Embryonic stem cells for therapeutic research – the ethical struggle

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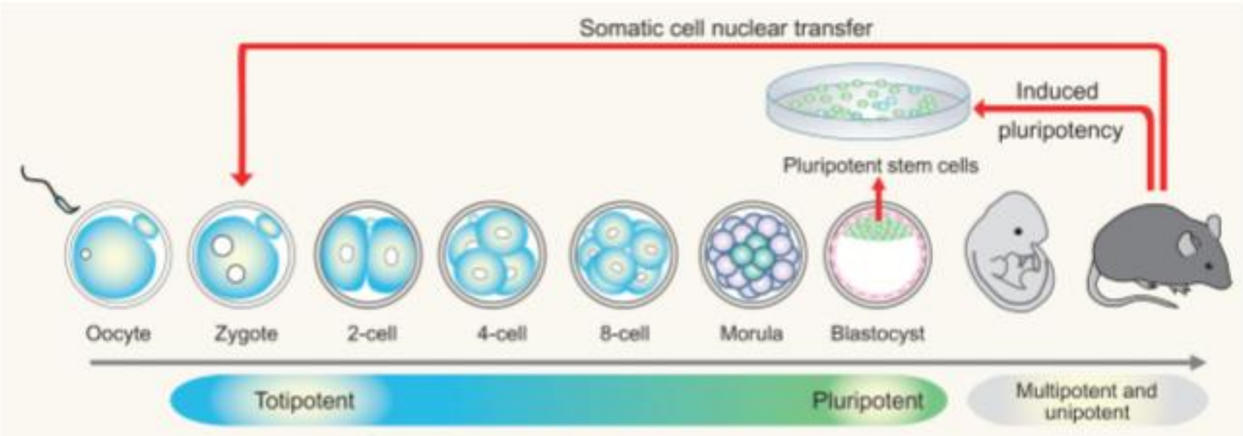

(Lu 2015)

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Summary

This report talks about the applications of embryonic stem cells in therapeutic research and the ethical implications surrounding it. It begins with an introduction that outlines the terms totipotency, morula, and blastomeres, and their relevance in stem cell research and therapeutics. It also briefly describes the reasons for ethical controversies surrounding this topic.

The body of the report further talks in detail about the processes following fertilization, development of blastomeres and the formation of a morula. It talks about totipotency and pluripotency, and the major differences between totipotent and pluripotent cells. It gives the reader an idea of why totipotent cells are preferred for stem cell research. The report goes on to describe the therapeutic applications of totipotent cells for treating human diseases relating to tissue damage or organ failure. Finally, the report describes the controversies surrounding the use of embryonic stem cells for therapy as it implies destruction of the embryo to harvest the stem cells.

The report concludes with a general consensus on the possibilities of using embryonic stem cells for therapy. It emphasizes the fact that if stem cell therapy can give a diseased patient a life filled with dignity it needs to be considered regardless of ethical considerations.

EMBRYONIC STEM CELLS FOR THERAPEUTIC RESEARCH – THE ETHICAL STRUGGLE

Introduction

Totipotency is a feature of cells that give them the ability to differentiate into multiple cell types including embryonic and extra-embryonic cells. This property is observed in embryonic cells about 24 to 48 hours after fertilization. Following fertilization, the resultant zygote undergoes several cell divisions to generate precursor cells for developing different organs and tissues. At these stages, every individual embryonic cell has the capacity to generate an entire organism (Lu 2015). Due to this totipotent ability of embryonic cells, they are extremely attractive candidates for stem cell research and therapy. Especially in cases where there is extreme tissue or cell damage, these embryonic cells can be cultured in a laboratory and used for replacement or transplantation procedures (Bhat, Bhat and Kour 2004). However, as the totipotent cells are generated only after fertilization, there is a lot of controversy surrounding the ethical implications of the use of cells from a developing embryo (Caulfield et al. 2015).

Early stages of embryonic development

The early stages of fertilization and embryo development have often been compared to the building of a house, where cells and extracellular secretions form the building materials from which an entire organism is created. Once an egg is fertilized by a sperm, a zygote is formed which undergoes a series of cell divisions without corresponding increase in zygote size. The resultant cells are known as blastomeres. Eventually, the blastomeres clump together to form a structure called the morula, which has a distinct outer layer of epithelial cells enclosing the blastomeres. Further cell divisions and development result in the formation of a blastocyst cavity within the morula, with movement of cells within the structure ready for differentiation into specialized cells (Pfeffer 2018).

Totipotency and pluripotency

The terms totipotency and pluripotency have been used extensively in medical research lately mainly because of the sheer possibilities of cells with these properties. It basically means that a single cell can develop into an entire organism if maintained in a suitable development environment. When a zygote undergoes the first cell division resulting in two blastomeres, both these cells are totipotent. This means that if these blastomeres are separated, each can develop into a complete organism and also produce extraembryonic structures (Condic 2014). Totipotency has been observed in the zygote upto the 4-celled stage. After this stage, the blastomeres are believed to gradually lose their totipotency and become more pluripotent (Mitalipov and Wolf 2009).

Pluripotency in a cell refers to its ability to differentiate into multiple cell types. Pluripotent cells can give rise to cells belonging to the outermost layer or the ectoderm, middle layer or the mesoderm, or the innermost layer or the endoderm. However, it does not have the capability to develop into an entire organism as it cannot positionally organize an embryo. A normal human body too has several pluripotent stem cells in the bone marrow that participate in tissue or organ repair in the body (Mitalipov and Wolf 2009).

Applications of totipotent and pluripotent cells

The most logical application of totipotent and pluripotent cells is in the field of therapeutics. From nerves to the brain, from the heart to the kidney, any type of cell or organ can be generated with the use of pluripotent cells. Extensive research has been carried out using mouse as the model organism and scientists have successfully been able to use pluripotent cells to regenerate myeloid and lymphoid cells in mice. Also, neural stem cells have been used to regenerate muscle cells under controlled conditions. Therefore, the use of pluripotent cells for therapeutic purposes has the potential to treat a considerable number of diseases through cell therapy and tissue regeneration. The most commonly used approach is to differentiate pluripotent cells into the desired cell type and then transplant these cells in the damaged tissue. Another approach is to directly transplant pluripotent cells into the damaged organ and induce its differentiation for restoring organ function. Both these approaches have proven promising for treating different types of diseases (Makhani and Siddiqui 2015).

Regardless of the idealistic possibility of using stem cells to treat diseases, there are still several available valid therapeutic options such as tissue grafting or organ transplantation. However, these approaches often face the risk of graft or organ rejection if transplanted in an immunocompromised individual leading to severe immunological consequences. Hence, the use of pluripotent stem cells in the field of therapeutics is being aggressively pursued by the medical community to eliminate the wait for a suitable donor and the risk of immunological incompatibility between the donor and the recipient (Taylor, Bolton and Bradley 2011).

Ethical implications of using totipotent cells for therapeutics

There is a lot of controversy among the people at large regarding the use of totipotent cells for therapeutics. Most people claim that in making use of totipotent cells, one has to destroy an embryo that under other circumstances could have developed into a normal human. In answer to this, some people argue that in this process the good outweighs the bad, and giving a diseased person the ability to live and function normally should be sufficient impetus to use totipotent cells for therapeutics. More than a decade of debate on this topic has not been able to resolve the issue of using embryonic stem cells (Condic and Rao 2010).

An alternative to using embryonic stem cells that are totipotent is to use adult pluripotent stem cells. However, these cells are limited in their ability to generate different cell types and may not be entirely applicable or useful for all types of disease conditions. Despite the controversy, human embryonic stem cells are currently considered to be the gold standard for use in medical research for the purpose of therapeutics for lack of better alternatives. However, there are several legal regulations and ethical implications involved and scientists need to provide clear justification and lack of alternative approaches for using these cells in their study (Zacharias et al. 2011).

Conclusion

In conclusion, the applications of embryonic stem cells in the field of therapeutics are huge and several preliminary studies have proved to be very promising. However, stem cell research is only limited by people claiming that using embryonic stem cells imply the destruction of an embryo, which is akin to killing what could become a fetus. A lot of nations are divided in this matter and there are no clear regulations for the use of embryonic stem cells for therapeutic research. In my opinion, when embryonic stem cells give a person the ability to lead a more functional and dignified life, it surpasses to a large extent the ethical consequences surrounding embryo destruction.

References:

Bhat, G M, Bhat, M A & Kour, K 2004, 'Stem cells: present status and future prospects', *JIACM*, vol. *5*, no. 2, pp. 149-156.

Caulfield, T, Kamenova, K, Ogbogu, U, Zarzeczny, A, Baltz, J, Benjaminy, S, Cassar, P A, Clark, M, Isasi, R, Knoppers, B, Knowles, L, Korbutt, G, Lavery J V, Lomaz, G P, Master, Z, McDonald, M, Preto, N & Toews, M 2015, 'Research ethics and stem cells', *EMBO Reports*, vol. *16*, no. 1. doi:10.15252/embr.201439819

Condic, M L 2014, 'Totipotency: what it is and what it is not', *Stem Cells and Development*, vol. *23*, no. 8. doi:10.1089/scd.2013.0364

Condic, M L & Rao, M 2010, 'Alternative sources of pluripotent stem cells: ethical and scientific issues revisited', *Stem Cells and Development*, vol. *19*, no. 8. doi:10.1089/scd.2009.0482

Lu, F 2015, 'Cell totipotency: molecular features, induction, and maintenance', *Natural Science Review*, vol. *2*, pp. 217-225. doi:10.1093/nsr/nwv009

Makhani, K & Siddiqui, S 2015, 'Therapeutic potential of totipotent, pluripotent and multipotent stem cells', *MOJ Cell Sci Rep*, vol. *2*, no. 5. doi:10.15406/mojcsr.2015.02.00041

Mitalipov, S & Wolf, D 2009, 'Totipotency, pluripotency and nuclear reprogramming', *Adv Biochem Eng Biotechnol*, vol. *114*, pp. 185-199. doi:10.1007/10_2008_45

Pfeffer, P L 2018, 'Building principles for constructing a mammalian blastocyst embryo', *Biology*, vol. *7*, no. 41. doi:10.3390/biology7030041

Taylor, C J, Bolton, E M & Bradley, J A 2011, 'Immunological considerations for embryonic and induced pluripotent stem cell banking', *Phil Trans R Soc B*, vol. *366*, pp. 2312-2322. doi:10.1098/rstb.2011.0030

Zacharias, D G, Nelson, T J, Mueller, T S & Hook, C C 2011, 'The science and ethics of induced pluripotency: what will become of embryonic stem cells?', *Mayo Clin Proc*, vol. *86*, no. 7, pp. 634-640. doi:10.4065/mcp.2011.0054

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Appendix III - Condic, M L 2014, 'Totipotency: what it is and what it is not', *Stem Cells and Development*, vol. *23*, no. 8. doi:10.1089/scd.2013.0364

Appendix IV - Condic, M L & Rao, M 2010, 'Alternative sources of pluripotent stem cells: ethical and scientific issues revisited', *Stem Cells and Development*, vol. *19*, no. 8. doi:10.1089/scd.2009.0482

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Appendix VI - Makhani, K & Siddiqui, S 2015, 'Therapeutic potential of totipotent, pluripotent and multipotent stem cells', *MOJ Cell Sci Rep*, vol. *2*, no. 5. doi:10.15406/mojcsr.2015.02.00041

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Appendix X - Zacharias, D G, Nelson, T J, Mueller, T S & Hook, C C 2011, 'The science and ethics of induced pluripotency: what will become of embryonic stem cells?', *Mayo Clin Proc*, vol. *86*, no. 7, pp. 634-640. doi:10.4065/mcp.2011.0054

Appendix I - Bhat, G M, Bhat, M A & Kour, K 2004, ‘Stem cells: present status and future prospects’, *JIACM*, vol. *5*, no. 2, pp. 149-156.

UPDATE ARTICLE

JIACM 2004; 5(2): 149-56

Stem Cells: Present Status and Future Prospects

Gh Mohd Bhat*, M Akbar Bhat**, Kulbeer Kour*

Introduction

Stem cells are undifferentiated cells which have the ability to divide for indefinite periods in culture and give rise to specialised cells on differentiation. Cells forming a whole conceptus are termed totipotent; whereas pluripotent cells have the ability to contribute several tissues of the foetus. Multipotent somatic stem cells, isolated from foetal and adult tissues, differentiate into effector cells of their tissue. However, recent studies imply that adult stem cells

Source and culture of stem cells

A) ***Embryonic Stem cells*:** Pluripotent embryonic stem cells were first isolated from murine teratocarcinomas[1]. Embryonic stem cells have been studied in various vertebrates from the sources mentioned below:

I. Mouse: From 8-cell embryos[2,3], dissociated blastomeres of morulae[4], inner cell mass of blastocysts[5,6], primordial germ cells[7]

Appendix II - Caulfield, T, Kamenova, K, Ogbogu, U, Zarzeczny, A, Baltz, J, Benjaminy, S, Cassar, P A, Clark, M, Isasi, R, Knoppers, B, Knowles, L, Korbutt, G, Lavery J V, Lomaz, G P, Master, Z, McDonald, M, Preto, N & Toews, M 2015, ‘Research ethics and stem cells’, *EMBO Reports*, vol. *16*, no. 1. doi:10.15252/embr.201439819

Science & Society

EMBO reports

Research ethics and stem cells

Is it time to re-think current approaches to oversight?

Timothy Caulfield[1,*], Kalina Kamenova[1], Ubaka Ogbogu[2], Amy Zarzeczny[3], Jay Baltz[4], Shelly Benjaminy[5], Paul A Cassar[6], Marianne Clark[1], Rosario Isasi[7], Bartha Knoppers[7], Lori Knowles[8], Gregory Korbutt[9], James V Lavery[10], Geoffrey P Lomax[11], Zubin Master[12], Michael McDonald[13], Nina Preto[14] & Maeghan Toews[1]

Few areas of scientific inquiry have received the amount of attention from politicians, the media and the ethics

receive federal funds, must comply with guidelines that were specifically created to govern human pluripotent stem cell (hPSC)

Cell Research (IC-SCR)—for basic science and clinical research in this field. A variety of approaches to heightened review and

Appendix III - Condic, M L 2014, 'Totipotency: what it is and what it is not', *Stem Cells and Development*, vol. *23*, no. 8. doi:10.1089/scd.2013.0364

STEM CELLS AND DEVELOPMENT
Volume 23, Number 8, 2014

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COMPREHENSIVE REVIEW

Totipotency: What It Is and What It Is Not

Maureen L. Condic

There is surprising confusion surrounding the concept of biological totipotency, both within the scientific community and in society at large. Increasingly, ethical objections to scientific research have both practical and political implications. Ethical controversy surrounding an area of research can have a chilling effect on investors and industry, which in turn slows the development of novel medical therapies. In this context, clarifying

Appendix IV - Condic, M L & Rao, M 2010, ‘Alternative sources of pluripotent stem cells: ethical and scientific issues revisited’, *Stem Cells and Development*, vol. *19*, no. 8. doi:10.1089/scd.2009.0482

STEM CELLS AND DEVELOPMENT
Volume 19, Number 8, 2010

DOI: 10.1089/scd.2009.0482

CONCISE REVIEW

Alternative Sources of Pluripotent Stem Cells: Ethical and Scientific Issues Revisited

Maureen L. Condic[1] and Mahendra Rao[2,3]

Stem cell researchers in the United States continue to face an uncertain future, because of the changing federal guidelines governing this research, the restrictive patent situation surrounding the generation of new human embryonic stem cell lines, and the ethical divide over the use of embryos for research. In this commentary, we describe how recent advances in the derivation of induced pluripotent stem cells and the isolation of germ-line-derived pluripotent stem cells resolve a number of these uncertainties. The availability of patient-matched, pluripotent stem

Appendix V - Lu, F 2015, 'Cell totipotency: molecular features, induction, and maintenance', *Natural Science Review*, vol. *2*, pp. 217-225. doi:10.1093/nsr/nwv009

REVIEW

National Science Review
2: 217–225, 2015
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Advance access publication 15 February 2015

MOLECULAR BIOLOGY & GENETICS

Cell totipotency: molecular features, induction, and maintenance

Falong Lu[1,2,3] and Yi Zhang[1,2,3,4,*]

ABSTRACT

In mammals, pluripotent stem cells can give rise to every cell type of embryonic lineage, and hold great potential in regenerative medicine and disease modeling. Guided by the mechanism underlying pluripotency, pluripotent stem cells have been successfully induced through manipulating the transcriptional and epigenetic networks of various differentiated cell types. However, the factors that confer totipotency, the ability to give rise to cells in both embryonic and extra-embryonic lineages still remain

Appendix VI - Makhani, K & Siddiqui, S 2015, 'Therapeutic potential of totipotent, pluripotent and multipotent stem cells', *MOJ Cell Sci Rep*, vol. *2*, no. 5. doi:10.15406/mojcsr.2015.02.00041

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Therapeutic Potential of Totipotent, Pluripotent and Multipotent Stem Cells

Abstract

The discovery of stem cells opened up a whole new arena of research for scientists. And the realizations of their therapeutic potential, promises sustainable cure for previously untreated diseases. Stem cells may broadly be classified into totipotent, pluripotent and multipotent and each of these classes show enormous therapeutic function. Totipotent stem cells can differentiate into 200 cell types of the body and also has the ability to reconstitute a stem cell-deprived organ, thereby opening ways to tissue regeneration and replacement therapies respectively. Similarly, Pluripotent stem cells have been made to differentiate into neural tissues, insulin secreting cells, cardiomyocytes, hematopoietic cells, osteoblasts, endothelial cells and hepatocytes successfully. Also, the prospects for reprogramming human somatic cells into induced Pluripotent Stem (iPS) cells have heralded a new era in the field of Stem Cell Therapeutics. In contrast, Multipotent stem cells also promises self-renewal as well as demonstrates plasticity to transdifferentiate into muscle, skeletal, liver, kidney, muscle, skin, neural, and cardiac cell lineages. Additionally, they are shown to serve as a gene

Review Article

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Appendix VII - Mitalipov, S & Wolf, D 2009, 'Totipotency, pluripotency and nuclear reprogramming', *Adv Biochem Eng Biotechnol*, vol. *114*, pp. 185-199. doi:10.1007/10_2008_45

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Totipotency, Pluripotency and Nuclear Reprogramming

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Abstract

Mammalian development commences with the totipotent zygote which is capable of developing into all the specialized cells that make up the adult animal. As development unfolds, cells of the early

Appendix VIII - Pfeffer, P L 2018, 'Building principles for constructing a mammalian blastocyst embryo', *Biology*, vol. *7*, no. 41. doi:10.3390/biology7030041

biology

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Review

Building Principles for Constructing a Mammalian Blastocyst Embryo

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Abstract: The self-organisation of a fertilised egg to form a blastocyst structure, which consists of three distinct cell lineages (trophoblast, epiblast and hypoblast) arranged around an off-centre cavity, is unique to mammals. While the starting point (the zygote) and endpoint (the blastocyst) are similar in all mammals, the intervening events have diverged. This review examines and compares the descriptive and functional data surrounding embryonic gene activation, symmetry-breaking,

Appendix IX - Taylor, C J, Bolton, E M & Bradley, J A 2011, 'Immunological considerations for embryonic and induced pluripotent stem cell banking', *Phil Trans R Soc B*, vol. *366*, pp. 2312-2322. doi:10.1098/rstb.2011.0030

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B

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doi:10.1098/rstb.2011.0030

Review

Immunological considerations for embryonic and induced pluripotent stem cell banking

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Recent advances in stem cell technology have generated enthusiasm for their potential to study and treat a diverse range of human disease. Pluripotent human stem cells for therapeutic use may, in principle, be obtained from two sources: embryonic stem cells (hESCs), which are capable of exten-

Appendix X - Zacharias, D G, Nelson, T J, Mueller, T S & Hook, C C 2011, ‘The science and ethics of induced pluripotency: what will become of embryonic stem cells?’, *Mayo Clin Proc*, vol. *86*, no. 7, pp. 634-640. doi:10.4065/mcp.2011.0054

SPECIAL ARTICLE

The Science and Ethics of Induced Pluripotency: What Will Become of Embryonic Stem Cells?

David G. Zacharias, BA; Timothy J. Nelson, MD, PhD; Paul S. Mueller, MD, MPH; and C. Christopher Hook, MD

For over a decade, the field of stem cell research has advanced tremendously and gained new attention in light of novel insights and emerging developments for regenerative medicine. Invariably, multiple considerations come into play, and clinicians and researchers must weigh the benefits of certain stem cell platforms against the costs they incur. Notably, human embryonic stem (hES) cell research has been a source of continued debate, leading to differing policies and regulations worldwide. This article briefly reviews current stem cell platforms, looking specifically at the two existing pluripotent lines available for potential therapeutic applications: hES cells and induced pluripotent stem (iPS) cells. We submit iPS technology as a viable and possibly superior alternative for future medical and research endeavors as it obviates many ethical and resource-related concerns posed by hES cells while prospectively matching their potential for scien-

resources), and human dignity (moral status and the ethical definition of personhood).[10,11] For research that necessitates embryo destruction, the verdict is still out among clinicians and researchers regarding one of the cardinal rules of medical ethics: “*Primum non nocere*” (First, do no harm). The principle of nonmaleficence takes into account the moral nature of the act, the agent’s intention, the means of the act, the possible adverse consequences, and the proportionality between the good and bad effects.[12] The ongoing dispute has worked its way into the global political arena such

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