Practical Bioethics of Modern Technology for Embryonic/Fetal Stem Cell Research and Transplantation

EMBRİYONİK/FETAL KÖK HÜCRE ARAŞTIRMA VE NAKLİ İÇİN MODERN TEKNOLOJİNİN UYGULAMALI BİYOETİĞİ

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Özet

Since 1930s scientists have used fetal tissues in research. Nowadays, the semi-opened secret of dissecting fetal tissue for sales reveal that aborted fetuses being harvested and sold in pieces to fuel a vast research enterprise. Because the severity of such a trend, there are many social, legal and ethical implications arisen. For these and other reasons, upon reflection, it is mandatory that all of us must take it very seriously. As such, this article aims to develop a theoretical foundation for establishing a middle ground for the emerging new technology of embryonic/fetal stem cell research and its application in potential therapy-the transplantation. This article provides in-depth discussion, arguments, and counter arguments on an ethical use of modern technology, especially that of molecular biology, in research and therapy (transplantation) of human beings.

Key Words: Bioethics, Embryonic/fetal stem cells, trasplantation, Parkinson's disease, oligodendroglia

Abstract

Bilim adamları, 1930lu yıllardan bu yana araştırmalarda fetal dokuları kullanmaktadırlar. Bugünlerde, yarı açık bir sır olan fetal dokuların satılmak üzere diseke edilmesi, abort olan fetusların parçalanıp satılarak geniş bir araştırma şirketini canlı tuttuklarını açığa çıkarmıştır. Böyle yoğun bir eğilim nedeniyle, birçok sosyal, yasal ve etik karışıklıklar artmaktadır. Bu ve diğer nedenler için, bu durum oldukça ciddiye alınmalıdır. Aslında bu makale, embriyonik/fetal kök hücre araştırması ve bunun potansiyel tedavi olan organ naklinde kullanılmasını sağlayan yeni teknoloji için orta bir zemin saptamak üzere teorik bir temeli geliştirmeyi amaçlamaktadır. Bu yazı, insanların, araştırma ve tedavide (transplantasyon) modern teknolojiyi, özellikle moleküler biyolojiyi etik olarak kullanmalarını tartışmakta, görüş ve karşı görüşler içinde vermektedir.

Anahtar Kelimeler: Biyoetik, embriyonik/fetal hücre, transplantasyon, Parkinson hastalığı, oligodendrogli

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In light of the current semi-opened secrets of dissecting fetal tissue for sales, in the mean time, due to heavy demands from the fetal/embryonic stem cell research circle, there are many social, legal and ethical implication in such a practice that deserve our attention. Scientist and the people in general need moral intensity these days. We all need to take the application of stem cell research extremely cautious.

Discussion

It is traditionally assumed that persons, who regard abortions to be usually not allowable, must (for the same reasons) are against fetal/embryonic stem cell research.

Nevertheless, a confirmed standpoint objecting abortion does not necessarily drive one to refuse fetal/embryonic stem cell research. Certainly, there is dissimilarity in potentiality between the embryos used in such researches and that are discussed in

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the abortion debate. Nevertheless, it can still make such researches acceptable even if one is convinced that abortion is not allowable. With regard to the aforementioned potentiality in vitro embryos, it has been argued that at times it is more morally alike to clonable somatic cells than they are to in vivo embryos.[1] In this author's humble opinion, this at the very least may endorse the concept that there is significant moral differentiation between embryos in vivo and that in vitro. Nevertheless, there are still others who refute such a concept.

In fact, stem cell research presents many technological and bioethical problems as well as future challenges. Conversely, stem cell therapy has been raised as a potentially and radically new way to treat some diseases and injuries, with possibly extensive medical benefits. Recently, a body of research has been done in this field on a global scale. Such a therapy could be a beginning of an age of medical discovery of cell-based treatments that in the future would reinstate certain function to people, whose lives are endangered. We are now still at the starting point of such a journey.

Because the US federal government refuses to fund research on the human embryonic stem cells and therapeutic cloning, several US states are trying to make up the emptiness. Notwithstanding their attempts are praiseworthy, the funds of most state budgets are minute as compared with that of federal source; further more, a gradual and statewide limited tactic cannot compensate for the requirement of federal funding.

With a cautious consideration of the political, social, ethical, and technological insinuations, we might distinguish the terms of a possible resolve that can maintain social agreement, whereas opportunities for technological and scientific development can still be met. The US President's Council on Bioethics publication (May 2003) entitled "Alternative Sources of Pluripotent Stem Cells", introduced four such suggestions.

One of these methods, altered nuclear transfer proposes to use the technology of somatic cell nuclear transfer (SCNT), but with a pre-emptive genetic or epigenetic alteration, that precludes the included and synchronized organization vital for natural embryogenesis. Its moral and scientific magnitudes of this suggestion are discussed as a way onward for the embryonic stem cell research.[2]

Bioethicist and lawyer Klotzko has written a book relevant to new technology on a topic timely to us all since the 1996 birth of Dolly, the first mammal cloned from an adult cell.[3] Her book, entitled *A Clone of Your Own?,* describes the new world of possibilities that can be peeked over the horizon. The human charm with cloning goes beyond science and its unusual medical insinuation. Klotzko explains why the view of human cloning activates our profound expectation and our serious doubts, and thus drives us to consider what it would signify for us to have a "clone of our own", with all the moral issues that surround it. There is a concern that, someday soon (if it has not happened already secretly), the first cloned human being will be born and the human being will go on board on a scientific and moral journey whose purpose cannot even be predicted.

For an example, in the light of lessons learned from the fraudulent Human Embryonic Stem Cell Research in South Korea,[4] it is as well worthwhile to note that there is a recent article by P Patel entitled *'A natural stem cell therapy? How novel findings and biotechnology clarify the ethics of stem cell research?'*.[5] Briefly, Patel's paper is written to obviate the need for a discussion of the "unfettered fetus industry"; the central thesis is that we can harvest totipotent stem cells from something other than an embryo (*Totipotency* means the ability of a cell, such as an egg, to give rise to unlike cells and thus to develop into or generate a new organism or part). The argument is that there is no need to develop an embryo, much less a whole fetus, before we can harvest these important stem cells – they may be derived from enucleated eggs, which are never fertilized, as well as parthogenically activated eggs that again, are never fertilized by a sperm. Hence, there will be never any need of "embryo harvesting" or "fetus harvesting" because

stem cells can be derived from non-embryonic tissue (*Parthenogenesis*-- Function: noun. Etymology: New Latin, from Greek pantheons + Latin genesis. Parthenogenesis: reproduction by development of an unfertilized usually female gamete that occurs especially among lower plants and invertebrate animals).

To address these concerns, the next step should certainly be cultivation of discarded tissue, i.e., utilization of "damaged ova" to create useful stem cells from growingly incapable destroyed cells. Now what matters is to found how to sift through an abortus to discover the destroyed ovum; and how to use this damaged ovum once we found.

It is as well noted that there is an-other issue like *'The problem is destruction of a human organism'*, according to Beverly B. Nuckols.[6] She stated that the blastocyst, with its inner cell mass, is by definition an embryo regardless of how that organism began. She observes that in animals (Dolly the sheep? and the cats, horses, mice, etc.) that have been cloned by somatic cell nuclear transfer, there is no immediate fertilization of the oocyte. Hence, she opines that, in nature, the generation of cell division is initiated by the penetration of the zona pellucida by the sperm. (It is noted that the **zona pellucida,** or **zona striata** in older texts, is an essential constitutive portion of an oocyte. It is a glycoprotein membrane surrounding the plasma membrane of an oocyte. Notwithstanding that it is external but not extraneous to oocyte. Zona pellucida binds spermatozoa.)

Perhaps, in the laboratory it could be the electrical stimulation of an enucleated oocyte, alternatively, even of the oocyte, itself, in some species to facilitate fertilization. Nevertheless, in Nuckols' opinion, the donor nucleus did remotely derive from the fertilization of an oocyte by a sperm. She thus regards that science fiction has dealt with the parentage of the clone; additionally, the consensus of these thinkers seems to be that the parents of a clone are both the donor and his/her parents. As such, this might be a philosophical issue, and the scientist and the ethicist, although allowed to pose it, unfortunately can not solve it, at least in this author's humble opinion.

Nevertheless, in Patel's article, there appears to be an effort trying to express some of the ideas behind what we should and should not value, irrespective of whether or not we call it an embryo. The argument that a blastocyst is untouchable with regard to full moral contemplation seems disproved by the appearance of "blighted ova" in Patel's article. More over, as for the deliberation of "in some remote sense", the somatically transferred nucleus constitutes an embryo is still not a good argument, since under that circumstance every single cell of the human body could have been called an embryo! This author agrees with Nuckols' viewpoint that it is important to define an embryo. Even though her critique may eventually have its merit, her argument seems lacking the reasons why we call "a blastocyst with an inner cell mass" an "embryo." Hence, her comment appears to miss the key point of Patel's paper, which is that we ought to establish technologies that may meet the middle ground, such as parthonogenetically created stem cells -- so that there will be no need for us to debate on where the stem cell actually comes from.[7,8] Unfortunately, embryonic stem cells from fetal/embryonic tissue applied to both clinical aspect and its experimentation thus far are only the first step. After it avails, the concept will possibly be accepted. Once the concept is accepted, what will be followed? How long before we have an unfettered fetus industry in which the organs of unborn babies are sought and then put up for sale as commonly as pints of blood?

As mentioned earlier, a lively example is to be illustrated and reflected as follows. Geoffrey Chamberlain received a professional award for his research (outlined in the March 1968 issue of the American Journal of Obstetrics and Gynecology), in which he took live aborted fetuses, attached them to an artificial placenta, perfused the fetuses with blood from the latter, to see whether he could keep the fetus alive, and then he pulled the plug off

on the fetus. No one objected to him at that time (in the late 1960's). Yet, the following discussion merits attention. Judge no one; the more the components of moral intensity that are present in an individual, including researchers, the more likely it is that that individual will recognize the existence of an ethical problem, with a subsequent effect on judgment, intentions, and behavior. Once more, judge no one - had moral intensity been positively impacted with stronger personal moral philosophy along with other related factors (variables), the conclusion of the event by Geoffrey Chamberlain at that time would have been completely different. It appears that there would have had lots of objection to his act at that time, notwithstanding, given judging no one.

Lindvall notwithstanding, there is an arguement that major scientific progress has been made in the field of embryonic/fetal tissue transplantation clearly documenting that cell replacement by transplantation can hopefully restore brain function for several years in the human being, there are still some of main problems that need to be solved for the further development of neural transplantation into a fully useful strategy in therapy.[9] One of the most serious problems is that large amounts of the human embryonic midbrain tissue are needed for therapeutic effects.

In fact, dopaminergic (DA) brain nerve cells, expanded from stem cells obtained from small quantities of early human embryonic tissue might become useful for transplantation in patients with Parkinson disease (PD), according to the current knowledge available. However, the deeply seated mid-brain tissue from at least three to four embryos needs to be implanted per brain hemisphere of any adult patient of PD in order to reach a significant clinical improvement!

All these indicate the main issue that early embryonic human tissue is needed. Issues on clinical application of embryonic/fetal tissue transplantation merit our further consideration. There are issues on clinical application of embryonic/fetal tissue transplantation are to be solved. Among such problems, one of the major concerns is as to how to increase the over-all result of functional recovery of the patients with embryonic/fetal tissue transplantation. For example, whether all the symptoms of PD can be completely cured by transplantations or not, and how this might be improved remain to be decided. Notwithstanding knowledge about the studies in animals has shown that grafts placed in different subregions of the deep location of an animal's brain can compensate for specific, but not all the symptoms of movement disorder. However, such topographic knowledge specifically on where to place the grafts in order to relief a specific symptom and sign of the human patients is still needed to be improved.

Some other practical considerations in neural transplantation in order to obviate ethical issues are as follow. For instance, the major problem will be as to how to reduce the amount of early embryonic and fetal tissues required for transplantation. Future transplantation strategies such as one of the studies has evaluated as follow. It is to assess the capacity of transplanted embryonic stem cell (ESC)-derived nerve cells to migrate into host brain and to assess these cells as a possible source for cell replacement therapy in neurodegenerative disorders such as PD. In short, such an experimental strategy has contributed to the future basic research regarding future transplantation approaches in neurodegenerative disease including but not limited to PD.[10] Other alternative approaches that would obviate these bioethical problems will be to use immortalized cell lines of the human embryonic/fetal central nervous system origin, or genetically manipulated cell suspensions into the deep portion of brain.[11-13] Further more, in contrast to the negligible inclination of the human neural stem cells to engender oligodendroglia (vide supra for its definition) reported hitherto, there is a most recent report of immortalized cell line bestowed with the natures of normal human neural stem cells. Such a cell line is also appropriate for establishing the novel, trustworthy analysis and re-constructible high-throughput gene and drug guarding that are important in research, diagnostics and cell therapy studies (It is noted that Oligoden-

droglia may be called interfascicular, perivascular, or perineuronal satellite cells according to their respective location. The most important recognized function of these cells is the formation of the insulating myelin sheaths of axons in the central nervous system. In contrast to Schwann cells of the peripheral nervous system, one oligodendroglial cell can myelinate more than one axon. It is as well noticed that **myelin sheath** is the insulating envelope of **myelin** that surrounds the core of a nerve fiber or axon, and facilitates the transmission of nerve impulses).

Obviously, elective abortions probably will continue to be the primary source of fetal/embryonic tissue for transplantation for some time until other tissue sources become available, therefore, continuing attention in evaluating the aforementioned issues are mandatory.

Conclusion

The embryonic/fetal tissue transplantation by itself is a complicated problem, so is embryonic stem cell research, furthermore, the source of embryonic/fetal tissues is another difficult dilemma to be settled; above and over, the use of primary human/embryonic fetal tissue in the treatment of neurodegenerative disorders, while promising, in reality, faces several difficult technical and bioethical issues.

Further assessment reveals that ethics for science of stem cell research has nothing in common with ethics (only if any) derived from the science of stem cell research, although one is unable to image what it is like such ethics, if any derived from embryonic stem cell research. Nevertheless, there can (if one wishes, should) be ethics for Stem Cell Research and Therapy. Therefore, the real issue is ethics FOR stem cell research and therapy. It can (and ought to) be ethics for it, exactly as it can and should be ethics for any other human activity: natural science, sports, arts, literature, management, and so on, and so on. For stem cell research and therapy, we certainly need very badly, at least for the time being, to take some middle ground for new technology, such as using parthonogenetically created stem cells, immortalized cell lines of the human embryonic/fetal central nervous system origin, genetically manipulated cell suspensions, etc for research and therapy. Hopefully, such a middle ground may serve as a framework for further studies in the developing biological technology in this era.[14]

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