Cloning For Embryonic Stem Cells

Defining the Terms

Types of cloning - There are three types of cloning: (1) reproductive cloning, (2) therapeutic cloning and (3) recombinant DNA technology or gene cloning. Only reproductive and therapeutic cloning have serious ethical issues.

1. Reproductive cloning is the most well known to the general public. It is used to generate another animal with the same DNA. The most famous case is that of Dolly the sheep. In this process, also called "somatic cell nuclear transfer" (SCNT), scientists transfer the genetic (DNA) material from the nucleus of an adult somatic cell (ex. a skin cell) to the female's egg whose own nucleus (DNA) material has been removed.

The reconstructed egg now containing the DNA from the adult somatic cell is treated with chemicals or electric current in order to stimulate cell division. Once this cloned embryo reaches a suitable stage of development, it is transferred to the uterus of a female "host" where it continues to develop until birth.

The Dolly experiment was not successful long-term and no one has successfully used cloning to make any primate. At this time, any chance of a cloned human embryo becoming a healthy baby is judged to be remote, if not impossible. In any event, human reproductive cloning is considered ethically wrong and is currently legally prohibited.

2. Therapeutic cloning is also called "embryo cloning" and is a current hot topic ethically and scientifically. (The ethical side will be treated below). Scientifically, the results are somewhat dubious. The so-called successes of Korean Dr. Hwang Woo Suk in cloning many human embryos were proven to be fraudulent and his published papers have been withdrawn. The great uncertainty surrounding stems cells from therapeutic cloning is whether or not they will be accepted by the patient's immune system. In such research trials on mice, the cells were rejected.

The stated goal of therapeutic cloning is not to create cloned human beings, but rather to create human embryos through cloning in order to harvest embryonic stems cells for research with the goal of possible use in the treatment of a variety of human diseases, e.g., Alzheimer's, cancer and heart disease.

Scientists are experimenting with two different therapeutic cloning procedures:

(1) The first is similar to the SCNT procedure described above in reproductive cloning. Some researchers choose to make a distinction between therapeutic cloning and reproductive cloning based on the intent not to produce a child, but only to produce an embryo in order to harvest its stem cells.

In November of 2001, scientists from Advanced Cell Technologies (ACT) announced that they had cloned the first human embryos for the purpose of collecting stem cells for

therapeutic research, using female eggs and adult skin cells. At the time of the report, none of the developing "embryos" reached a stage where stem cells could be derived.

(2) The ACT scientists also reported a second type of therapeutic cloning in which human eggs were stimulated in a way known as parthenogenesis. That is, the eggs were coaxed into developing as if sperm had fertilized them, when in fact sperm fertilization had not take place. Some of these stimulated eggs were maintained in a culture for seven days and seemed to develop normally.

It is claimed that these parthenogenetically produced embryos could not under any circumstances produce a viable pregnancy that would result in a child. However, they could be used to harvest stem cells. Thus the label therapeutic cloning rather than reproductive cloning was based not only on the intent not to produce a child, but also on the seeming impossibility of producing a child.

The research goal of these therapeutic cloning procedures is to extract stem cells from the fertilized human egg, after cell division of about five days (blastocyst stage). Stem cells at this stage of development are described as "pluripotent", which means that they have the potency to become the various parts of the human body. After extracting the stem cells, the research goal is to find a way to "guide" these pluripotent cells to differentiate in such a way so that they can become the kind of body cells (somatic cells) that are needed to treat specific diseases. Some say it may eventually be possible to produce whole organs from single, pluripotent stem cells.

Stanford University plans to use the SCNT procedure (described in 1, above) to clone human embryos to study diseases. By studying the development of cloned human embryos made from the cells of people with juvenile diabetes, cystic fibrosis, autism, Tay-Sachs, sickle cell, muscular dystrophy and many other genetic maladies, they hope to begin to understand what goes wrong during the development that eventually produces these diseases.

3. Recombinant DNA technology or gene cloning has been around since the 1970's and is a common practice in molecular biology labs. It is used in such things as the production of vaccines and the modification of crop plants. It is a type of genetic engineering in which the characteristics of an organism are altered by inserting a gene from another organism into its DNA. This altered DNA is known as "recombinant DNA."

Stem cells defined - Stem cells are undifferentiated human cells present at all stages of human life. At the embryonic stage, they have the ability to differentiate in order to become the specialized cells needed to create all the tissues of the human body. In adults, they can perform such tasks as strengthening the immune system or repairing damaged parts of the human body. At the early embryonic stage they even have the power to generate a completely new embryo (twinning).

Stem cells are classified as to their "plasticity" or "potency", that is, their ability to differentiate and form various cell types of the human body. In order of their potency they are called totipotent, pluripotent, multipotent and unipotent.

Totipotent cells are cells that can form a new embryo (in twinning) or differentiate to become all parts of the human body. These are available only in the early embryonic stages.

Pluripotent cells are cells that are able to differentiate to form most or all tissues of the human body. These are present in the embryo and recently some adult stem cells have been given this designation.

Multipotent cells are cells that are able to differentiate to form many, but not most of the cells of the bodily organs and tissues. These are present in adults.

Unipotent cells are able to form only one differentiated cell type and are also present in adults.

A stem cell line is a family of constantly dividing cells, the product of a single parent group of stem cells. They are obtained from human or animal tissues and depending on their type can replicate in vitro indefinitely or for an extended period of time.

Focus on Embryonic Stem Cells

Given the ethical and political problems with embryonic stem cell research, especially the questions about using or creating human embryos as a source for stem cells, why is there such great interest in this research? The answer is partly historical. The interest in embryonic stem cells was given a jump-start in 1998, when James A. Thompson, a biologist at the University of Wisconsin, isolated embryonic stem cells for the first time.

This step was hailed as the beginning of a process that could quite possibly result in the cure of such diseases as Parkinson's, Alzheimer's and many others. The hope was based on the fact that the cells of a 4-5 day old embryo, (blastocyst), are as yet undifferentiated (pluripoent) and thus have the potential to become any part of the human body. Once isolated and reproduced, in theory, they could then be given "appropriate signals" to differentiate into various specialized cell types like blood, bone, and brain cells and then "guided" into becoming specific body tissues that could replace or repair many kinds of diseased tissues.

At this early stage of research, most scientists were of the opinion that since adult stem cells seemed to be relative few in number and because they were already differentiated (not pluripotent), their potential was limited relative to the pluripotent embryonic stem cells. However, in the years following 1998, new research has given adult stem cells a brighter future and real hope that they may eventually prove to be as potentially effective as embryonic stem cells for the treatment of many diseases, thus solving the ethical issues surrounding the harvesting of embryonic stem cells.

Ethical Issues

While all parties to the debate concerning the ethics of cloning agree that the research goal or end of curing disease is most laudable, the debate focuses on the means employed in the research. There are a few who would argue that this is a scientific issue, not an ethical issue, however most would agree with President Clinton who was quoted in a 1977 *Hastings Center Report* as saying: "Any discovery that touches upon human creation is not simply a matter of scientific inquiry, it is a matter of morality and spirituality as well".

Creation and Destruction of the Embryo -- In the case of cloning, when the somatic cell nuclear transfer (SCNT) procedure is used, an ethical problem arises when, after the extraction of the stem cells, the embryo (zygote) is destroyed. The question arises as to whether it is ethical to terminate human life at this stage of its development. This same question arises in other forms of embryonic stem cell research.

While all ethiticans agree that it is unethical to directly destroy innocent human life, there is disagreement on a question of *fact:* At what point in the reproductive process -- fertilization, after 14 days (the advent of the primitive streak) or at some other point -- is human life now individual or individual and personal human life? All agree that when individual, personal human life is present, it is unethical to destroy it even as a means to the end of advancing the science of medicine in its fight against disease. This is the classical moral dilemma: does the end justify the means?

While neither science nor philosophy is able to definitively determine when personal, individual human life is present, a conservative ethical view would hold that the "safer course" must be followed, because human life is at stake. Therefore, according to this view, direct destruction of the embryo at any stage after conception is considered to be ethically unacceptable.

An extreme liberal view was expressed by Dr. Michael Gazzaniga in the *New York Times* when he referred to the early cloned embryo as just a "hunk of cells" and that human dignity resides in a "lifetime of experiences and discovery". Commentators Robert George and Eric Cohen replied that newborn infants do not have a "lifetime of experiences and discovery" and no one would imagine they are fit subjects for destructive research.

To the untrained eye the embryo does look like a "hunk of cells". However, it is the focus of research precisely because it contains all the elements of a complete human being, lacking only development.

A more reasoned liberal view would be that while developing human life begins at conception, it is unlikely that individual, personal human life is present during the first 14 days. This view is based on the phenomenon of twinning and the possibility of recombination, a process in which the "twins" can be recombined into a single embryo.

Also since it is observed that about 35% to 50% of all fertilized eggs are spontaneously aborted, it is argued that a settled human individuality does not seem to be in place at the moment of conception. As so it is argued that during this first 14 days the individuality of the embryo is not a settled matter and so it does not have the moral status, and thus the inalienable human rights, of a truly individual human being.

Others argue that since these cloned embryos have a near zero chance of ever becoming developed human beings, their destruction for the purposes of research is not destroying potential adult human life and thus is ethically permissible, especially in lieu of the potential to cure many human diseases.

A more conservative approach is that the creation of any form of human life to be used solely for it parts and then destroyed is unethical and is, in principle, an attack on all human life, because human life is now seen as disposable property, albeit in a good cause.

And so, while all parties to the debate agree that the goal of curing a variety of human diseases is a laudable end, disagreements arise in evaluating the ethical means of obtaining that end. Again the question: does the end justify the means? And with the developments in adult stems cell research, a research and funding focus on this research could well make embryonic research unnecessary in the quest to cure many human diseases.

Manipulation of the Embryo -- While the above argument is based on the ethical principle that it is unethical to directly destroy innocent human life, there is another ethical principle that states that: "it is ethically wrong to use another human person as a mere means to our ends and not an end in themselves". This principle can certainly be applied to cloning.

This principle has been cited relative to an article published on August 24, 2006 in *Nature* magazine, concerning the reported research of Dr. Robert Lanza, the medical director of Advanced Cell Technology in Worcester, Mass. In this report, Lanza states that he can now harvest stem cells without destroying the embryo.

Lanza uses a procedure similar to that commonly used for pre-implantation genetic diagnosis, to check for genetic disorders during the process of in vitro fertilization (IVF). Lanza says that he was able to pluck out one totipotent cell of an embryo at the 8 to10 cell stage, without destroying the embryo. He was able to devise a way to co-culture the cell with other cells and he reported that "they have been growing for over eight months, are entirely normal genetically and they were able to generate all of the cell types of the body".

He expressed hope that this procedure - where the embryo is not destroyed - will pave the way for federal funding, which at the present time is restricted to stem cell lines derived from embryos that had been already destroyed before the limit was set by President Bush in 2001.

However, in a September 6th *Nature* magazine online article, it was reported that, in fact, all 16 of the embryos used in the Lanza research had been destroyed and that more than one cell had been taken from each embryo. What Lanza did show is that a human embryonic stem-cell line can be created from a single cell, extracted from a very early embryo comprising 8-10 cells.

Lanza's work has also been critiqued on several counts by Arthur Caplan, Ph.D., director of the Center for Bioethics at the University of Pennsylvania. He does not see Lanza's work as a breakthrough and recommends using stem cells from unwanted extra embryos generated in IVF procedures. (for details see: www.msnbc.msn.com/id/14502237/)

In any event, the ethical principle invoked by a conservative ethical view is that, even if Lanza's procedure proves to be successful and does not destroy the embryo, this process involves a manipulation of human life that amounts to using another human life as a means to the ends of others and therefore, is not permitted.

Ethical Issues in Egg Procurement - In an analysis of the fraudulent claims of Dr. Hwang Woo Suk, the problems surrounding egg procurement surfaced. In this attempt to clone human embryos, hundreds of human eggs had to be harvested. Many young women working in the lab were pressured to donate their eggs and others were paid. To procure these eggs the women had to undergo ovarian hyper-stimulation and then had to endure a risky procedure of the insertion of a needle into their ovaries.

The question then arose: if cloning research would continue in Korea and other parts of the world, how many thousands of women would need to be recruited or paid to become egg donors? Could the research industry and the public condone, as an ethical practice, the buying and selling of human eggs on the open market and the risks to donors?

A Procedural Recommendation

Given the fact that, as of yet, there have been no medical success stories with embryonic stems cells and given the ethical issues involved in the various research methods for isolating embryonic stem cells, one reasonable recommendation is to use stem cells from other sources which, as sources, pose no ethical issues and have already demonstrated some success.

Here are two examples.

Adult stem cells - Adult stem cell research has been a long process. It took approximately 25 years between discovery and routine clinical application of adult stem cell therapy. In truth, a few years ago researchers thought that there were relatively few adult stem cells present in the body. They also seemed difficult to isolate and grow in culture and seemed to be extremely limited in their capacity to generate new cell types. It was thought that they were limited to forming more cells only from their tissue of origin.

However, a number of reports in recent years have changed these opinions, because adult stem cells are proving to be remarkably flexible. In a 2001 publication, evidence was presented that a single adult bone marrow stem cell could contribute not only to formation of cells for marrow and blood, but also to the formation of liver, lung, digestive tract, skin, heart and muscle cells.

Several examples now exist of some adult stem cells demonstrating pluripotent flexibility. These examples include cells from bone marrow, peripheral blood, the inner ear, umbilical cord blood, etc. These pluripotent cells can multiply in culture for extensive periods of time while still retaining their ability to differentiate and provide sufficient numbers of cells for clinical treatments.

While all these research results hold great promise, yet on the clinical side, there are still only a few adult stem cell treatments that have been fully tested in all required phases of clinical trials in order to be approved by the U.S. Food and Drug Administration. These approved adult stem cell therapies are considered powerful and life-saving, but the clinical applications are basically limited to blood disorders and specific blood cell-derived cancers such as leukemia, lymphoma and multiple myeloma.

Some strong advocates of adult stem cell research, like Senator Brownback, are claiming high numbers of success stories. Brownback uses a list created by David Prentice of the Family Research Council, which claimed that adult stem cells have now helped patients with at least 65 different human diseases. However, other researchers point out that only 9 of the conditions on the Prentice list have been fully clinically tested and the others still await clinical validation and FDA approval.

However, because of the actual, clinical tested success stories involving adult stem cells, a number of other diseases are being targeted, such as problems from spinal cord injury, Parkinson's disease and coronary artery disease. Researchers and funding agencies see a bright future for adult stem cell therapy.

For example, this bright future resulted in a $100,000 grant from Joan's Legacy, a lung cancer foundation, given to Kansas State University researchers Masaaki Tamura and Deryl Troyer. They isolated stem cells from the cushioning material of the umbilical cord and successfully used these cells in treating lung cancer in mice. Their long-term goal, financed by this grant, is to use this therapy to cure cancer in humans.

Another example, at the June 2006 meeting of the International Society for Stem Cell Research, Shinya Yamanaka and Kazutoshi Takahashi of Kyoto University reported that they were able to turn adult mouse skin cells back to an embryonic state by adding four biochemical messenger molecules found in early embryos. Assuming that their methods will work on human adult cells, they would be able to grow replacement cells and tissues, genetically matched to individual patients, thus effectively producing embryonic stem cells without using an embryo at all.

(Information above taken in part from a paper by Dr. David A. Prentice, "Current Science of Regenerative Medicine with Stem Cells" from a symposium sponsored by The Family Research Council and Center for Clinical Bioethics, Georgetown Medical Center, Washington, DC 2001, a July, 2006 article in *Science*, the *New Scientist* and the K-State Collegian Newspaper).

Amniotic stem cells - With embryonic stems cells at one end of the potency spectrum and adult stem cells on the other, the recently reported success with isolating stem cells from amniotic fluid may provide a middle course, by making pluripotent stem cells available without either destroying or manipulating an embryo.

In a recent article in the journal *Nature Biotechnology,* Dr. Anthony Atala, director of the Institute for Regenerative Medicine at the Wake Forest University School of Medicine in Winston-Salem, N.C., reported that: "So far, we've been successful with every cell type we've attempted to produce from these stem cells."

Amniotic-fluid stem cells (AFS cells) are found in both the placenta and the liquid that surrounds growing fetuses. The potency of these cells is judged to be somewhere between embryonic and adult, but have been described as pluripotent and seem to be very close in potency to embryonic stem cells. Like embryonic stem cells they multiply quickly and are remarkably long-lived.

Amniotic-fluid stem cells are collected by the process of amniocentesis in which some of the fluid surrounding the fetus is drawn out through a hollow needle inserted into the uterus. They can also be taken from the placenta or from tissues shed after birth.

Conclusion - Because of the important ethical concerns surrounding embryonic cloning and all other research involving embryonic stem cells and given the success, availability and lack of ethical concerns relative to research involving non-embryonic stems cells, e.g., adult and amniotic, a reasoned approach would suggest that the most logical and ethical course to follow at this point would be to continue to allow, support and fund adult stem cell research.