



## DO EMBRYONIC STEM CELLS GIVE A NEW DIRECTION FOR THERAPEUTIC PURPOSES?

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### ABSTRACT

In recent years there has been an increasing amount of genuine research for using human embryonic stem cells worldwide. However, a number of the current arguments in legal and ethical philosophy still contest the morality of these studies in terms of harvesting stem cell from the non-implanted foetus. This review explores on one hand the importance of these cells in therapeutic purposes ignoring all the different standpoints which are involved in these arguments, including ethical debates and medical safety. It argues with the purpose of assessing the importance of embryonic stem cells for giving a new direction in the treatment of the most common chronic and incurable diseases in human beings. However, patient safety still represents one of the obstacles facing this new biotechnology beside it is important to give specific concerns to the moral and public considerations regarding to this issue. Further study could examine alternative solutions for minimising the intractable debates about the ethical status of embryonic life. Therefore, ultimately solving for this issue might be through much future scientific research on this issue paralleling with relevant clinical applications would be necessity.

Keywords: ethical issue; stem cell therapy; embryonic stem cells, harvesting stem cells, non-implanted foetus .

### Introduction

The past two decades have witnessed dramatically rapid advances in the biotechnology of human embryonic stem cells (HESCs). This innovation is one of the most significant developments in biomedical science in recent years/this century/decades. HESCs can be isolated from non-implanted embryos which can adapt and ultimately specialize into different cells and tissues of the human body. This has been exploited by vast majority of biomedical global scientists for research and medical purposes, as well as gaining the attraction of public attention as an important source of alternative treatment for incurable and chronic diseases (Lewis et al., 2020). However, these developments may raise debates in relation to the ethics of harvesting cells from the foetus and medical safety of patient life (Volarevic et al., 2018). A few popular instances or newsworthy examples, such as attempts to legalise the use of human embryos for research.

In recent years ESCs have become an important and promising technology for indorse regenerative medicine and that is not merely due to their biologic properties, but as well because they be able to be produced in large quantities in the laboratory (Akopian et al., 2010, Candan and Kahraman 2010). This promising has achieved in the study of foetal abnormalities and for drug innovation also provoked a new direction in regenerative medicine(Olee et al., 2014, Khan et al., 2018). The dispute that the beneficial effects of studying ESCs study outbalance foetal damage and ethical issue which is counted in healthiness results that could be elucidated or rebutted just in case if the study is authorized to persist. But by continuity of studies on this cell represented as one of the most arguments that isolation is moral (Taylor, 2005, Hyun, 2010). Creating much dispute and disagreement with proponents and adversaries ESCs research have raised anxieties around the sacredness of human embryonic life (Manzar et al., 2013). The purpose of this paper is to explore the disputes over extracting human embryonic stem cells (ESCs) from unborn children and using them for the treatment in medical applications, and their potential ethical, healthy and financial on consequences. This includes discussions as to the potential benefits of ESCs for research into many incurable and chronic diseases such as heart disease, Alzheimer's disease, diabetes and their

potential to be sources for various others cells and tissues in human body. This review will follow the most variations would be happen in embryonic development and causes mutation or cancer cells .

## **Background**

In 1998 the academic journal *Science* (vol. 282) in the United States published probably one of the most significant biotechnological discoveries of the 20th century. Thomson et al. (1998) stated that they had extracted and cultivated Embryonic Stem Cells (ESCs) originated from a human foetus despite legislation preventing the use of the federal treasury for research on the foetal structures of human embryos. To avoid violating of National Institutes of Health Thomson et al. managed their development on ESCs by utilizing a private company for the biological research institution (Resnik 1999). This research explored a new direction in tissue engineering of human organs. Although ESCs had been obtained primarily from mouse embryos since 1981, the major achievement of human ESCs is considered to be a beginning for the future of replacement therapy (Nikoliskii et al 2007). However, Jensen (2008) argues that a controversy of embryonic stem cell research starts from the isolation of ESCs from human embryos in the early stages of development between 72-120 hours of its life. As a result, the inquiry initiated with why it is ethically admissible to kill a human embryo and harvest stem cells for experimental and therapeutic purposes. Nikoliskii et al. (2007) argued that increasing utilization of the number of human ESCs had engendered considerable political, moral and social arguments. The research also revealed a number of ethical debates regarding both viewpoints, the comprehension of the quintessence of the human ESCs beginning in the first stage of foetal development and have differences in religious standpoints. In particular, the use of human ESCs provokes ethical dilemmas due to essential moral rules such as sacredness of life that are extremely valued by communities (Swazi 2010). Additionally Hug and Hermerén (2011) have highlighted that the dilemma of HESCs is frequently more complex due to the current gaps in our knowledge relating to the safety of patient life (Funato et al., 2014). Wert et al. (2002) have discussed that according to British law in 1990s, any such specific study on human embryos must illustrate to the HFEA (Human Fertilisation and Embryology Authority) to be requisite or qualified for the following objectives: to enhance advancement in the curing of infertility, to investigate the causes of most congenital disorder or the reasons of abortion, and finally to promote further effective methods for preventing fertilization or discovering abnormal preferable chromosome before implantation of foetus inside the uterus. Since 2004, there has been a controversy of which ESCs lines are suitable to be used in the treatment of most chronic diseases because the periodic verification of embryonic stem cell line should be in fact has genetic stability as it is quite possible that unspecialized ESCs may not be used for replacement therapy, because there is a hazard of their carcinogenic transmutation (some embryonic stem cell converted to cancer cells through mutation of their genes). The majority of attempts will be localized on the extraction of human ESCs which may have a highly significant value for development and differentiation cells to become more suitable for therapeutic transplantation (Nikoliskii et al. 2007).

## **Discussion and Analysis**

### **Ethical debates for using embryonic stem cells**

It is becoming untenable to ignore the controversial issue of (human) embryonic stem cells (HESCs) as moral debates and due to legislation and public objections. In this aspect of the controversial issue, it will argue the doubts about bioethical debates of HESCs and clarify the potentiality of it to be more acceptable from the general public and to show the different perspectives which may be used HESCs in therapeutic purposes. Recently, there has been an increase interest in the use of HESCs in for biomedical therapeutics despite some debates regarding to the ethical dilemma of destruction foetus life (Volarevic et al., 2018). Also, some scientists who support the use of HESCs for therapeutic research studies have highlighted that in term of religious stand points not all of them grant complete ethical status to the first stage of

development, but it would be after implantation of the foetus (Zoloth, 2001). In 2006, Lysaght et al. (2006) set out to explore the ethical issue of HESCs. Their research examined the use of HESCs from two aspects of the ethical debate: one centralized on the possible medical and curative usefulness of hESCs research, which raised few moral objections, and the second less concerned in the issue of human ESCs in comparison to many ethical problems, such as in the marketing of human organs. Denker (2008) suggested resolving the moral issue of HESCs by the reprogramming of HESCs (reprogrammed ESCs have less debates than stem cells harvested from the umbilical cord after birth) and improving the potential for using these cells (induced pluripotent stem cells) for use in therapeutic research. Moreover, Steinbock, (2011) highlights that respect for foetal life does not contest with use of HESCs for therapeutic research; in spite of some limitations regarding to ethical debates and religious for using hESCs from unborn children. Brouillet and Turner (2005) carried out a number of investigate in relation to the morality of HESCs. They argued that in ethical science, there are many spiritual denominations which debate that the human soul is sacramental at different developmental stages of a human being. This view is supported by Hug and Hermern (2011) who state that the basis of human rights is to respect human embryonic life in different developmental stages as it is one of the religious reasons .

A centre of debate in regards to HESCs research is whether protection of human embryonic life extends to un-implanted foetus from (1-8 days) or implanted foetuses. Therefore, the destruction of foetus for harvesting has emerged this argument relate specifically to human dignity which is denounced any practical study may effect on human respect (Greenpeace, 2013, Arakelyan, 2017). In fact, the perspectives of human dignity and human rights, it would be esteemed human embryonic life even if HESCs extracted from unborn children. What is more, Swazo (2010) stated that most of HESCs studies encounter ethical debates due to the destruction of human foetus and harvesting of a prospective human life that could be considered desecrating the commitments of human rights for relieving or rejecting any harmful of human being. Therefore, these studies on HESCs could be considered unacceptable by the general public. However, Chapman (2009) argue that in spite of debates about the harvesting of HESCs, it is difficult to have complete rights of non-implanted foetus because it is related to human dignity and religious. Indeed, they argue that the ethical obligation of HESCs research is to cure and to reduce pain brought about by human sickness and disease such as congenital diseases. Another important finding was that there is a strong relationship between organ donation and extraction of embryonic stem cells to be utilized for curative patients from chronic diseases. Whittington (2012) demonstrates the possibility of using embryonic stem cells under specific conditions where the donation of embryos for therapeutic purposes is performed ethically in parallel with the organ donation of a dying person to help the life of another person.

Studies to date have tended to centre on therapeutic purposes and/or research rather than a moral issue of HESCs (Wysoczynski and Bolli, 2020, Aly, 2020, Sivaraman, 2019). Thus, Manzar et al. (2013) in their study of moral debate of HESCs suggested that the bioethics of HESCs ought to be integrated into therapeutic studies to allow discussion/rationalisation of HESCs use in tandem with therapeutic research. Therefore, they could possibly give an opportunity in near future to expand and achieve in the biomedical therapies. As a result, it appears from these arguments regarding the morality of HESCs that future research into biomedical therapies may need to consider the ethical issues regarding this kind of treatment (Lysaght et al., 2006). Additionally, they must also attempt to look objectively at the potential effectiveness of hESCs in order to find better treatment for chronic diseases which are currently difficult to cure, such as cancer or diabetes. If more ethical consideration is needed, more detailed discussion and investigation of the ethics is necessary, contrasted with the benefits of HESC use. This as well as an analysis of what legislature is already in place that limits the use and harvesting of HESCs.

### **The suitability of embryonic stem cell in medical therapy**

Another significant perspective concerning embryonic stem cells debate is a medical aspect. Here, in this section it might be taken into account the subject of safety from several directions, for instance the formation of tumour, the difficulty of immune reflexion, or another point is that unexpected receiving negative impacts appear after treatment with HESCs. Adversaries HESCs therapy have concerns about the side effects of such method on patient safety. It has been argued that such technology will causes pathological complications after treatment as in the case of mutation carcinogenesis (Funato et al., 2014, Chen et al., 2019) and this debate has raged unabated for over the last two decades. However, proponents for HESCs therapy believe these new biotechnological methods of HESCs hold the promise to solve many difficult diseases and help to repair injured tissues and else. This aspect explains these debates and will illustrate the most interesting applications in medical therapy and it would give clear evidences for future promising in human medicine (Wysoczynski and Bolli, 2020). Raikwar et al. (2006) stated that one major achievement of HESCs will be accomplished by a comprehensive study on the genetic features of hESCs due to the therapeutic potential for human hereditary illnesses. In addition, Ameen et al. (2008) conclude in their study on future applications that HESCs are unparalleled and immortal sources for cryotherapy of different untreatable diseases such as cardiac repair (Wysoczynski and Bolli, 2020). Such diseases have affected globally on human and resulting in prolong serving therapy and finally precocious death, for instance, congestive heart failure, a common consequence of heart muscle and/or valve damage, impacts millions, as nearly 5 million people in the United States, and more than 400,000 new cases diagnosed annually as well as 1.5 million people each year suffer myocardial infarction, and about one-third of them die (Zoloth, 2001). There was a noble prize awarded for Nano medicine (Janowski et al. 2012). This invention has reducing the gap knowledge and open the door for scientists to find the opportunity for using this biotechnology in biomedical therapy; it also might be useful to explore the tracking of these cells in human and animal medicine. Jensen et al. (2009) and Joseph (2013) state that HESCs are able for growing and specializing all the mature cells in the human body (Inzunza et al., 2005, Trounson, 2006). These characteristic features of HESCs have been employed for the treatment of various diseases for instance damage of spinal cord (Faulkner and Keirstead, 2005), retrogression of eye muscles, heart muscle diseases and diabetes (Wysoczynski and Bolli, 2020, Kroon et al., 2008), and else. The debates concerning scientific evidence for HESCs therapy and people safety have remained continuous for more than ten years. In an investigation into HESCs safety, Hug and Hermerén (2011) argued that there might be a variance between the scholars who agree to accept the integrity of HESCs in treatment and others scientist who thought that there is inadequate scientific knowledge to be filled with safety studies. Furthermore, Aznar and Sánchez (2011) states in some cases that have been treated by ESCs might lead to occurrence of cancer cells. He mentions that there is one patient who has been recorded for cancer. This case occurred after four years from treatment with ESCs. He finally concludes that this therapy could be effect on patient safety (Prokhorova et al., 2009). This might be happen due to inadequate processing of ESCs or requiring more empirical study on this technological method. However, Yang and Shyr (2009) establish an interesting refinement in ESCs therapy, as measured by the possibility to repair and regenerate the tissue damage for important vital organs in the human body, for example, the heart and the brain tissue as well as treat insufficiency immune system. This rapid development in biomedical therapy clarifies in great outcomes of this technology to face obstacles of ESCs as it gives a promising to be a magical treatment for those suffering from treatment for a long time. In another motivating study, Denecke and Schwengberg (2011) demonstrate that in spite of ESCs using for curative the patient from difficult diseases, it could be use these cells as a specific method to determine the efficacy of drug toxicity through their action on a new medicine. This test will facilitate the potentiality for evaluating drug safety. In another words, this assay by using ESCs will lead to protect human and keeping them safe from side effects of drug toxicity by minimizing the hazard of human life. Undoubtedly, many studies which are backing ESCs depend on the capability of this technology to provide an appropriate chance for applying in clinical applications (Nikolskii,



2007). There are many novels that have been done theoretically which hold up a great promise in near future to be empirical study. It is appear from this argument and rebuttal, in spite of the biotechnology containing some risk in regarding to some cases might develop to cancer, it is possible to set up complete investigations and validations of ESCs before utilizing in clinical implementations. Thus this technology may be become a key which relieve suffering of many patients from threatening of untreatable diseases such as dysfunction of heart muscle, Alzheimer, diabetes and else. Therefore, it is likely that the current future will bring an exciting new trend of biotechnology in order to fit the scientist demand of medical therapy. Therefore, according to the scientific responses of the current new biotechnology, there remain objections, doubts, and knowledgeable insufficiency in relation to the safety and therapeutic efficiency of HESCs.

### References

- Akopian, V., Andrews, P. W., Beil, S., Benvenisty, N., Brehm, J., Christie, M., Ford, A., Fox, V., Gokhale, P. J. & Healy, L. 2010. Comparison of defined culture systems for feeder cell free propagation of human embryonic stem cells. *In Vitro Cellular & Developmental Biology-Animal*, 46, 247-258.
- Aly, R. M. 2020. Current state of stem cell-based therapies: An overview. *Stem Cell Investigation*, 7.
- Ameen, C., Strehl, R., Bjourquest, B., Lindhal, A., Hyllner J. And Sartipy, P. 2008. 'Human embryonic stem cells: Current technologies and emerging industrial applications'. *Critical Review in Oncology and Haematology*, 65, 54-80 .
- Arakelyan, N. 2017. Contemporary Challenges in Protection of Human Dignity of a Human Embryo. Charles University in Prague Faculty of Law Research Paper No.
- Aznar, J. And Sánchez, J. 2011. 'Embryonic stem cells: are useful in clinic treatments?'. *Journal of Physiology and Biochemical*, J, 67, 141–144.
- Brouillet, M. and Turner, L. 2005. 'Bioethics, religion, and democratic deliberation: policy formation and embryonic stem cell research'. *HEC Forum*, 17, 1, 49-63 .
- Candan, Z. and Kahraman, S. 2010. Establishment and characterization of human embryonic stem cell lines, Turkey perspectives. *In Vitro Cell Development Biobiology—Animal*, 46, 345–355.
- Chapman, A. 2009. The ethics of patenting human embryonic stem cells. *Kennedy Institute of Ethics Journal*, 19, 3, 261-288.
- Chen, H. J., Poran, A., Unni, A. M., Huang, S. X., Elemento, O., Snoeck, H.-W. & Varmus, H. 2019. Generation of pulmonary neuroendocrine cells and SCLC-like tumors from human embryonic stem cells. *Journal of Experimental Medicine*, 216, 674-687.
- Denecke, B. and Schwengberg, S. 2011. Embryonic stem cells as a tool for drug screening and toxicity testing. G.M. Artmann et al. (Eds.), *Stem Cell Engineering*, IZKF "BIOMAT.", RWTH Aachen, Germany, 473-500.
- Denker, H. 2008. Human embryonic stem cells: The real challenge for research as well as for bioethics is still ahead of us '. *Cells Tissues Organs*, 187, 250–256.
- Faulkner, J. &Keirstead, H. S. 2005. Human embryonic stem cell-derived oligodendrocyte progenitors for the treatment of spinal cord injury. *Transplant immunology*, 15, 131-142.
- Funato, K., Major, T., Lewis, P. W., Allis, C. D. &Tabar, V. 2014. Use of human embryonic stem cells to model pediatric gliomas with H3. 3K27M histone mutation. *Science*, 346, 1529-1533.
- Greenpeace, B. 2013. Embryonic stem cell research and the European court of justice's new found morality'. *Medical Law Review*, 21, 310–319.
- Hug, K. and Hermerén, G. 2011. 'Do we still need human embryonic stem cells for stem cell-based therapies? epistemic and ethical aspects'. *Stem Cell Reviews and Reports*, 7, 761–774.
- Hyun, I. 2010. 'The bioethics of stem cell research and therapy'. *The Journal of Clinical Investigation*, 120, 171-175 .
- Inzunza, J., Gertow, K., Strömberg, M. A., Matilainen, E., Blennow, E., Skottman, H., Wolbank, S., Ährlund-Richter, L. &Hovatta, O. 2005. Derivation of human embryonic stem cell lines in

- serum replacement medium using postnatal human fibroblasts as feeder cells. *Stem cells*, 23, 544-549.
- Janowski, M., Bulte, J. and Walszak, P. 2012. 'Personalized nanomedicine advancements for stem cells tracking'. *Advanced Drug Delivery Reviews*, 64, 1488-1507.
- Jensen, D. 2008. 'Abortion, embryonic stem cell research, and waste'. *Theoretical Medicine and Bioethics*, 29, 27-41.
- Jensen, J., Hyllner, J. and Rquist, P. 2009. 'Human embryonic stem cell technologies and drug discovery'. *Journal of Cellular Physiology*, 219, 513-519.
- Joseph, B. 2013. 'Human embryonic stem cell research: Its importance in the culture wars'. *Christian Bioethics*, 19, 1, 60-71.
- Khan, F. A., Almohazey, D., Alomari, M. &Almofty, S. A. 2018. 'Isolation, culture, and functional characterization of human embryonic stem cells: Current trends and challenges'. *Stem cells international*, 2018.
- Kroon, E., Martinson, L. A., Kadoya, K., Bang, A. G., Kelly, O. G., Eliazar, S., Young, H., Richardson, M., Smart, N. G. & Cunningham, J. 2008. 'Pancreatic endoderm derived from human embryonic stem cells generates glucose-responsive insulin-secreting cells in vivo'. *Nature biotechnology*, 26, 443-452.
- Lewis, P., Silajdžić, E., Brison, D.R. and Kimber, S.J., 2020. 'Embryonic Stem Cells'. *Cell Engineering and Regeneration*, pp.315-365.
- Lysaght, T., Ankeny, R. and Kerridge, I. 2006. 'The scope of public discourse surrounding proposition 71: Looking beyond the moral status of the embryo'. *Bioethical Inquiry*, 3, 109-119.
- Manzar, N., Manzar, B., Hussain, N., Hussain, M. and Raza, J. 2013. 'The ethical dilemma of embryonic stem cell research'. *Science and Engineering Ethics*, 19, 97-106.
- Nikolskii, N., Gabai, I. and Somova, N. 2007. 'Human embryonic stem cells: problems and perspectives'. *Cell and Tissue Biology*, 1, 375-383.
- Olee, T., Grogan, S. P., Lotz, M. K., Colwell Jr, C. W., D'lima, D. D. & Snyder, E. Y. 2014. 'Repair of cartilage defects in arthritic tissue with differentiated human embryonic stem cells'. *Tissue Engineering Part A*, 20, 683-692.
- Prokhorova, T.A., Harkness, L.M., Frandsen, U., Ditzel, N., Schröder, H.D., Burns, J.S. and Kassem, M., 2009. 'Teratoma formation by human embryonic stem cells is site dependent and enhanced by the presence of Matrigel'. *Stem cells and development*, 18, 47-54.
- Raikwar, S., Mueller, T. and Zavazava, N. 2006. 'Strategies for developing therapeutic application of human embryonic stem cells'. *Physiology*, 21, 19-28.
- Resnik, D. 1999. 'Privatized biomedical research, public fears, and the hazards of government regulation: Lessons from stem cell research'. *Health Care Analysis*, 7, 273-287.
- Sivaraman, M. A. F. 2019. 'Ethical guiding principles of "do no harm" and the "intention to save lives" in relation to human embryonic stem cell research: finding common ground between religious views and principles of medical ethics'. *Asian Bioethics Review*, 11, 409-435.
- Steinbock, B. 2011. *Life Before Birth: The Moral and Legal Status of Embryos and Fetuses*, 2nd Ed., Oxford University Press, 327-335 .
- Swazo, N. 2010. 'Just one animal among many? Existential phenomenology, ethics, and stem cell research'. *Theoretical Medicine and Bioethics*, 31, 197-224.
- Taylor, P. 2005. *Science and Engineering Ethics*, 11, 589-616 .
- Taylor, P. L. 2005. 'The gap between law and ethics in human embryonic stem cell research: overcoming the effect of US federal policy on research advances and public benefit'. *Science and engineering ethics*, 11, 589-616.
- Thomson, J., Itskovitz-Eldor, J., Shapiro, S., Waknitz, M., Swiergiel, J., Marshall, V. and Jones, J. 1998. 'Embryonic stem cells derived from human blastocysts'. *Science*, 282, 1145-1147.

- Trounson, A. 2006. The production and directed differentiation of human embryonic stem cells. *Endocrine reviews*, 27, 208-219.
- Volarevic, V., Markovic, B.S., Gazdic, M., Volarevic, A., Jovicic, N., Arsenijevic, N., Armstrong, L., Djonov, V., Lako, M. and Stojkovic, M., 2018. Ethical and safety issues of stem cell-based therapy. *International journal of medical sciences*, 15, 36-45.
- Wert, G., Berghmans, R., Boer, G., Andersen, S., Brambati, B., Carvalho, A., Dierickx, K., Elliston, S., Nunez, P., Osswald, W. and Vicari, M 2002. 'Ethical guidance on human embryonic and fetal tissue transplantation: A European overview'. *Medicine, Health Care and Philosophy*, 5, 79–90.
- Whittington, R. 2012. Embryonic stem cell research: A pragmatic roman catholic's defence. *Christian Bioethics*, 18, 3, 235–251.
- Wysoczynski, M. & Bolli, R. 2020. A realistic appraisal of the use of embryonic stem cell-based therapies for cardiac repair. *European heart journal*, 41, 2397-2404.
- Yang, K. and Shyr, M. 2009. Are stem cells the magical medical therapy of the future?'. *Tzu Chi Medical Journal*, 21, 12-17.
- Zoloth, S. H. K. L. L. 2001. *The human embryonic stem cell debate: Science, ethics, and public policy*, MIT Press.