Omega
II (2003)2, 72-82

Stem Cell Research
Ethical Considerations

- S. John Britto[1]

Abstract: *In recent times stem cell research has been making much hue and cry in scientific, religious, political and ethical circles. Today this field is at the cutting edge of scientific research. This paper attempts to go in some depth into the various aspects of this controversy. It gives a panoramic view of the ethical, religious and social impact of this important scientific development.*

Key Words: *Stem Cell, Embryonic Germ Cell, Blastocyst, Cloning, Somatic Cell Nuclear Transfer*

Introduction

The issue of stem cell research appeared on the scientific scene in November of 1998 when researchers first reported the isolation of human embryonic stem (ES) cells. However, knowledge on stem cells has been accumulating for more than 30 years. The discovery made by Dr. James A.Thomson, a biologist at the University of Wisconsin, Madison, USA, offers great promise for new ways of treating diseases of the heart, cancer, Parkinson's disease, Alzheimer's disease and others. ES cells can be theoretically differentiated into virtually any type of human cell, from blood cells to skin cells. Scientists hope to find ways of using them to repair damaged tissues. Although it is impossible to predict the outcomes, scientists and the public will gain new knowledge in the biology of human development with significant potential for therapies and cures. Derivation of ES cells from early human embryos and the use embryonic germ (EG) cells and fetal stem cells from aborted fetal tissues raise

fundamental ethical and religious questions about what it means to be human and what restrictions, if necessary, should be placed on research in this area. This paper will briefly review the current status of human stem cell research and its ethical and religious implications.

Current Status of Human Stem Cell Research

"Stem Cells" refer to precursor cells that can give rise to multiple tissue types and can divide indefinitely. The embryos from which the embryonic stem cells (ES) are derived are typically 4-5 days old - a hollow microscopic ball of cells called blastocyst.[2] Totipotent cells give rise to fully functional organism as well as to every cell type of the body. Pluripotent stem cells are capable of giving rise to any tissue type but not a full-grown organism. Multipotent stem cells are more differentiated or determined to give a specific tissue.[3]

There are two directions of research: one is reproductive cloning (controversial) and the other is therapeutic cloning (chiefly by Somatic Cell Nuclear Transplantation (SCNT) after reprogramming).[4] The interest now lies on ES cells. The sources of stem cells are as follows: The Embryonic Carcinoma (EC) cells are derived from the cells of testicular tumors; ES from the pre-implantation embryos and Embryonic Germ (EG) cells from Primordial Germ Cells (PGC).[5]

Stem Cell Derivation

The isolation, culture and partial characterization of stem cells isolated from human embryos were reported in November 1998.[6] Human embryonic stem cells are derived from the inner cell mass of a 4 or 5 day old blastocyst which consists of three structures. The trophoblast, the layer of cells that surrounds the blastocyst; the blastocoel, the hollow cavity inside the blastocyst; and the inner cells mass, a group of nearly 30 cells at one end of the blastocoel. Human embryonic germ (EG) cells are derived from 5 to 10 week old fetuses. The above two are sources of reproductive cloning, while the other multipotent entity lies with the success of adult stem cell research.

Adult stem cells (alternatively called somatic stem cells) typically generate the cell types of the tissue in which they reside. They are

found in developed tissue, regardless of the age of the organism, as for example the hematopoletic stem cells of blood. More recently, Mesenchymal stem cells (MSC) (a type of multipotent adult stem cells required for the maintenance of bone, muscle and other tissues) have been discovered.[7] Experiments have also raised the possibility that adult stem cells from one tissue may be able to generate cell types of a completely different tissue, which is known as plasticity or transdifferentiation, which is applied in regenerative medicine. Examples of plasticity include blood cells becoming neurons, liver cells producing insulin, hematopoietic stem cells becoming heart muscle. Thus use of adult stem cells for cell-based therapies has become an active area of investigation by researchers.[8] Benefits of such research range from chronic heart disease, stroke, diabetes, burns, osteoarthritis, rheumatoid arthritis, Parkinsons's and Alzheimer's diseases and cancer.[9] The noteworthy advantage is that it avoids the hassle of immune rejection because cells are from the patient's own body.

Properties of stem cells are threefold: i) they can replicate indefinitely without senescence or mutation, ii) they appear genetically normal, iii) they possess the property of differentiation into other cell types of the body. The promise of stem cells lies in their ability to be cultured in the laboratory and ultimately directed to become specific types of cells or tissue that can be used to treat a host of cell-based diseases.[10]

Techniques of Stem Cell Research

Nuclear Transfer (NT): this is the primary method based on transfer of nucleus from one cell to another. The nucleus of the stem cells needs a kind of reprogramming before transfer occurs, which will lead to the regeneration of cells and tissues of an individual. The genetic modification of somatic cells prior to NT provides a new route for modifying and targeting the germ line. In this approach the cells are selected and tested for the genetic modification prior to SCNT.[11] Nuclear transfer can be through three processes. One is the usual reproductive mode by sexual reproduction. The other two are in vitro processes which include the reproductive cloning and SCNT, also known as therapeutic or biomedical cloning.

In reproductive cloning, the blastocyst is put into an adult animal's (surrogate mother) hormonally "prepared womb" and is allowed to develop normally. In therapeutic or biomedical cloning, a donor nucleus is transferred to an egg that has its own nucleus removed; the cell divides then to form blastocyst.[12] The clusters of cells are then removed from the blastocyst and they go on to be the embryonic stem cell line, while the developing blastocyst is destroyed. This destruction is different from that of reproductive cloning, where the blastocyst gets into surrogate mother's hormonally prepared womb.

Scientists adopt this biomedical cloning to form human embryonic stem cell lines that carry DNA with disease causing mutations. By studying how these cell lines grow, divide and respond to factors such as drugs, it would be possible to understand and treat diseases. The term "human embryonic cloning" is now being replaced by the term "nuclear transplantation/transferal" to produce human pluripotent stem cell lines. This research is endorsed by the different government organizations as a necessary step in the development of new and novel therapies for cancer, diabetes, Parkinson's disease and others.[13] Cloning by nuclear transfer was first successfully applied in cultured somatic cells introducing targeted changes into the genome of livestock while cloning Dolly.[14]

Pluripotent stem cells present hope for the cure of several diseases. In theory, stem cells can be collected, grown, and stored to provide a plentiful supply of healthy replacement tissue for transplantation into any body site. As said earlier, they have the potential to react or cure a myriad of diseases. However many political and religious groups strongly oppose the stem cell research.

A Brief Review of the Reactions to Stem Cell Research

Europe's catholic Bishops have called on the council of Ministers of the European Union to reject the proposed new EU guidelines on the funding of future research on embryos.[15] They said: "We believe that human life has an intrinsic and absolute value at every stage, and it should not therefore be used as 'new material.' A good end cannot be used to justify any means." President George W. Bush declared that research on stem lines might receive government funding subject to

certain conditions, and he freed up some 64 stem cell lines in laboratories across the country.[16] Scientists in Britain and in the United States (National Institutes of Health) have definitively expressed a scientific preference for embryonic stem cells over any other source of research. King's college, London has announced the establishment of a line of human embryonic stem cells, the first to be grown in Britain. Embryonic stem cell research is considered illegal in Italy, Austria, Portugal, Spain, Germany, France and Ireland. However, Sweden, Finland, Greece, the Netherlands and Britain allow harvesting of embryonic stem cells. In other parts of the world, specifically in Singapore and in Mainland China, human stem cell research is forging ahead with no apparent ethical guidelines. Biologists at the Second Medical University in Shanghai have reprogrammed human cells by fusing them with rabbit eggs emptied of their genetic material.[17]

Ethical Considerations of Reproductive Cloning

The deliberations of international, national and state regulatory bodies in most cases favoured the prohibition of reproductive cloning in which a cloned human embryo is created with the intent that a human clone will be borne.[18] But they differ considerably over what has been termed research cloning. The latter involves the creation of a cloned human embryo for the purpose of scientific investigation of early human development or for medical research aimed at developing treatments for diseases.[19] Cheshire *et al* contend that human cloning should not be permitted whether for research or reproductive purposes. Though importance has to be given for medical research and healing of people, yet the many harmful consequences of human cloning would exceed the anticipated benefits.[20]

Reproductive human cloning is hazardous to the gestating clone and the surrogate mother. The status of non-human animal cloning technology is still rudimentary. There have been high occurrences of severe physical and genetic defects and premature aging in cloned offspring.[21] Embryologists estimate that a single successful human cloning might come at the cost of hundreds of failed attempts.[22] Even if the issues of safety were overcome, which is unlikely, ethical objections remain.[23]

Human cloning would signify an egregious disrespect for human dignity and personal autonomy, in addition to profound emotional problems. The cloned individual would not be born with the special privilege of having a unique genetic identity, but would live in the shadow of the other person whom the clone was intended to duplicate genetically. There would be stigma of being known as a clone, with a confused parentage and expectations to measure up to the level of the genetic original or of 'replacing' a deceased person. All these could result in unforeseen psychological turmoil.[24]

Public opinion justifiably regards human cloning to be a hazardous departure from the intimate and richly meaningful process of natural procreation. It is not technology that is objected to but its misuse that enables some people to wield nearly absolute control over the genetic makeup of others. This substitution of human genetic replication for procreation would amount to a perilous affront to human dignity. Human cloning, whether practiced occasionally or otherwise, would be a grave devaluation of humanity and would create a shift in societal attitudes away from appreciating people as distinct individuals but sizing them up as useful or attractive products of technology.[25] Proposals to ban human cloning for purposes of reproduction have received broad support. However, enacting a ban solely on reproductive cloning, while simultaneously permitting research cloning, would lead to several unforeseeable consequences, and hence is undesirable.[26] A ban on human cloning for both research and reproductive purposes would be the most effective and ethically responsible safeguard against the births of human beings by cloning.

Ethical Implications of Therapeutic Biomedical Cloning

Scientists use SCNT which involves enucleating a cell and replacing it with a donor nucleus. This raises two basic ethical dilemmas. In enucleating the cell, an important value is destroyed, since an individual's uniqueness lies in the genetic material and it is directly linked to the identify of the person. Besides, the importance and the centrality of reproduction in the life of an individual or couple is undermined. Human life is sacred from the beginning and so genetic material cannot be ignored as a mere bundle of molecules. In human society, family lineage

and ancestral relationship are cherished values which are thwarted by this approach. The Pontifical Academy of Life states that this extreme form of manipulation would destroy the complementary and personalist nature of human reproduction, violate the human right of equal dignity by selective reproduction, reduce the role of women to a mere biological function, destroy natural family relationships and cause psychological suffering for the cloned subject as a copy of somebody else.[27]

In replacing the cell with a donor nucleus the mitochondria of one cell is used by the donor nucleus to grow. Mitochondria provide four essential pathways for energy transformation. Damage to any of them accelerates aging in children and adults.[28] Judging from the range of problems that cloned animals have, there are indications that somatic cell nuclear transfer damages mitochondrial genes in the egg. It must be concluded that the present process of therapeutic cloning presents serious risks and can be only described as experimental. Such non-beneficial experimentation cannot be justified ethically. The basic ethical rules of respect, consent, avoidance of risks, absence of harm either to the subject of research or to those who use this research can hardly be adhered to by this process. In fact, it brings harm to both the person involved and society because it lessens the respect for life in society.[29]

Destroying the blastocyst to remove its stem cells is a more serious act than enucleating a cell, since the cell is now organized by its DNA and its biological potentiality is clear. This step could be immoral.[30] The declaration of the Pontifical Academy of Life on the production and use of embryonic stem cells for scientific or therapeutic research points out that this conclusion is clear from the encyclical *Evangelium Vitae* and the instruction *Donum Vitae*, which hold that the fruit of human generation must be respected from the very first moment of its existence. Pope John Paul II declared that therapeutic cloning is not morally acceptable since it involves the manipulation and destruction of human embryos.[31]

Analysis of Divergent Schools

From the above analysis of reproductive and therapeutic cloning, two broad and somewhat opposing themes emerge. On the one hand, there is a moral commitment to healing and to relieving suffering caused

through injury and illness. On the other hand, we need to be cautious in pursuing the promise of stem cell research, which involves moral and ethical problems. There are possibilities of longer-term harm to society such as damage to our respect for the sanctity of human life and the problems arising from the appropriation or privatization of stem cell resources. Other issues of contention are the status of the fetus and the embryo, complicity on the part of the researcher and the alternative of concentrating on the stem cells found in adults.

Doerflinger[32] and others hold that fetuses and embryos have moral status as individuals, and so must not be treated as instruments and as a means to an end. Being innocent they are inviolable. A researcher using fetal tissues is not necessarily a supporter of abortion. Those who harvest embryos and use the cells are necessarily complicit in the destruction of the embryo. He is critical of the view that derivation of stem cells from 'spare' embryos obtained through fertility clinic differs morally from using embryos created solely for research purposes.

Margaret Fasley[33] and others seem to postulate a liberal view. According to her, the moral status of the embryo is not that of a person, and its use for certain kinds of research can be justified. Developmental view of personhood is strongly adhered to.[34] Since it is a form of human life, it deserves some respect.[35] She refuses to equate the destruction of embryos that already exist with the creation of embryos in order to destroy them subtly for the benefit of third parties.

John C. Robertson[36] and others deny moral status to fetuses and embryos. However they are not to be harmed by research or destruction when no transfer to uterus is planned. Symbolic value accorded to pre-viable fetuses should not override a pregnant women's choices. Gene Outka[37] and others assert that we should resist the creation of embryos for research purposes only, yet we may engage in research on 'excess embryos.' There is opposition by some to governmental involvement in stem cell research since embryo or fetal destruction is involved.[38]

Conclusion

It is clear now that there is significant disagreement on stem cell research and human cloning. Some believe that the human embryo has

moral value from the beginning, while others hold that moral value develops gradually. There is a strong contention that human cloning should not be permitted, whether for research or reproductive purposes. The religious circles affirm the importance of medical research and support the goal of healing people, yet many believe that the harm human cloning would bring would exceed the anticipated benefits. The way scientists think is often so fundamentally different that the answers to bioethical issues proposed by a non-scientific community are perceived as minimally relevant by scientists.[39] Another factor is that most countries in Europe and elsewhere are moving towards allowing derivation of ES cells. There is general agreement that it might be neither necessary nor desirable to harvest more embryos, if 'spare' frozen embryos are available for donation. The benefits from SCNT would be affordable by the rich only and may not prove economical for routine treatment. Attempts are being made to hype adult stem cells over ES cells. Scientists working on either adult or ES cells opine that both lines of research should be actively pursued.

Notes

1. Dr. S. John Britto is Professor of Life Sciences at St. Joseph's College (Autonomous), Tiruchirappalli.
2. Quoted in "*Stem Cells*: 1999. *A Primer,*" NIH publications, USA.
3. Quoted in, "*Stem Cells*: 2000 : *Scientific Progress and Future Research Directions,*" NIH publications, USA.
4. Sanjit Dey, "Buoyancy of Stem Cell Research," *Science and Culture,* 69 (2003), p. 99.
5. P. J. Donovan and J. Gearhart "The End of the Beginning for Pluripotent Stem Cells," *Nature,* 414 (2001), pp. 92-97.
6. J. A. Thomson, M. A. Waknitz, J. J. Swiergieal and U.S. Mareshall, "Embryonic Stem Cell Lines Derived from Human Blastocysts," *Science,* 282 (1998), pp. 1061-1062.
7. NIH publications,1999.
8. Sanjit Dey, p.100.
9. Ibid. p.100.
10. NIH publications, 1999.

11. P. J. Donovan and J. Gerarhart, pp. 92-97.
12. T. Reya, S. J. Morrison, M.F Clarke and I. L. Weissman, "Stem Cells, Cancer and Cancer Stem Cells," *Nature,* 414 (2001), pp. 101-105.
13. Anne McLaren, "Ethical and Social Considerations of Stem Cell Research" *Nature,* 414 (201), pp. 129-131.
14. A. E. Schneike, A.J. Kind, W. A. Richie, K. Mycock, A. R. Scott, M. Ritchie, I. Wilmut, A. Colman and K. H. S. Campbell, "Human factor in Transgenic Sheep Produced by Transfer of Nuclei from Fetal Fibroblasts," *Science* 278(1997), pp. 2130-2133.
15. See *Tablet* (2003) 26th July, p. 26.
16. See *Tablet* (2003) 2nd August, p. 6.
17. Ibid., p. 6.
18. W. P. Cheshire, D. Edmend, Pellegrino, Linda K.Bevington, O. Ben Mitchall, Nancy L. Jones, Kevin T. Fitzgerald and C. Everett Koop, "Stem Cell Research: Why Medicine Should Reject Human Cloning," *Mayo. Clin. Proc.* 78 (2003), pp. 1010-1018.
19. W. P. Cheshire, p. 1010.
20. W. P. Chespire, p. 1011.
21. See S. P. Westpahl, "Cloned Embryos Are a 'Gallery of Horrors,'" *New Scientist,* (2001, December 12).
22. R. Jaesnisch and I. Wilmut. "Developmental Biology: Don't Clone Humans!" *Science,* 291 (2001), p. 2552.
23. W. P. Cheshire, p. 1011.
24. L. R. Kass, "*Human Cloning and Human Dignity*: *The Report of the President's Council on Bioethics*" (New York: Public Affairs, 2002).
25. W. P. Cheshire, p. 1011.
26. J. F. Kiner. "Human Cloning," in J. A. Kilner, P. C. Cunningham, W. D. Hager (eds.), *The Reproductive Revolution*; *A Christian Appraisal of Sexuality, Reproductive Technologies and the Family* (Grand Rapids Michigan: WB Eerdmans, 2000), pp. 124-139.
27. Quoted in Peter Jeffrey, "Ethical Issues Raised by Stem Cell Research," *The Catholic Medical Quarterly,* June 30, 2002.
28. The cycles are the citric and respiratory cycles, oxidative phosphorylation and fatty acid oxidation.

29. See Peter Jeffrey.

30. Norman Ford argued in the *Tablet* that the status of the human embryo is not settled in catholic theology. N. Ford, 9th December, 2000.

31. Address to 18th *International Congress of the Transplant Society*, Rome 29th August, 2000.

32. R. Doerglinger, "Destructive Stem Cell Research on Human Embryos," *Origin,* 28 (1999), pp. 697-711.

33. Margaret Farley (1999), " *Roman Catholic Views on Research Involving Human Embryonic Stem Cells,*" paper presented to the National Bioethics Advisory Commission.

34. T. A. Shannon and A. B. Walter, "Reflections on the Moral Status of the Pre-embryo," *Theological Studies,* 51(1993), pp. 603-626.

35. M. J. Myer, L. J. Nelson, "Respecting What We Destroy: Reflections on Human Embryo Research," *Hastings Center Report*, 31/1 (2001), pp.16-32.

36. J. A. Roberson, " Ethics and Policy in Embryonic Stem Cell Research," *Kennedy Institute of Ethics Journal,* 9/2 (1999); pp. 109-136.

37. Outka, "The Ethics of Stem Cell Research", *Kennedy Institute of Ethics Journal*, 12/2 (2002), pp.174-213.

38. Letter to Senators by Cardinal Willam H. Keller, Chairman, National Conference of Catholic Bishops, USA, 2003.

39. Nancy L. Jones, "*The Interface between Science and Ethics: Probing the Deeper Questions,*" panel discussion on "Artificial and Asexual Human Embryos," held on October 24-27, 2002, in Baltimore.