Alternatives to Human Embryonic Stem Cells

Keva Green

"How can we advance stem cell research without destroying human life in the process? This question confronts scientists, lawmakers and many others in society today. Stem cells, found in the human embryo and the adult body, are distinguished from other cells in the body by their unique ability to renew their own population indefinitely and their capability to turn into specialized cells when given the right signal. These remarkable features have important applications in advancing scientific knowledge about normal and abnormal human development and in the regeneration and repair of damaged or diseased organs. However, for several decades, stem cell research has received much criticism and opposition mainly because critics believe destroying human embryos to extract the stem cells they contain is morally wrong. My goal is to compile an extensive discussion of the more ethical sources of stem cells. If the stem cell debate is to end, it is important that members of society realize that there are numerous alternatives to human embryonic stem cells. In an attempt to meet my goal, my paper will focus on answering the following questions:

1. How do scientists obtain stem cells?
2. How are stem cells being used to advance the field of medicine?
3. Are there less controversial ways of obtaining stem cells from embryos?
4. Can the adult body together with the organs facilitating the development of the human fetus provide reliable alternatives to HESCs?

How do scientists obtain stem cells?

The morula (a solid ball of about sixteen cells formed from cell division of the fused egg and sperm) is the premier source of stem cells. This is because the cells of the morula are totipotent, meaning they have the ability to transform into all the cell types needed to produce a complete living being. Immediately preceeding the formation of the morula is blastulation, a process during which the cells of the morula get rearranged, creating a hollow, fluid-filled interior called the blastocoel, which is surrounded by a ring of cells called the trophoblast. The entire structure is known as the blastocyst. The trophoblast will later give rise to the placenta, and a mass of cells found in the blastocoel called the inner cell mass [ICM] will eventually give rise to the body of the embryo (Shier, Butler & Lewis, 2004, pp. 881-882). The fact that the morula can produce any cell in the human body, as well as the structures that facilitate the development of the embryo, such as the placenta, means it is able to produce a complete living being (Cogle et al., 2003, p. 994). Thus, it is possible for scientists to use this small mass of cells to derive any cell type they

may need for research.

In contrast, stem cells taken from the ICM of the blastocyst are pluripotent, which means they have the ability to produce all the cells of the body but cannot produce a living being because they cannot produce a placenta. According to Campbell and Reece (2005), the cells of a very early mammal remain totipotent until the 16-cell morula stage but any descendant of the morula produced thereafter is pluripotent (p. 1005). Shier, Butler and Lewis (2004) pointed out that during their extraction, the pluripotent stem cells of the ICM, called human embryonic stem cells [HESCs], are separated from the trophoblast that gives rise to the placenta (p. 882). Thus, while these cells are capable of differentiating into all cell types in the human body, they cannot produce an entire living being because they lack the trophoblast which is needed to produce the placenta and its supporting tissues (Cogle et al., 2003, p. 993). Nevertheless, the fact that human embryonic stem cells [HESCs] can produce any cell type in the human body is the main reason why scientists marvel at them and are pursuing their use (Fitzgerald, 2003, p. 28).

The adult body is becoming a more important stem cell source due to the recent discovery of pluripotency and plasticity among adult stem cells. Unlike HESCs and morulas that are pluripotent and totipotent respectively, adult stem cells were believed to be multipotent (i.e., having the ability to transform into some, but not all cell types). Stem cells are found in various parts of the adult body, namely: the bone marrow, the intestine, the umbilical cord, the liver, the pancreas and most recently the brain, where their role is to replace specialized cells in the body as needed (Cogel et al., 2003, pp. 995-997). These stem cells are limited in that they are not able to transform into any cell type (Campbell & Reece, 2005, p. 418). This means that stem cells from the bone marrow, for example, can give rise to all types of blood cells, but cannot give rise to brain cells. However, according to The Domestic Policy Council (2007), "scientists have also reported that adult stem cells may, in some cases, exhibit the ability to form specialized cell types of other tissues, a characteristic known as transdifferentiation, or plasticity. Some experiments have even suggested that certain adult stem cell types may be pluripotent" (p. 12). Thus, in addition to being a superb source of multipotent stem cells, the adult body may be a possible source of pluripotent stem cells.

How are stem cells being used to advance the field of medicine?

Stem cell research gives scientists the opportunity to better understand human developmental processes. Fitzgerald (2003) pointed out that since every multicellular organism develops from stem cells, scientists are growing stem cells in the lab in order to better understand how humans develop from a one cell zygote to a multicellular organism. Also, by watching the development of stem cells in the lab, scientists will gain insight into bodily processes like aging and the formation/onset and progression of diseases (Fitzgerald, 2003,

p. 27). Cogle et al. (2003) added that stem cells play a role in the formation of certain cancers and that cancer cells have certain similar features to stem cells (p. 997). Thus, by observing stem cells in the lab, scientists can gain profound insights about normal and abnormal processes that occur in humans.

Stem cell research eliminates the use of animals and humans as guinea pigs in an attempt to develop safe and specific drugs. Fitzgerald (2003) argued that since animals are different from humans and may not accurately reflect the interaction of medicinal drugs with human tissues, using organs grown from stem cells in the lab to determine the safety of new drugs is better than testing the drugs on animals (p. 27). Information about how the drug interacts with human cells will thus be obtained even before clinical trials on humans are done. Fitzgerald (2003) also pointed out that stem cells from different people can be used to grow organs in order to see how different people react to the same drug (p. 27). Thus, scientists can determine which drug is suitable for which set of people.

Stem cell research has practical applications in the field of regenerative and repair medicine. Organs grown from stem cells in the lab can be used to repair or replace damaged or diseased organs. According to Kline (2003), this eliminates the major problem faced by people waiting for an organ donor, i.e. the scarcity of compatible donors. Since it may take several years to find a compatible donor, many people succumb to their illnesses before they are able to receive organs (p. 48). Also, in situations where cells are malfunctioning, stem cells can be programmed to create normal versions of the malfunctioning cells. Scientists can then use these resulting specialized stem cells to replace the malfunctioning cells. According to a report from The Domestic Policy Council (2007), stem cells can be used to replace the malfunctioning dopamine producing cells in the brains of people with Parkinson's disease, replace damaged heart muscles resulting from a heart attack with new cardiac muscle cells and create new insulin-producing cells for people with type 1 diabetes (p. 12). According to Prentice (2003) using stem cells, new bone marrow cells can be created for people with "certain cancers [like leukemia]; autoimmune diseases such as lupus, multiple sclerosis and arthritis; anemias such as sickle cell anemia; and immunodeficiencies" (pp. 17-18). Thus, stem cells are very advantageous to regenerative medicine because they can be used to cure otherwise incurable diseases.

Are there less controversial ways of obtaining stem cells from embryos?

Human embryonic stem cells [HESCs] possess many of the features that define a good stem cell line. HESCs are relatively easy to grow in the lab, are able to generate all the cell types scientists will ever need for research, and even after many cell divisions, they maintain relatively long telomeres, which are nucleotide sequences at the end of chromosomes (Garg, 2008, pp. 6-7). (By allowing themselves to be eroded, telomeres prevent the erosion of

genes that would result from the shortening of chromosomes that unavoidably happens during the process of cell division.) But while HESCs possess many good features there are also many problems with them. According to The Domestic Policy Council (2007), HESC-derived organs are not currently being used by humans in replacement therapeutic procedures mainly because of the high risk of them being rejected by the patient's immune system. Also, HESCs have the tendency to form benign tumors when cultured in the lab. As a result, all the experiments with HESCs so far have been done using animals (p. 12-13). Moreover, the use of HESCs is very controversial because obtaining them involves the destruction of human embryos (The Domestic Policy Council, 2007, p. 14). The shortcomings of HESCs have forced scientists to explore more ethical and less problematic sources of pluripotent stem cells for research.

One area of exploration is obtaining pluripotent stem cells from embryos in three (3) non-harmful ways. Firstly, pluripotent stem cells can be extracted from embryos that died spontaneously in in-vitro fertilization [IVF] clinics. An embryo can be classified as dead if it is no longer growing because its cells have stopped dividing and differentiating (Hinman, 2009, p. 9). With this definition of embryonic death in mind, "approximately one-fifth of all the embryos generated for use in IV clinics could be re-classified as dead" (The Domestic Policy Council, 2007, pp. 18-19). Since the embryo is already dead before the stem cells are extracted, a valuable source of human embryonic pluripotent stem cells could be obtained without destroying a single living embryo (p. 19). However, according to Hinman (2009), the main problem with this technique is that it is intrinsically difficult to determine if an embryo is 'truly dead' because there is a possibility that in the process of screening for embryonic death, the embryo may be hurt or killed (p. 10). Nevertheless, if scientists can screen for embryonic death without harming or killing any of the embryos, dead embryos from IV clinics could potentially serve as a stem cell source for scientists. Another reasonable apprehension is that stem cells obtained from dead embryos might not be as viable as those obtained from live ones. While more research is being done to address this issue, the process of obtaining stem cells from dead embryos can be seen as analogous to obtaining viable organs from the deceased (The Domestic Policy Council, 2007, p.18-19). Hinman (2009) is also concerned that the use of dead IV embryos as a source of stem cell will encourage doctors to produce a surplus of embryos in IV clinics, an act deemed unethical by many critics (p. 10). But if strict limits are set on the number of embryos scientists can produce, dead IV embryos can be used as stem cell sources without much controversy.

Secondly, the totipotent cells extracted from non-harmful biopsies of early human embryos can be used to produce pluripotent stem cells. According to The Domestic Policy Council (2007), one or two cells can be extracted from an embryo at the morula stage and the removed cells can be cultured in the laboratory to produce HESCs (p. 19). The key to this process is to extract

the cells at a very early stage in the development of the embryo before cell fate is established. Since at the morula stage cell fate is not yet determined, (i.e. all the cells are identical and there is not yet any specialization into heart cells, brain cells or blood cells etc), it is highly likely that removing a cell or two will not result in the death of the embryo because any cell removed can be replaced by the remaining cells. Additional evidence that this technique will work comes from Vargo (2007), who argued that the cells can be extracted from the morula without killing the remaining embryo because doctors use this technique during pre-implantation genetic diagnosis [PGD] to screen embryos for genetic diseases. However, while the cells can be extracted without killing the embryo, other side effects of the procedure later on in the baby's life are currently unknown because the technique is new (Vargo, 2007). Also, Hinman (2009) believed that since the cells extracted from the morula during the biopsy are totipotent and can give rise to a complete human being, using them as a stem cell source is no better than the current destructive method of obtaining stem cells (p. 12). But if all the totipotent cells in the embryo were left untouched, only one fetus would form nonetheless. Thus, capturing these totipotent cells to generate pluripotent cells does not take away the potential for a new human being in the population.

Thirdly, human embryonic pluripotent stem cells can be obtained from non-embryonic entities that are made to function like embryos. According to The Domestic Policy Council (2007), "artificially created biological entities that resemble embryos but engineered to lack the essential elements of an embryo" can be created for the sole purpose of supplying pluripotent stem cells (p. 14). Since these artificial entities lack the essential elements of an embryo, they cannot develop into a human being and so they are not considered as 'real' embryos. However, they will still have the potential to produce the pluripotent stem cells that real embryos produce (p. 20). One manifested example of this technique was performed in a study with mice. The Domestic Policy Council (2007) stated that researchers at the Massachusetts Institute of Technology [MIT] turned off a certain gene in a mouse embryo and the result was "a laboratory-constructed biological entity that could not implant in a uterus and was morphologically unlike a natural embryo. This non-embryonic entity nonetheless yielded fully functional pluripotent stem cells with the same characteristics as those obtained from real embryos" (p. 21). This procedure does not hurt an embryo in any way since the producer of the stem cells is not essentially a real embryo. It is simply an entity designed to carry out some of the processes that normal embryos carry out. Even so, this technique is deemed unethical by critics who view the procedure as the intentional creation of a disabled embryo rather than the creation of a non-embryo (Vargo, 2007). Consequently, scientists today are attempting to create this biological entity without the fusion of an egg and a sperm. This will eliminate the debate over whether or not the biological entity is a disabled embryo or a non-embryo since no fusion of egg and sperm occurred during its formation. However,

scientists have not yet succeeded.

Can the adult body together with the organs facilitating the development of the human fetus provide reliable alternatives to HESCs?

The adult body, as well as two lifeline tissues that support a developing fetus, the amniotic fluid and the umbilical cord blood, are gaining importance as promising alternatives to HESCs. Garg (2008) stated that stem cells obtained from the amniotic fluid (i.e. the fluid within the amniotic cavity that surrounds the developing fetus) possess certain features that make them qualify as an alternative to HESCs (p.3). Firstly, amniotic fluid stem cells [AFSCs] represent a less controversial source of stem cells than HESCs because AFSCs are obtained from the amniotic fluid which would otherwise be discarded after births (Garg, 2008, p. 4). Secondly, AFSCs are easier to grow than HESCs (The Domestic Policy Council, 2008, p. 2). Since AFSCs do not take a long time to divide, populations of stem cells can easily be generated in a relatively short period of time in the lab (Garg, 2008, p. 3). Thus, using AFSCs, scientists can obtain large numbers of stem cells in a short time period. In addition, the fact that AFSCs can maintain long telomeres even after 250 cell divisions means they have a longer reproductive life span than adult stem cells [ASCs] and HESCs which stop dividing after forty to sixty divisions (Garg, 2008, p. 4). When cultured in the lab, AFSCs are able to multiply and generate more stem cells than ASCs or HESCs are capable of producing. Garg (2008) pointed out that another impressive feature of AFSCs is that they do not form tumors, which is a major issue with HESCs (p. 4). In addition to having several advantages over HESCs, AFSCs posses many of the features of HESCs (The Domestic Policy Council, 2007, p. 2). These two factors cause scientists to consider AFSCs as a potential alternative to HESCs.

Pluripotent stem cells derived from the umbilical cord blood [UCBs] have two important features that make scientists regard them as potential alternatives to HESCs. Firstly, Kline (2003) pointed out that "with four million births per year in the United States, the umbilical cord blood is virtually a limitless source of pluripotent stem cells" (p.48). And since umbilical cords are usually discarded after births, using umbilical cord blood as a source of stem cells does not impose any risk to an embryo or fetus. Thus, their use is more ethical than the use of HESCs (p. 48). Secondly, Garg (2008) explained that because UCBs do not elicit severe responses from the recipient's immune system, organs derived from them are ideal for use in regenerative medicine (p. 3). In fact, UCBs are so promising to regenerative medicine that in many countries umbilical cord blood banks have been established to collect umbilical cords after births, and UCBs are currently being used to provide non-immunogenic stem cells for use in bone marrow transplants (Garg, 2008, p. 3). Thus, the use of UCBs places less pressure on doctors to find compatible donors for patients in need of bone marrow transplants. However, one major

disadvantage of using umbilical cord blood as a stem cell source is that it can transmit genetic diseases that are undetected in the fetus (Kline, 2003, p. 48). The chances of this happening can be significantly reduced by doing routine follow-ups with the child donor about six to twelve months after birth to screen for any medical problems (pp. 48-49).

Of all the alternatives, adult stem cells [ASCs] may offer the most possibilities. Firstly, ASCs are less likely to form tumors than HESCs and their use elicits fewer ethical concerns (Garg, 2008, pp. 6-7). Secondly, according to The Domestic Policy Council (2007), organs generated from ASCs are less likely to experience immune rejection than organs formed from HESCs because the ASCs used to make the organs can be taken from the recipient's own body. Hence, the organs created will be genetically identical to the recipient's body cells and so should not be rejected when introduced into the recipient's body. The fact that scientists still aren't sure how to prevent a patient's body from rejecting the organs created from HESCs causes clinical trials with HESCs to lag behind clinical trials with ASCs. In fact there are 1371 clinical trials with adult stem cells, while there are no reported clinical trials with HESCs (p.12).

Plasticity or trans-differentiation is another trait exhibited by ASCs that makes it possible for them to replace HESCs. According to The Domestic Policy Council (2007), by monitoring the medium into which the stem cells are cultured, adult stem cells of one tissue type can be used to produce cells of a different tissue type (p. 12). Specifically, stem cells from the bone marrow can transform into not only blood cells, but cells of other tissues like the liver, the heart and the pancreas (Cogle et al., 2003, pp. 996-997). Thus, even though adult stem cells were thought to be limited because they are multipotent, the recent discovery of plasticity deems adult stem cells more versatile than they were once thought to be. It is unclear if plasticity enables adult stem cells to generate virtually all cell types in the body, a criterion for pluripotency, but scientists are sure that plasticity allows adult stem cells to give rise to at least some cell types. Meanwhile, The Domestic Policy Council (2007) pointed out that recent experimental evidence, unrelated to plasticity, is leading scientists to believe that some adult stem cells are in fact pluripotent (p. 12).

Perhaps the most fascinating characteristic of adult body cells that qualifies them as a potential replacement for human embryonic stem cells is their ability to be reprogrammed back to pluripotency. Reprogramming these adult cells to function like embryonic stem cells produces a source of pluripotent stem cells that bypasses the need for embryo destruction. By using certain chemical factors adult body cells can be programmed to act like the embryonic stem cells from which they were derived (The Domestic Policy Council, 2007, p.2). Garg (2008) further explained that the chemical factors are proteins called transcription factors that are used to activate certain genes in fully differentiated adult body cells, causing them to function like embryonic stem cells. These reprogrammed cells, called induced pluripotent stem cells [IPSs], represent a milestone in stem cell research and according to Garg

(2008) are by far the most impressive proposed alternative for HESCs (p. 4). This is because, unlike HESCs, induced pluripotent stem cells can be obtained without the need to hurt any being in the process. Hence, there are no ethical controversies surrounding the use of IPSs. And since these cells will be taken from the recipient's own body, patient-specific organs can be created from IPSs. This may lower the probability of the organ suffering immune rejection. But while researchers were able to induce human fibroblasts (cells making up the connective tissue) to act like embryonic stem cells, IPS technology still needs more research because immune rejection and tumor formation are not completely out of the question (Garg, 2008, p. 5).

Further research

Despite the remarkable pluripotent ability of HESCs, scientists are being challenged to develop safer and more ethical ways of obtaining pluripotent stem cells. Three major alternative sources of stem cells were mentioned in this research paper. Obtaining stem cells from embryos in three (3) non-harmful ways is the first proposed alternative. While most of the sources agreed that it is feasible to obtain human pluripotent stem cells from dead IV embryos, from artificially created non-embryonic entities and from a biopsy of the morula, they disagree with each other over whether the pluripotent stem cells obtained will have the same quality as those obtained from normal living embryos. Hence, before clinical trials with humans are begun, scientists need to construct experiments that will enable them to determine if the qualities of the stem cells harvested from these methods are comparable to those obtained from normal living embryos. Also, more research is needed to determine if biopsy of the morula to obtain the totipotent stem cells really doesn't hurt the embryo because the team of researchers who claimed that they successfully extracted stem cells from the morula actually hurt all the embryos involved in the process (The Domestic Policy Council, 2007, pp. 19-20). As this was partly due to the poor extraction techniques of the researchers, more research is needed to determine the best method that should be used to extract the stem cells without hurting the embryos, since strong evidence that morula extraction can be done without destroying the embryo comes from the preimplantation genetic diagnosis that doctors perform (Vargo, 2007). Thus, these techniques are not being ruled out: they just require more development.

Meanwhile, obtaining stem cells from the tissues that support a developing fetus is another proposed alternative that seems very promising. Researchers were so far able to grow brain, bone, liver and muscle tissues from amniotic fluid stem cells (The Domestic Policy Council, 2007, p. 17). Umbilical cord blood stem cells are being used to derive bone marrow stem cells for use in bone marrow transplants (Kline, 2003, p. 48). In addition to being able to generate many of the cell types that HESCs can produce, amniotic fluid stem cells and umbilical cord stem cells possess many other characteristics desired by scientists when they are seeking a stem cell line. As a result, amniotic fluid

stem cells and umbilical cord blood stem cells are among the better potential alternatives to HESCs. The only drawback of these two stem cell lines is that they are involved in very few reported clinical trials with humans (Garg, 2008, pp. 3-4). Thus, in order to increase the reliability of amniotic fluid stem cells and umbilical cord blood stem cells, they need to be used in more clinical experiments.

Adult stem cells have so far captured the interest of scientists and have been used in clinical trials with humans for over 30 years (Garg, 2008, p. 4). While adult stem cells were once seen as multipotent, the discovery of plasticity among these cells and their ability to be reprogrammed back to pluripotency means scientists can generate virtually any cell type they may need using these adult stem cells. Thus, these features make adult stem cells the most promising of the proposed alternative for HESCs.

While each proposed alternative has advantages and disadvantages, with further research in the areas identified, many scientists are optimistic that they can conduct more ethical stem cell research in the near future.

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