

CROSSROADS: WHERE MEDICINE AND THE HUMANITIES MEET

Embryonic Stem Cell Research: Is it merely the means to an end?

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I. INTRODUCTION:

To some people, the promise of embryonic stem cell (ESC) research may seem a scientific messiah, one in its infant stage and currently under the threat of being killed by Herod—a political decree of its death before its potential may never be known. A religious metaphor is used here precisely because the arguments revolving around ESC research are so powerful as to evoke an opinion from all: religious leaders, politicians, the legal community, scientists, and ethicists. While the various views are intimately related, we will attempt to categorize them for the sake of simplicity.

The goal of this paper is not to convince the reader of the opinion of its authors. Our purpose is to present an objective overview of all the relevant issues surrounding embryonic stem cell (ESC) research, including the anticipated benefits, religious, legal and ethical arguments. Although we recognize that other issues concerning reproduction technology, including human cloning as an alternative means of having a child, pre-implantation diagnosis, and abortion are all intimately linked to the question of ESC research, we have chosen to concentrate on the issues surrounding therapeutic cloning, and ESC research.

II. WHAT IS CLONING?

Reproductive cloning is the cloning of an entire organism (whether sheep, dog or human) to yield a fully developed fetus (24, 28). Reproductive cloning is a subset of cloning research that can be used to aid infertile couples as well as other applications discussed

later. Another subset of cloning research is therapeutic cloning (17). This latter area studies how cloning of specific cells, such as embryonic stem (ES) cells, could be used to treat diseases (17). This type of cloning research does not involve the production of offspring, and is therefore considered ethically different from reproductive cloning (17). It is important to understand the difference between these two areas of scientific investigation, since they have altogether separate aims and therefore different results or consequences.

III. TECHNIQUES CURRENTLY USED FOR CLONING:

A) Splitting of the Morula

During the cleavage period, each individual blastomere is totipotent, and can therefore generate an entire organism on its own. The fetuses arising from each blastomere would be clones of each other, but not clones of their parents, since each arose from one fertilized ovum (24, 5, 11).

B) Somatic Cell Nuclear Transfer (SCNT)

SCNT is a technique used to produce a clonal child that is effectively a delayed identical twin of its parent. The donor is first given oral contraceptives for approximately two weeks, providing a clean slate to begin from. The donor's pituitary gland is then pharmacologically prevented from secreting gonadotropins. Finally, the donor is injected with FSH and LH to promote follicular maturation. Once follicles have matured, a mature oocyte is aspirated from the donor's ovary using a needle. The genetic material of the oocyte is then removed via the insertion of a small needle through the zona pellucida, into the cell, removing all of the chromosomes and some of the surrounding cytoplasm (ovum enucleation) (5).

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In addition, a somatic cell from the "parent" is isolated via skin biopsy, which involves the removal of fibroblasts from the skin of the donor. A fibroblast nucleus is isolated and immediately injected into the enucleated ovum. The "fertilized cell" is then stimulated to begin mitosis. After several days, the cleaving embryo is a human clone of its donor parent. However, this embryo cannot be allowed to develop beyond 14 days according to ethics guidelines (5).

The embryo is allowed to develop only up to day 14 because during the first two weeks of development, the embryo has not yet begun to construct its nervous system, and therefore cannot have a consciousness (11,28). Furthermore, in utero, the embryo would not normally implant before the second week and is therefore still independent of the mother. Spontaneous abortions are common in nature prior to implantation and thus some ethicists do not see the killing of an embryo up to the implantation stage as an immoral act (5).

C) Cloning existing stem cell lines

These stem cell lines have been previously isolated from embryos which were discarded during fertility procedures, such as IVF (in vitro fertilization), IUF (intra-uterine fertilization) etc (6). These cells are induced to replicate via morula separation, but it needs to be mentioned separately since, in some countries (e.g. the United States (U.S.) and Germany) it is the only research technique approved for public research (6, 27, 16).

III. ANTICIPATED BENEFITS OF HUMAN EMBRYONIC CLONING

Human cloning in general, and the use of ES cells specifically, have been the sources of much recent public debate. If allowed to become widely used, these procedures would have serious ethical implications, precisely because they can have a significant impact on the development of the entire human race. Decreasing the genetic variation of future human populations can reduce our capability to adapt to environmental changes and thus severely endanger the future of our race (15). So why even consider such potentially hazardous research? Because all of the aspects of human cloning research which make it potentially dangerous also give it beneficial potential. Both therapeutic and reproductive human cloning can be tools for improving the lives of many sick or infertile people.

A) Therapeutic cloning: Using ES cells to treat disease

Researchers are desperately trying to discover methods of differentiating stem cells into specific types

of cells, which can then be used to replace dysfunctional and/or damaged cells in diseased patients. If scientists manage to develop ways to produce mature nerve cells from ES cells, these healthy cells can be implanted into Alzheimer's, Parkinson's, Multiple Sclerosis or nerve-injured patients (31). The implanted cells would then take on the jobs of damaged neurons and restore partial or complete functioning to the individual.

Furthermore, ES cells could replace heart muscle cells that are damaged or destroyed after a myocardial infarction (17). Damaged cartilage (e.g. osteoarthritis) or bone (e.g. trauma or surgery) could also be replaced by implanted ES cells (17). These stem cells could also be used as sources of pancreatic cells and replace dysfunctional pancreatic cells in Diabetes Mellitus patients (17). They may no longer require chronic insulin medication and may be at reduced risk for heart disease, pregnancy complications, and many other long-term effects of diabetes mellitus. Stem cells may even be capable of generating entire organs, which could be used for transplants in patients in dire need for these structures (17).

ES cells could improve the conditions of cancer patients. Cancer treatments such as chemotherapy and radiation often cause damage to the bone marrow, resulting in an underproduction of blood and immune cells. This effect could be counteracted by injections of hematopoietic stem cells (pluripotent cells capable of giving rise to red blood cells as well as cells of the immune system) (17). Replacement of immune cells would also treat many diseases of the immune system, such as AIDS (17).

If embryonic cells could be collected and frozen from each newborn, they could provide a non-depletable source of cells and/or organs for that individual should the need arise (17). Something similar has already been done in the U.S., where a Colorado couple screened 15 embryos for one whose tissue type matched those of their 6 year-old daughter suffering from Fanconi's Anemia (17). The resulting fetus would not only be the little girl's sibling, but her blood donor. Cloning one's own ES cells would provide a faster, easier and less ethically questionable way to derive the same benefit (17).

B) Reproductive cloning: another tool to increase fertility

The fertility of first world populations has been rapidly declining over the recent past. More and more couples are looking to science to help them conceive and scientific research has made many births feasible where they would not have been otherwise. Human embryonic cloning can serve as an additional method of conception for homosexual couples as well as couples

with one severely infertile person (15, 28). Furthermore, an increasing percentage of people in developed countries remain single but still desire to conceive a child on their own. This cohort of the population would also benefit from reproductive cloning procedures.

PART II: THE RELIGIOUS, LEGAL, AND ETHICAL ARGUMENTS SURROUNDING CLONING AND EMBRYONIC RESEARCH

Although beneficial, the cloning techniques mentioned above must be placed under ethical scrutiny before being clinically implemented. Even though they may increase the lifespan of many and the fertility of some, these outcomes do not come without a price. The consequences must therefore be considered in their entirety and have in fact been the source of much public debate. Some of the ethical concerns around human cloning are considered below.

The arguments for and against stem cell (SC) research are numerous and diverse. Often it depends on the standpoint of the individual making them. A catholic scientist, for example, may have a great deal of internal conflict depending on which aspect of him- or herself is presenting the argument. However, no matter how we define ourselves and our views, whether by profession, religious background, or politically, eventually there must be some element of consensus to determine if, and how far we as individuals and as a human society are willing to permit this type of research to proceed. The following presents an overview of the current religious and legal arguments, followed by a longer discussion of the ethical debate on embryonic research.

IV. AN OVERVIEW OF THE RELIGIOUS ARGUMENTS

The religious argument about ESC research tends to circle around a central question: when does life begin (4, 9)? For those who believe that life begins at the moment of conception there is little need for debate: any research involving the destruction of the embryo is tantamount to murder. For others the answer is not so uni-dimensional. In this section, we present the current thinking on ESC research of three major religious traditions: Christianity, Judaism, and Islam. Although none of these religions have uniform thinking across all their denominations, there are certain commonalities to their thinking that will be presented here. For a more thorough discussion of this subject, please refer to the reference list.

In the Instruction *Donum Vitae*, issued in 1987 by the Vatican's Congregation for the Doctrine of the Faith, "The human being is to be respected and treated as a person from the moment of conception; and therefore

from the same moment his rights as a person must be recognized, among which in the first place is the inviolable right of every innocent being in life...No objective can in any way justify experimentation on living human embryos or fetuses, whether viable or not, either inside or outside the mother's womb." (25)

A) The Roman Catholic Church

The Roman Catholic perspective may be considered the most dogmatic of religious positions. Its contention is that no form of contraception, reproductive technology or ESC manipulation, whether for research, therapeutic, or cloning purposes is permissible (25). Thus, from the Roman Catholic viewpoint that there is no debate: From the moment of conception, there is life; if there is life then destruction or manipulation of said life is murder-end of story. However, if one delves further into Catholic doctrine, one discovers that the current and popular view is not the only one available. Until Pope Pius IX's declaration in 1869, the belief remained, in accordance with Aristotle, that the conceptus was not considered to be animatus, or with a soul, until it had acquired formatus, an obvious human form. For boys this occurred at 40 days gestation; for girls at 80 days (25). Although the reason for this strange discrepancy between male and female fetuses is beyond the scope of this paper, the relevance is in the discussion as to when life begins. For those Catholics who maintain this belief that a soul must be conferred upon a fetus before it is to be considered as a person, the question of ESC research is more open to debate. No longer dealing with the heinous crime of murder, the debate delves further into the realm of ethics, which will be dealt with in a subsequent section.

B) Protestant Denominations

Protestant beliefs are very diverse. Some traditions hold a similar view to that of the Roman Catholic Church: life begins at conception. Other views may hold that an embryo gradually acquires full human status, therefore research on ESC may be considered permissible. "It is, in fact, part of the Protestant ethos that moral questions are determined by the individual conscience, and there is therefore room for a variety of stances on this point. Protestant thought, therefore, may accept that this is an issue on which Christians may have very differing views, with these differing views being compatible with Christian beliefs." (22)

C) Judaism

Jewish law is set by the Torah. According to Jewish tradition, "... a person becomes a person, only upon birth." (10, 21) Other sources suggested that an embryo only acquires the status of personhood after forty days

of gestation.¹⁰ It may at least be concluded, therefore, that Judaism does not grant full moral status to an embryo from the moment of conception (10).

From our research, Judaism comes out as the religion strongly in favour of ESC research (10, 4) In the Torah, there are 613 commandments or good deeds that a person should follow. Among these "mitzvahs" is the command: "Thou shalt be fruitful and multiply..." This has been cited in favour of in vitro fertilization techniques (21). More important to the ESC debate is the clause indicating that almost any Jewish law may be broken in order to save a life. Those who are sick, or too young, or pregnant do not participate in fasts because it could bring them harm; and those stem cells from frozen embryos should be researched as they may prevent the death of those suffering from illness. Furthermore, "Never having been implanted into a woman's uterus, Jewish law does not even accord these embryos the limited status of an ordinary fetus. And yet, flushing them down the sink seems to dishonour their potential for human life...Even though the destruction of the embryo may be a sin, that act is massively overridden by the drive to save another life." (21)

D) Islam

Islamic tradition holds that ensoulment of the fetus does not occur until four months of gestation, according to the Qur'an and Sunnah (4). In a news release accompanying a recent poll held by the Islamic Institute, a political body in the U.S., the following statement was made, "Under the Islamic principle of the 'purposes and higher causes of the Shari'ah (Islamic law)', we believe it is a societal obligation to perform research on these extra embryos instead of discarding them." (4) However, there is still controversy surrounding the question of whether or not embryos should be created for the sole purpose of research." (4)

V. LEGISLATION

Legislation on new technology often tends to lag behind its scientific development. However, the controversy surrounding cloning and other forms of embryo research, including therapeutic, has caused a great deal of public outcry. Politically speaking, the general view is that cloning is unacceptable. Nonetheless, there remains a much greater divide amongst both law makers and the public as to whether ESC research for therapeutic purposes should be legal.

Canada

On Dec 3, 2001, following the publication of a research paper reporting the first cloning of human embryos in the E-journal of Regenerative Medicine, the

Canadian Medical Association (CMA) issued a statement suggesting the need for an independent regulatory agency. This statement suggests, on behalf of the Assisted Human Reproduction Health Care Providers Coalition, that there is concern that the proposed draft legislation as written would inadvertently prohibit some potentially beneficial research which Minister Rock is in favour of: "Research using human reproductive materials has the potential of bringing significant benefits to Canadians and, therefore, this research should be encouraged." (6) An independent coalition would have the ability to procure input from both the public and experts (6). Its proposed responsibilities include accrediting facilities, issuing licenses, and monitoring the physicians and scientists according to national standards of research on human subjects.

At this time, there is no comprehensive legislation on ESC research. In May 2001, Health Minister Allan Rock presented draft legislation to the Standing Committee on Health. If accepted as a law, the cloning of human beings, the sale and purchase of human embryos, and paying women to act as surrogate mothers would be considered illegal. It would further act to regulate reproductive technologies and permit limited ESC research to those who obtain a license. The minister has requested a report on the legislation by the Committee in January 2002. Currently no research is permitted on any embryo beyond the age of 14 days (23).

United States of America

In August 2001, President George Bush approved federal funding of research conducted on pre-existing ES cells. Much controversy has stemmed from the number of reported existing lines. No federal funding would be given for research on embryos whether created for research purposes, or left-over from in vitro fertilization techniques.

Aside from bans of federal funding, it would appear that all types of research are permissible within the United States as long as the finances are available from sources outside of the government.

VI. THE ETHICS OF EMBRYONIC RESEARCH: IS IT MERELY THE MEANS TO AN END?

It is incredible the number and nature of scientific discoveries and advancements the world has seen in the last quarter of a century. What was once merely the stuff of science fiction novels, movies, or cartoons is now a part of daily discoveries. A sheep was cloned, a test tube baby was born, the mysteries of the human genome are well on their way to being catalogued and characterized, and now to the question of what to do

with the very beginning of human life itself. How do we, the human race, proceed? The following is a discussion of the ethical issues and concerns surrounding embryo research: is ESC research merely a means to an end?

Is it ethical to do research on embryos with the intent of finding the potential cures to human illnesses? First, let us define ethics. Ethics is the secular or human moral contemplation of good conduct. Thus, the question becomes, "Is it right, according to human morals and values, to conduct research on embryos?" The next obvious question follows, "What are embryos?" From a scientific standpoint, embryos are the result of the union of an ovum and sperm thus creating a zygote, which then divides to become an embryo. Arbitrarily, past three months of gestation, an embryo is termed a fetus. However, it is not the scientific definition we are interested in here. What we really should be asking ourselves is, "What is the moral status of an embryo?" (1) Or, "Is an embryo a person?" (1) There are those who feel that an embryo is no more than a ball of cells. As such, it has no moral value at all. If a scientist is just mixing up gametes in a petri dish, and he or she is lucky or skillful enough to create an embryo, and even to encourage it to divide outside of a uterus, then what is the harm? The answer to that question is in another, "Would you care for some human caviar?" If this question does not give you any feeling of disgust, then clearly there is no problem with the harvesting of human eggs for any purpose. However, it is likely that there is a feeling a revulsion finishing the reading of that question for most readers. If that is the case, then surely there is at least some moral status to be given to human embryos.

How is moral status defined? Mary Ann Warren has described moral status as having seven criteria: 1) Respect for life; one should not kill or harm another living creature without a just cause, 2) Anti-cruelty; harm or pain should only occur to another sentient being when there is no other way of furthering the goals of one with higher moral status, 3) Agent's rights, 4) Human rights, 5) Ecological importance, 6) Interspecific communities, and 7) Transitivity of respect; moral agents should respect another's moral attribution of moral status (1). According to these criteria, the embryo has a weak moral status for two reasons: It is alive and because of the respect, we must accord to others attribution of moral status on the embryo. It is not a sentient being. It cannot live without the support of a woman's uterus, but it does have the potential to become a human being and therefore it must be respected (1).

Still, is there not an inherent conflict between the concepts of respect and destruction? Certainly, there is

for those who believe that life begins at conception and that there is never any reason great enough to offset the devaluation of destroying life. Yet, this treats the concept of respect as a black and white issue. Preserving life equals respect. Destroying life equals murder. Black. White. No gray. Yet, human life itself presents us with its own shades of gray. A female fetus develops approximately 6 to 7 million oocytes, but by the time she is born, only a million or so remains. By the time she reaches puberty and begins menstruating, a mere 40% of what she had at birth remains. Nature has destroyed approximately 95% of the oocytes that the fetus once had. Furthermore, when a woman's ovaries are being prepared for ovulation, anywhere between 5 and 15 follicles begin to develop. Only one, or on a rare occasion two, is ovulated and available for fertilization. Then, should fertilization occur, there is a large possibility that the woman will never even know she was pregnant, since the majority of embryos never even implant. Thus, one could argue that nature itself does not revere life such that it cannot be destroyed. Ah, yes, but that is nature, and who are we, mere mortals, to interfere with nature then? We all have our choice as to how to live. There are certain cultures that attempt to respect our place in nature ignoring the advancement of science. But that is not the question here. The question still before us is, "Can we respect life and still destroy it?"

We can respect life by how we choose to conduct research on it. The training of many health care professions requires the study of anatomy. This study is enhanced by the use of cadavers and prosections; those who have died and given their body for teaching. Students show their respect in the way the bodies are treated, and in many institutions, such as McGill University, there are ceremonies to commemorate the lives of those who have generously contributed to students' learning. If this is an acceptable practice, then why would we not be able to afford such respect to embryos that are being experimented upon?

The decision each person must make for him or herself is whether experimentation on embryos that would lead to their destruction is inherently wrong? If it is then we need not go further. No benefit of this research could possibly outweigh the detriment that would be done to human society by the undertaking of this research. But if we maintain that we can respect human life at the same time as conducting this research, then we must move onto what are the reasons for undertaking this research in the first place? In other words, "What are the anticipated benefits of ESC research?" This topic was covered in scientific detail in a previous section. What we are concerned with here is whether the ends justify the means. Surely, one of the

greatest human virtues is compassion. To want to help another who is suffering is often one of the most compelling reasons one has for going into health sciences or into a health care profession. That being said, how do we propose to alleviate suffering by ESC research?

There is obvious potential to find cures for diseases such as Alzheimer's and Parkinson's from ESC research. However, that is all it is: potential. There is also potential to do the same type of research with adult stem cells. Here, there is much less cause for ethical alarms to sound. There is little or no harm to the donor and it may be done with the donor's fully informed consent. So why is this avenue of research not being pursued as fiercely as that of ESC? Because, scientists claim, it is more difficult to isolate the cells and it will take too long. Why is it that humans have come to demand that everything be available to them today, and if not today then tomorrow?

Allowing that we accept there is better potential from ESC to alleviate suffering, and that it is not considered inherently wrong to do research on them providing they are allocated a minimum amount of respect, the question then becomes, "Where do we get the ES cells from?" There are several sources that could potentially serve this purpose: cloning existing stem cell lines, from "left-over" embryos no longer being used for in vitro fertilization, from the ova of a woman who chooses to donate her ova for profit, from the ova of aborted fetuses, from the umbilical cords of aborted fetuses, or by creating embryos from gametes in the lab with no intention of use for implantation. This is simply a list, but it raises a lot of questions and ties in some other ethically problematic subjects, namely reproductive technology, cloning, and abortion.

The purpose of most reproductive technologies is to enable an individual or couple who cannot achieve pregnancy by natural means to become pregnant. For example, a single mother or lesbian couple who wish to have a baby may choose to be artificially inseminated. A gay couple may choose to have a child by a surrogate mother. A heterosexual couple that has fertility problems may choose to attempt in vitro fertilization. The same couple may also wish to have pre-implantation diagnosis if either or both partners or their first child has a genetic disease. There are ethical questions inherent to all of these examples that are beyond the scope of this paper. What is relevant is when a couple chooses to undergo in vitro fertilization. In order to increase the chance of having a successful pregnancy, several ova are collected from the woman and fertilized. Some of the resulting embryos are implanted, and others are maintained in stasis by freezing them with liquid nitrogen. Should the woman

become pregnant, she, or the couple, may choose to keep them for the chance to have another child later on, or they may be discarded. What if, instead of discarding them, the woman, or couple, consented to having them used for research? Is there a problem with this? It becomes a problem when one realizes that often the clinics that perform in vitro fertilization are also involved in research. Thus, there is a question as to whether there would be pressure to create a greater number of embryos than needed in order to ensure there would be some left over to do research on. Another possibility is that this could become a method of coercion for infertile individuals or couples who do not have the financial means to have a child by in vitro fertilization. The clinic will provide the treatment free in exchange for a couple of extra embryos.

So, if there is a possibility that donating embryos for research could become a corrupt business, then why not just clone them? Of course, we are not suggesting that we permit reproductive cloning, as to most people, this notion is reprehensible. If the goal of therapeutic cloning is to alleviate human suffering, then what better way to accomplish that than by cloning a dead child? Here comes the slippery slope argument. There can be no doubt as to the emotional anguish that comes from losing a loved one, especially a child. If we permit the cloning of embryos as a source of material to create a new heart for someone who will otherwise die, then how can we justify not removing the suffering of a mother whose child has died? If we permit one type of cloning, aren't we just opening the door to all others? If so, have we succeeded in completely devaluing all forms of human life?

And what, then, about the young girl who finds herself in trouble? She cannot have this baby, so she seeks out an abortion. Although her world has been turned upside down, can't at least some good come out of this by allowing the stem cells of her baby, or better yet, if a female, its ova? What would be the harm in that? Perhaps it may even become a way for those in unfortunate financial circumstances to earn a little extra money: get pregnant and have an abortion.

So many questions remain unanswered in the minds of so many individuals. At heart in all of these is what the value of human life is in all its forms, from its earliest days to the time we die. More pertinent here is if we can find an acceptable balance in which human life maintains its value and allow scientific progress to continue. Dr. Margaret Somerville suggests there is such a thing as "ethics time" that is needed to determine how to proceed when science, law, and ethics do not keep pace with each other:

"A minimum amount of time is also needed for the public to become familiar with the benefits, potential

benefits, risks, and harms of a new scientific development, not only at the physical level, but also at the level of its potential impact on values, norms, traditions, customs, culture, beliefs, and attitudes."

What seems clear is that we, both as individuals and as a society, have not had adequate ethics time to determine what role embryonic research should play in a human society.

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