number and therapeutic effect of researches in order to obtain the expected benefit from the hESCs. Since a greater number of trials are required to evaluate the positive outcomes of studies, voluntary female donors are needed to donate for the procurement of female gamete. Such evaluations require the analysis of researches in terms of bioethics and women's rights. The fact that hESCs precisely effectuate the targeted treatment, have a very broad treatment area and do not form an immune system response could be considered among their advantageous aspects. However, there are also some disputable subjects such as the potential of containing infectious agents, transfer of genetic disorders, violations of privacy and patient rights, risk for a great number of women, consent, abuse of women's body, accessibility to treatment due to expensiveness, making the embryos a merchandise and instrument.[22,37-40]

Even though the studies give hope to incurable diseases, this should not be turned into a hope mongering. There is a requirement for hESC guides and laws that are explained with clear and detailed items and prepared in cooperation of not only healthcare professionals, but also those who have the competence of objective evaluations such as politicians, lawyers and theologians.[21,22]

Apart from all these, it could also be considered to conduct researches and studies aimed at the production of pluripotent SCs and include evaluations in terms of benefits/harms. This choice is important in terms of presenting other options that end many disputes, which obstruct the hESCs researches and treatments and are thought to be caused by the use of "human embryo", in terms of attaining hESCs without using the human embryo.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

All authors contributed equally while this study preparing.

REFERENCES

1. Arda B, Acıduman A. An evaluation regarding the current situation of stem cell studies in Turkey. Stem Cell Rev Rep. 2009;5:130-4.[Crossref]
2. Backhouse D, Deckha M. Shifting rationales: the waning influence of feminism on Canada's embryo research restrictions. Canadian Journal of Women and the Law. 2009;21(2):229-66..[Crossref]
3. Beksaç M. Kök hücre araştırmalarında güncel kavramlar. Ankara: Türkiye Bilimler Akademisi Raporları; TÜBA Yayınları; 2004. p.15-6..
4. Gardner RL, Brook FA. Reflections on the biology of embryonic stem (ES) cells. Int J Dev Biol. 1997;41(2):235-43. [PubMed]
5. Bruce A, Harmon SHE. Discursive typologies and moral values in stem cell politics, regulation and commercialisation: some preliminary observations (Part I). Journal of International Biotechnology Law. 2009;6(2):61-6. .[Crossref]
6. Cameron C, Williamson R. In the world of dolly, when does a human embriyo acquire respect? J Med Ethics. 2005;31(4):215-20. [Crossref] [PubMed]
7. European group on Ethics in science and New Technologies Ethical aspects of human Cell Research and use European Commission Brüssels,14 Nov. 2000. .[Link]
8. European group on Ethics in science and New Technologies Ethical aspects of human stem Cell Research and use European Commission Brüssels,p:13.2000. .[Link]
9. ESF Science Policy Briefings 14. 1st ed. 2001 and 18. 2nd ed. 2002. .[Link]
10. Sökmensüer LK. Embriyonik kök hücreler ve tedavi amaçlı kullanımları.Embryonic stem cells and their therapeutic uses Hacettepe Tıp Dergisi. 2007;38:15-9.
11. Vatansever HS. Embriyonik kök hücreler. Human embriyonic stem cell. Sağlıkta Birikim Dergisi. 2009;1(5):25-44.
12. Martin J. Human embryonic stem cells: ethics, myths and realities. Australian e-Journal of Theology. 2005;5:1-6.
13. Mertes H, Pennings G. Elective oocyte criyopreservation: who should pay? Hum Reprod. 2012;27(1):9-13. .[Crossref] [PubMed]
14. Özel HB, Ozan E, Dabak E. [Embryonic stem cells: review]. Turkiye Klinikleri J Med Sci. 2008;28(3):333-41.

15. Simonstein F. Embryonic stem cells: the disagreement debate and embryonic stem cell research in Israel. J Med Ethics. 2008;34(10):732-4. .[Crossref] [PubMed]
16. Solbak JH, Holm S. The ethics of stem cell research: can the disagreements resolved? J Med Ethics. 2008;34(12):831-2. .[Crossref] [PubMed]
17. Solbak JH, Zoloth L. The tragedy of translation: the case of "first use" in human embryonic stem cell research. Cell Stem Cell. 2011;6;8(5):479-81. .[Crossref] [PubMed]
18. Sousa PAD, Galea G, Turner M. The road to proving human embryo stem cells for therapeutic use: the UK experience. Reproduction. 2006;132(5):681-9. .[Crossref] [PubMed]
19. Stojkovic M, Lako M, Strachan T, Murdoch A. Derivation, growth and applications of human embriyonic stem cells. Reproduction. 2004;128(3):259-67..[Crossref] [PubMed]
20. Steinbock B. What does "respect for embryos" mean in the contex of stem cell research? Womens Health Issues. 2000;10(3):127-30. .[Crossref] [PubMed]
21. Görkey Ş, Kutlay N, Başağaç Gül RT, Güven T, Sert G, Gün M, et al. Kök Hücre Araştırmalarının Etik ve Hukuki Boyutu. Türkiye Biyoetik Derneği Kök Hücre Araştırmaları ve Uygulamaları Kurulu. 1. Baskı. Ankara: Dizgi Matbaacılık; 2015. p.40.
22. Gün, M. Embriyonik kök hücre Araştırmaları/ tedavileri ve olası etik sorunlar. Turkiye Klinikleri J Med Oncol-Special Topics. 2015;8(2):141-7.
23. Mackie JE, Taylor AD, Finegold DL, Daar AS, Singer PA. Lessons on ethical decision making from the bioscience industry. PLoS Med. 2006;3(5):e129. .[Crossref] [PubMed]
24. Robertson JA. Embryo stem cell research: ten years of controversy. The Journal of Law, Medicine and Ethics. 2010;38(2):191-203.[Crossref]
25. Saltzberg J. The current embryonic stem cell research federal funding policy. Undue respect to minority ethical considerations? The Journal of Legal Med. 2008;29(4):505-21..[Crossref]
26. Schechter J. Promoting human embryonic stem cell research: a comparison of policies in the United States and the United Kingdom and factors encouraging advancement. Texas International Law Journal. 2009;45: 603-29.
27. Shum J. Moral disharmony: human embryonic stem cell patent laws, warf and public policy. Boston College International and Comparative Law Review. 2010;33(1):153-78.
28. de Wert G, Mummery C. Human embriyonic stem cells research, ethics and policy. Hum Reprod. 2003;18(4):672-82. .[Crossref] [PubMed]
29. Dhar D, Ho JHE. Stem cell research policies around the world. Yale J Biol Med. 2009;82(3):113-5. . [PubMed]
30. Green RM. Political interventions in U.S. human embryo research: an ethical assessment. Journal of Law, Medicine and Ethics. 2010;38(2):220-8. .[Crossref]
31. Halliday S. A Comparative approach to the regulation of human embryonic stem cell research in Europe. Medical Law Review. 2004;12(1):40-69..[Crossref]
32. Sugerman S, Douglas S. Ethical aspects of stem cell-based clinical translation: research, ınnovation,and delivering unproven ınterventions. Hug K. Hermerén G, eds. Translational Stem Cell Research: Issues Beyond the Debate on the Moral status of the human Embryo. New York: Humana Press; 2011. p.128-35..[Crossref]
33. Great Britain. Human Genetics Advisory Commission. Cloning Issues in Reproduction, Science, and Medicine: A Report from the Human Genetics Advisory Commission and the Human Fertilisation and Embryology Authority. London: The Commission; 1998. p.50.
34. Hovatta O, Stojkovıc M, Nogueıra M, Varela-Nieto I. European Scientific, Ethical, and Legal Issues on Human Stem Cell Research and Regenerative Medicine. Stem Cells. 2010;28:1005-7..[Crossref]
35. Overwiew of international human embriyonic stem cell laws. Australian eJournal of Technology and society. Winter. 2012;129-46. .[Link]
36. Türkmen HO, Arda B. Ethical and legal aspects of stem cell practices in Turkey: where are we? J Med Ethics. 2008;34(12):833-7. .[Crossref] [PubMed]
37. Devolder K. Human embryonic stem cell research: why the discardedcreated-distinction cannot be based on the potentiality argument. Bioethics. 2005;19(2):167-86. .[Crossref]
38. Harris J. Hayatın Değeri. Tıp Etiğine Giriş. 1. Baskı. İstanbul: Ayrıntı Yayınları; 1998. p.39:162,163,329.
39. Okka B. Ethical conflicts in stem cell research and education. Procedia - Social and Behavioral Sciences. 2015;176:1071-77. [Crossref]
40. Petrisor TM. Overview of embryonic stem cell research, postmodern openings. Editura Lumen, Department of Economics. 2016;7(2):59-77. .[Crossref]