Feature Article

Stem Cell Research and Health Education

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ABSTRACT

Stem cells are being touted as the greatest discovery for the potential treatment of a myriad of diseases in the new millennium, but there is still much research to be done before it will be known whether they can live up to this description. There is also an ethical debate over the production of one of the most valuable types of stem cell: the embryonic form. Consequently, there is public confusion over the benefits currently being derived from the use of stem cells and what can potentially be expected from their use in the future. The health educator's role is to give an unbiased account of the current state of stem cell research. This paper provides the groundwork by discussing the types of cells currently identified, their potential use, and some of the political and ethical pitfalls resulting from such use.

INTRODUCTION

Stem cells are believed to be one of the greatest untapped resources currently available for the prevention and treatment of many diseases. Inasmuch as current knowledge of stem cells is a combination of scientific reality and cautious speculation, considerable research is required to identify the true, long-term potential for medical advances from these cells. As health resources professionals, communicators, and advocates,[1] health educators are in a position to advance the public dialogue about this promising technology. This article offers a general overview of stem cells, their potential for extending life and improving its overall quality, and some thoughts on the role of health educators with regard to professional and lay audiences.

WHAT ARE STEM CELLS?

Stem cells are template cells found throughout the body that can grow to become cells with specialized functions.[2-6] These cells replicate to generate "offspring" cells that can be either stem cells (and hence, self-renewing) or specialized cells (i.e., differentiated cells) that play a specific role—becoming blood, bone, brain, or skin cells, among others.[7] Stem cells, therefore, have the potential to act as repair systems for replacement of damaged cells.[2-6] The field in which a great deal of research is currently underway to determine the use of stems cells in the treatment of diseases and injuries is called "regenerative medicine." Under "normal" conditions stem cells continue to replicate until they receive a signal to differentiate into a specific cell type.[8] When stem cells receive such a signal they first become progenitor cells, and later, the final mature cell type. Determination of the different signals that cause the stem cell to become a specific type rather than just continue to replicate is important (and, in some cases, it is the absence rather than the presence of a signal that is the important factor).[8] The ability of

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stem cells from one area to differentiate into another completely different type is known as plasticity, and embryonic stem cells appear to be the "most plastic" of the four types discussed below.[2-6]

Stem cells are described as being of a specific cell line, dependent on the characteristics and location of the original template cells from which all future offspring cells have grown (reflecting the self-renewing capability of the cells). Assuming that no contamination of the cell line occurs as a result of mutations or infections, and no differentiating triggers occur, the cell lines could potentially grow ad infinitum.[2]

DIFFERENT TYPES OF STEM CELLS

There are several types of stem cells: embryonic stem cells, fetal stem cells, adult stem cells, embryonic germ cells, and amniotic and umbilical cord stem cells. These stem cell varieties and their distinct properties are discussed below.

Embryonic and Fetal Stem Cells

The development of an organism can be compartmentalized into several stages.[9] Following the union of the egg and sperm, the initial four to five days from conception are characterized by a period of rapid cell division. A "ball" of 50 to 150 cells known as a blastocyst is created, so named because it is a hollow sphere. The blastocyst is composed of three parts: the trophoblast or outer surface, the blastocoel or inner cavity, and the inner cell mass found inside the blastocoel which is composed of stem cells.[9] These inner-lying cells are said to be "embryonic" even though the term embryo does not technically apply until after this initial two-week stage.

The next eight-week stage is characterized by cell growth and multiplication. Following this eight-week stage, the organism has recognizable structures and is classified as a fetus. At this time, embryonic stem cells continue to proliferate and are said to be pluripotent or plastic, meaning that they can differentiate into almost any type of cell that makes up the body.[10] The embryonic stem cell is believed by many scientists to be the most useful for potential medical treatments, but its use is restricted by federal legislation (described later in this article). Existing stem cells for medical research can come from four primary sources: existing stem cell lines, aborted or miscarried fetuses, discarded embryos from fertilization treatments, or cloned embryos. Only the first source can be used in federally funded research programs, however.[11,12]

The cloning of embryos is another controversial area of research. The cloning of humans to full term is banned almost worldwide.[13,14] In some cases, short-term cloning has been performed to allow for the generation and extraction of stem cells, followed by the termination of the cloned embryo by the sixth day after fertilization. Cloning of some animals has been allowed to proceed to full term; the first and most famous example was the work of Scottish scientists resulting in the creation of a sheep known as "Dolly."[15] That achievement became the driving force for new regulations to prevent a similar event occurring with human cells. The latest evidence suggests that cloned cells do not "reset their longevity clocks," thus resulting in reduced lifespan. Furthermore, not only is the success rate of cloning low, but the cloned organism is beset with problems, some of which may not become apparent until adulthood, assuming life extends to that age.[16,17]

For research to occur with embryonic stem cells, the inner cell mass of the blastocyst is extracted (thus destroying the embryo) and grown in cell culture.[18,19] This process enables cells to grow on plates coated with a feeder layer that provides anchorage and nutrients. The stem cells become attached to the plate and grow in the nutrient broth (i.e., cell culture media tailored to the specific needs of the cell line being grown).[18,19] As the cells proliferate they fill the plate until a point is reached where they would be forced to compete for space and nutrients. Shortly before such competition breaks out, the cultures are replated at the original cell density (meaning that one starting plate could be divided across two or more plates) and the process is repeated. This procedure is known as "passaging."[20]After several months, the cells will number in the billions without differentiating or changing in any detectable way. They can either be frozen for storage or continue replicating. However, there is some evidence that with continued passaging, a point may be reached in which the cells become less stable with respect to their ability to replicate, differentiate, or avoid mutations.[21] This instability seems to be particularly true when adult and embryonic stem cells are compared (see below).

Fetal stem cells, typically obtained following abortion or miscarriage, are believed to be as pluripotent as their embryonic counterparts, though they occur at a later stage than the true embryonic stem cell.[22] Several biotechnological companies are experimenting with these cells as treatments for a myriad of diseases. For instance, ReNeuron, Inc. (UK) has several cell lines derived from the fetal brain that they are testing for the treatment of neurodegenerative disorders, including stroke, Parkinson's disease, and Alzheimer's disease.[23,24]

Adult Stem Cells

A small number of stem cells can be found in adult humans at specific locations, such as in the bone marrow or the subventricular zone of the brain.[25,26] Until the discovery of these and other cells in the central nervous system, it was believed that the brain was the only organ that could not replicate. However, it is now clear that certain regions of the brain may have some limited capability to replace damaged or dead cells as a consequence of endogenous stem cells.[27,28]

Whereas embryonic stem cells are derived from the inner cell mass of the blastocyst, knowledge of the origin of the adult stem cell is less certain. Its source could potentially be the same, with the adult stem cell being many generations removed from the original source. If this speculation is true, then one would expect the body to have large numbers of these cells, which it does not. It has therefore been suggested that halting of replication is the means by which the number of stem cells found in the organs of the body is limited.[29] The stem cells are said to have entered a state of quiescence, until they receive an activation signal due

to cell damage. Determination of the signal that triggers adult stem cells to "wake up" is critical to maximizing their benefit. In addition, identification of what makes the cells quiescent is of considerable merit. One study revealed the presence of a "master switch" that can trigger the change from embryonic to adult stem cell characteristics, suggesting that this signal may originate from the same source.[30]

There is considerable debate as to how pluripotent adult stem cells are. The original belief was that they were not as versatile, healthy, or durable as embryonic stem cells because they appeared to be limited to forming only cells of a similar origin (e.g., bone marrow stem cells could only produce blood cells). Consequently, these cells became known as multipotent cells. These characteristics meant that adult stem cells would be harder to manipulate or control compared with embryonic cells. Also, due to their presence in adults, it is likely that the cells could have accumulated abnormalities through continuous exposure of the organism to environmental hazards (such as viruses) or to replication errors.[31,32] The latter problems are normally corrected, but with the aging organism, the ability to correct replication errors is believed to diminish.[32,33] In the majority of cases, the ability of adult stem cells to replicate also appears to be limited compared with embryonic stem cells, thus reducing their usefulness.[34] However, these cells do have an advantage over embryonic stem cells: theoretically, they can be removed from a patient, grown in culture, and then returned to the patient.[35] Therefore, they would not induce an immunological rejection response that may be seen with embryonic stem cells.[35,36] In addition, there is more flexibility in using these cells than human embryonic stem cells, especially with regard to federal funding.

Some research shows that certain adult stem cells can differentiate into a number of varied cell types, including neurons[37-39] of the peripheral and central nervous system. However, this observation may not be true of all adult stem cells, and more research is required to determine how useful these cells might be for use in treating human disease and injury.

Most research on adult stem cells is based on mesenchymal cells, i.e., cells from regions originally derived from the mesodermal layer of the embryo. These cells include connective tissue and, in particular, bone marrow and muscles. They are multipotent cells and are a relatively homogeneous population of mononuclear progenitor cells that can be made to differentiate into specific cell lines following environmental cues. Additionally, there are stromal stem cells found in the bone marrow, which are a more heterogeneous population of different cell types with varying degrees of proliferation and differentiation potential.[40] Adult stem cells also can be found in children, in the placenta, and in blood from the umbilical cord. These specialized cells are discussed below.

Embryonic Germ Cells

Germ cells are the precursors to the gametes (egg and sperm) and are therefore found in adult testes and ovaries, and in the areas of the embryo that ultimately differentiate into testes or ovaries.[41] These cells appear to be as pluripotent as other embryonic stem cells. However, they have been found to differentiate spontaneously, which would suggest that there is less control over their development than with other stem cells.[42]

Two studies[43,44] suggest that adult stem cells can be easily derived from germ cells of both sexes. Further research is needed to explore the validity of this hypothesis, though the findings are certainly intriguing and potentially useful.

Amniotic Fluid (or Placental) and Umbilical Cord Blood Stem Cells

The amniotic fluid that surrounds and protects a developing fetus in its mother's uterus, as well as the placenta, have also been shown to contain stem cells.[45] An amniocentesis procedure—where amniotic fluid is collected through the insertion of a long, thin needle into a pregnant woman's abdomen to check for abnormalities, including Down syndrome—is generally considered safe for both the mother and embryo.[46] The collected amniotic fluid is normally discarded once testing is complete, but now that it has been found to contain stem cells, there is potential for further research and storage of such fluid. The current belief is that amniotic fluid contains a mixture of embryonic and adult stem cells.[47,48] Testing of these cells has been limited to date. It is believed that they are able to differentiate into a variety of cell types, but it is not known whether they are as pluripotent as other types of stem cells. Some authorities have suggested they could be used as a potential treatment for diabetes.[49]

Umbilical cord blood contains low levels of stem cells as well as a number of hematopoietic (blood forming) cells, including lymphocytes and monocytes. There is a considerable amount of research focusing on umbilical cord blood for the treatment of stroke, myocardial infarction, and a variety of blood-related disorders, with some degree of success.[50-53] The benefits of such blood have already been demonstrated in the treatment of hematopoietic disorders, with over 6,000 transplants being performed worldwide since it was first used to treat a five-year-old child afflicted with Fanconi anemia in 1988.[50] And there is good experimental evidence that it can help with other disorders as well.[53,54] However, it is unclear precisely how these benefits are obtained. Current evidence suggests that in many cases it is not the stem cells per se that provide the benefit, but rather the growth factors these cells release. Some research shows that umbilical cord blood cells do seem to have the ability to become neuronal-like cells in vitro, but do not appear to produce neurons of any significant number in animal models of stroke.[53,54]

The current research interest in umbilical cord blood cells[53,54] has resulted in the formation of many companies worldwide that allow public and private storage of these cells. As a result, at least 18 states have proposed legislation to encourage and inform the public about this potential resource, and in several cases to provide funding for the setting up and/or running of umbilical cord cell banks (see http://www.ncsl.org/programs/health/genetics/geneticsDB.cfm for a searchable database of such legislation).

Additionally, official Japanese, European, and Australian banks exist, as well as the many private companies that are currently "getting in on the act."[55-57] This resource could prove to be valuable. Although the potential benefit of these cells still remains relatively unexplored, the practice of banking them already has at least one undeniable benefit: providing donors with a source of their own cells, which considerably reduces the chance of rejection if they ever do need them for medical reasons.

Two other recent papers have demonstrated an additional potential source of adult multipotent stem cells: menstrual blood.[58,59]

POTENTIAL USES OF STEM CELLS

Adult stem cells derived from bone marrow (i.e., the hematopoietic system) have been used frequently over the past 30 years for successful treatment of numerous blood-based disorders. Current treatments include nuclear radiation exposure and transplantation for the treatment of genetic diseases or cell cancers of the blood and the blood-forming system.[40,60-63]

According to a White House report, there are currently more than 1,200 non-embryonic stem cell clinical trials under way, while none are being performed using embryonic cells.[64] The freeze on federal funding to support embryonic studies, rather than a lack of efficacy, is most likely a major factor behind this statistic. It is important to remember, however, that embryonic stem cell research has never been *illegal* in the United States; it just cannot be funded from federal sources other than those lines that were approved in August 2001. It is also noteworthy that adult stem cells have been researched for three decades, whereas embryonic stem cell research is considerably more recent, with the first human embryonic stem cell being isolated in 1998 at the University of Wisconsin–Madison by James Thomson.[18] That discovery led to several patents/licenses by the Wisconsin Alumni Research Foundation (WARF), further restricting the use and research of such cells, given the expense of purchasing them. These patents were revoked in April 2007 by the U.S. Patent and Trademark Office,[65] but WARF appealed the decision. In March 2008, WARF's appeal was upheld.[66] To provide cells to researchers, the National Institutes of Health has established a subsidy that allows the purchase of cell lines approved in August 2001, at much reduced rates, thus resolving some of the previous issues related to their use.

Many of the adult stem cell trials are also oncology studies rather than regenerative medicine studies.[67,68] Ongoing clinical studies include phase II trials in which patients suffering from myocardial ischemia have their own adult bone marrow stem cells transplanted into their heart, theoretically increasing revascularization of the affected areas.[69,70] Additional cardiac therapies are summarized in a review by Ramos and Hare.[71]

A myriad of basic research is underway worldwide on both embryonic and non-embryonic stem cells derived from a number of sources. This research encompasses treatment of various disorders including organ regeneration, cardiovascular improvements, diabetes, and neurodegenerative conditions. They comprise the complete continuum of research from preliminary explorative studies through preclinical and clinical trails. Promising results include the promotion of liver regeneration by bone marrow stem cells in patients with hepatic malignancies,[72] the formation of blood vessels in mice from human embryonic stem cells that have been made to differentiate into endothelial precursor cells,[73] the treatment of stroke and heart ischemia animal models by human umbilical cord blood transplants in rats,[51,53,54] and the ability of embryonic stem cells to differentiate into functioning heart tissue (myocytes).[74] Adult stem cells also have been used for the latter purpose, but the differentiated cells appear to impair heart function. However, preliminary data from a clinical phase I trial of an intravenous formulation (Provacel) of adult bone marrow–derived mesenchymal stem cells appears to demonstrate some benefit in decreasing subsequent problems among heart attack patients (Schaer, American College of Cardiology's Innovation in Intervention, March 25, 2007). Also, Yacoub[75] announced that his team has been able to grow a heart valve from bone marrow stem cells using a collagen scaffold. This procedure has yet to be tested to determine if the valve is functional *in vivo*, but it clearly represents a promising discovery. Similarly, preliminary testing of the recently discovered stem cells in amniotic fluid for treating heart disease has demonstrated some encouraging results that require further study and verification.[76] Unfortunately, transplantation of these cells has been accompanied by a strong immunological response.

Elsewhere, a study using embryonic stem cells has shown considerable improvement in mice specially bred to exhibit symptoms of Sandhoff disease, a childhood disorder.[77] The implanted cells appear to function by replacing the neurons killed by the disease, as well as restoring normal levels of the enzyme hexosaminidase (low levels cause the disease). The disease was found to eventually return, but Lee et al.[78] believe that additional treatments could inhibit recurrence and are conducting further research in this area.

Preliminary findings from other studies involving fetal neural stem cells in culture and in animals have shown rescue of retinal cells after injury or disease.[79] This observation appears to demonstrate a restorative rather than a replacement action by these cells.

In general, considerable research is underway to ensure that the development of treatments involves only those cell types being sought, and that it includes ways of ensuring desired outcomes—i.e., controlling the stem cells so that they form the desired cells and do not proliferate indefinitely, which could lead to malignancy once transplanted. Achieving such outcomes may constitute one of the biggest stumbling blocks to stem cell research. One possible method would be to differentiate the cells before transplantation; Keller[79] has summarized various attempts at this method. Yet, a study involving transplantation of stem cells obtained from the human central nervous system into a primate Parkinsonian model resulted in behavioral improvements

and integration of cells without tumor formation.[80] Therefore, predifferentiation of cells before transplant may not be necessary, though further research is required to be sure that this is the case. This avenue of research is likely to see many initiatives, given the anticipated dividends.

Additionally, study of the body's ability to reject "foreign" tissue is also important because certain embryonic tissue is likely to have the ability to induce a significant immunologic response. Some studies are now suggesting that immature embryonic stem cells and umbilical cord blood cells are not as likely to cause an immunological reaction as differentiated adult stem cells.[81-83] With adult stem cells, harvesting from the same patient undergoing the transplant generally eliminates this problem.

A few studies have found that co-transplantation of two or more different types of cells has resulted in a synergistic effect that maintained their survival and execution of beneficial effects. For instance, the co-culture of amniotic epithelial and neural stem cells promoted neuronal differentiation of the latter.[84] Both trophic support and direct contact between the two cell types appeared to have important but independent effects on the neuronal survival and differentiation.

One caveat to consider in stem cell treatment of disease is that the replacement of dying cells by new ones is only a temporary solution because whatever resulted in the death of the cells initially—unless purely intrinsic to the dying cells themselves or only a onetime event—will eventually prove lethal to the new cells, too. This phenomenon has been demonstrated in a paper on fetal tissue grafts for the treatment of Parkinson's disease.[85] Consequently, calling stem cells a "cure" for diseases is really a misnomer; instead, calling them the "best available treatment" may be more accurate at present. This caveat makes the assumption that stem cell transplants are replacing the dying cells. Studies on stroke models using umbilical cord blood–derived stem cells do not support the idea of replacement, but do show an improvement in the size of the stroke lesion and behavioral markers.[53,54] Some of their benefit may be more related to controlling the inflammatory response that causes cell death or to promoting more rapid healing. A study by Capone et al.[86] demonstrated that stem cells do act in this fashion, modifying the microenvironment following stroke to afford neuroprotection, rather than replacing "sick" cells. Similar findings have been observed in other studies, including the eye experiments mentioned previously. Thus, stem cells may help to support the cells that are already present and protect them from further injury or death due to the factors that cause or perpetuate the initial disease or injury. This support in turn leads to another consideration: are pluripotent cells necessarily better than multipotent ones? Assuming that adult stem cells from a specific source (e.g., adult stem cells from the brain) can differentiate into the required replacement cell (e.g., neural cells) or provide the required supporting factors, they do not need to be pluripotent. Therefore, pluripotent (embryonic stem) cells would only be required when adult stem cells are not present or cannot differentiate into the cell of interest or produce the necessary factors to give the desired result. Consequently, research on both pluripotent and multipotent cells would seem to still be necessary.[87]

Not only does stem cell research provide direct cell replacement benefits or improve the survivability of "sick" or "injured" cells, it also offers considerable insight on what causes cells to proliferate and differentiate—an important phenomenon to understand in the fight against cancers and in general research dedicated to the development and normal life cycle of cells.[88-92] Studies of stem cells could, therefore, have far-reaching implications that are not limited to just disease treatment.[88-94] Finally, stem cells could also be used to model organs for the testing of drugs or new surgical techniques—another potentially powerful benefit of stem cell research.[95,96]

PREDOMINANT CONTROVERSIES ABOUT STEM CELL RESEARCH

There are four main controversies currently surrounding stem cells. Perhaps the most significant involves moral arguments regarding the use of embryonic material to harvest stem cells. The focus of this controversy is on when life begins—which some consider to be at conception—and whether any individual has the right to terminate a life. Strong spiritual and religious beliefs are frequently central to this controversy, and the practice is considered unacceptable by many. One study[97] suggested the possibility of removing one or a few stem cells without harming an in vitro–fertilized embryo prior to implantation, thus maintaining its viability. As of yet, however, it is unclear exactly what impact this action has on the growing organism and whether such studies can be confirmed. Consequently, because of the controversy over when life begins, many countries either ban embryonic stem cell research or severely restrict it. As indicated previously, only those embryonic stem cell lines approved for study in August 2001 can receive federal funding and support in the United States.

Three connected groups of scientists reported success in transforming normal mouse skin cells into embryonic stem cell–like cells via genetic manipulation.[98-100] Further research is required to confirm these findings and those of other studies[101,102] have translated this technique to human cells. Additionally, the transformed cells are prone to tumorigenesis, and therefore, would not be useful for transplantation in humans in their current form. This technique would not necessarily replace the use of embryo-derived stem cells, as further characterization is necessary to confirm that the cells do possess all of the same characteristics—including the same receptors and response to treatments. Nevertheless, it is a small step in the right direction for those opposed to embryonic sources.

A second controversy surrounding stem cell research is the apparent groundbreaking outcome of studies performed by a research team in South Korea. In 2004, this team reported in *Science* that they had obtained human embryonic stem cells from the nuclear transfer of oocytes (i.e., the replacement of the nucleus of an egg with that of

an already differentiated cell). The following year, this team again reported in *Science* that they were able to generate patient-specific immune-matched embryonic stem cells for the treatment of diseases. In the end, the data were found to be fraudulent, and some of the female researchers had apparently been coerced to donate their own eggs for the process of obtaining stem cells, a significant ethical breach in the field.[103] As a result of these findings, both papers were retracted in 2005, and significant penalties were imposed on the researchers. This scandal cast a large shadow over the competitiveness in the field and the possible unethical means of obtaining stem cells for research purposes.

A third controversy has to do with stem cells' alleged potential to produce malignancies once implanted due to their theoretically immortal nature (viewed as such because stem cells can reproduce *ad infinitum*). Some research suggests that certain kinds of stem cells could cause cancer because a small number of defective stem cells have been found in tumors, where they may have acted as a seed.[104] Given their ability to proliferate continuously, these cells carry an increased likelihood of mutations, which in turn increases the probability that they will grow out of control and become cancerous. Therefore, their use in treatments could be fraught with problems, at least until a clearer understanding emerges regarding the signals that turn them on and off in their growth cycles. Adult stem cells are normally quiescent, meaning that identification of the process by which mutations occur could prove to be vitally important in preventing transplant tumorigenicity or in preventing cancers altogether.

Interestingly, studies using embryonic carcinoma cells—which are malignant, similar to stem cells, and generally derived from germinal cells—have provided some neurodegenerative improvement in animal models.[105] These cells can be made to differentiate into human neurons under retinoic acid treatment. When this conversion occurs, the cells appear to lose their malignant properties.[105] Once the mechanism for this process has been determined, it could be tested in stem cells, perhaps creating the ability to turn off the malignant characteristics of these cells.

At the same time, another recent study suggested that although stem cells—specifically, those obtained from bone marrow—may look like malignant cells, they do not necessarily function like them. In other words, stem cells may not be cancerous and may not be able to seed tumors.[106] Further research is required to determine whether this is true for all stem cells found in tumors, and whether they are acting as "developmental mimics" or seed tumors.

The fourth main controversy concerns whether adult stem cells are as beneficial as embryonic stem cells. A seminal paper from a group led by Catherine Verfaillie (see Jiang et al.[107]) reported that adult stem cells from the bone marrow of rats, which they called "multipotent adult progenitor cells" (MAPCs), had the potential to differentiate into almost every type of cell in the body, a claim that previously applied only to embryonic stem cells. Unfortunately, little success has been made in replicating these results. More recent evidence suggests that the paper was flawed, adding further consternation to this area of investigation.[108,109] Subsequent research from a number of teams reported that when MAPCs could be successfully isolated from bone marrow using a different technique than that originally proposed, they did have the ability to become any type of blood cell but not other cells. But overall, it is still unclear whether this and other types of adult stem cells are as efficacious as originally proposed.[110-112] Criteria that stem cells have to meet to be classified as pluripotent have been proposed,[113,114] and few studies have actually met these criteria, with the majority being explained by cell fusion[115] and incorrect interpretation.[111,116] Thus, many researchers still believe that embryonic stem cells may provide more benefit due to their hypothetical ability to differentiate into all cell types, though most would prefer both avenues to be explored, acknowledging that adult stem cells could be useful in some circumstances.

Two independent studies by the groups of Yamanaka[101] and Thomson[102] may make this controversy a moot point. Expanding on the mouse studies[98-100] mentioned in an earlier section, they reported two similar methods of converting adult human skin cells into embryonic-like stem cells. This was achieved by the insertion of 4 genes that led to the reprogramming of the cells (interestingly, two of the genes differed between the research groups but had similar functions). This research has great potential but requires considerable additional testing to ensure that the embryonic-like stem cells behave in a similar fashion to embryonic stem cells obtained in the "normal" fashion. Additionally, there is the concern that one of the genes the researchers inserted was a cancer gene, which could increase the likelihood for tumorigenesis using this approach. There is also concern over the retroviruses used to insert the genes, which can have potentially carcinogenic and other detrimental effects due to their ability to randomly insert the gene of interest into the genome. A major bonus of this approach is the ability to take the cells from the patients themselves and therefore reduce the likelihood of transplant rejection. There is also the potential to model a disease more directly by removing the affected cells from a patient and growing them in culture so that they can be characterized and compared with healthy cells. Research by Jaenisch's group[117] has demonstrated that reprogrammed skin cells can treat the sickle cell anemia mouse model, thus confirming the potentially beneficial effects of such cells.

STATUS OF LEGISLATION ON STEM CELL USE

In the United States, federal funding for embryonic stem cell research from sources such as the National Institutes of Health is restricted by congressional legislation, which mandates that only cell lines approved in August 2001 be used in funded research. At that time, there were more than 60 lines, but only 20 have proven to be viable and available for general use. All of these cell lines have been grown on a mouse fibroblast feeder layer to restrict differentiation and only allow replication. Unfortunately, it has been

found that these stem cells are likely contaminated with mouse proteins and sugars that could generate severe immunological responses following transplantation into humans to treat diseases.[118] However, some studies suggest that the proteins and sugars can be removed or cultured out to make the cells safer for human transplantation.[119] Newer procedures that use completely human components have been developed, so any future cell lines are unlikely to have this problem. Research involving adult stem cells is not limited under the current federal restrictions.

The 20 embryonic cell lines that are federally permissible represent only a small fraction of the genetically and immunologically heterogenous population of the world.[120,121] This limitation casts doubt over whether any treatments derived from these cell lines will be suitable for treating all of the ethnically diverse populations that exist in the United States and abroad. This limitation is both an incentive for developing additional cell lines and an important factor that should be considered with respect to all types of stem cells. The genetic diversity inherent in the world's different ethnic groups implies that different ethnicities may respond in different ways to these cell lines. Therefore, any success found with these cells would need to be replicated using cell lines derived from other ethnic groups to determine their general use among the world's population.[122]

In 2006, a congressional bill was proposed to allow research on stem cells derived from embryos discarded after in vitro fertilization treatments. This bill was vetoed by the president based on ethical, moral, and religious concerns. The bill resurfaced following the 2006 midterm elections in which Democrats regained control of the House and Senate, but no change to the veto is likely under the current administration.[123]

The restriction on federal funding for embryonic stem cell research led New Jersey to appropriate state funding for research on both embryonic and adult stem cells in early 2004. Ohio had previously proposed funding dedicated to adult stem cell research. The most well known example of funding at the state level is California, which proposed its own legislation in 2004 (Proposition 71) involving the sale of $3 billion in bonds to provide $295 million annually for 10 years to the funding of stem cell research.[124]

Since then, several other states have sought endorsement of similar propositions (Tables 1 and 2). Currently, at least 33 states have specific guidelines with respect to the use of embryos in research, which in several cases (e.g., Arizona, South Dakota, Texas) conform to federal legislation. However, there is considerable variation among these states regarding their support of separate initiatives for stem cell research.

The International Society for Stem Cell Research recently proposed international guidelines for the use of embryonic tissue to ensure uniform research and experimental practice worldwide.[125] At the core of these guidelines is that embryonic research should be rigorously overseen by sponsoring organizations or regulatory bodies with specific policies and procedures that conform to the recommendations of the scientific community. In all policies, no cloning is to be undertaken to create humans. The society's policies also recommend the establishment of an institutional oversight committee to review and determine approval of all stem cell research. The use of "chimeras" (i.e., animals created with human cells) is allowed with approval from this committee. Further, the use of any cells donated for research purposes should require consent from those donating them. Regulations pertaining to stem cell use by state and country are kept reasonably up to date at the following websites:

- http://www.ncsl.org/programs/health/genetics/embfet.htm
- http://isscr.org/public/regions

Initially, the federal funding restriction was seen as detrimental to stem cell research. However, some scientists are now suggesting that the restriction has actually opened other funding opportunities that may be more helpful to the research community. As Table 1 shows, federal restrictions have created unprecedented state funding far exceeding any that the National Institutes of Health would likely provide. This alternative funding source has also piqued the interest of pharmaceutical companies. Such companies may be able to position themselves for a larger share of patents and licenses from state-funded research—they already have a near monopoly on drug therapies derived from this research. This apparent paradox was discussed in an opinion piece in *The Scientist* by Dr. Paul Sanberg.[126]

STEM CELL RESEARCH AND HEALTH EDUCATION PRACTICE

Health educators are charged with numerous roles and responsibilities in the public sector.[1] These essential tasks intersect with current and anticipated research involving stem cells. What follows is an iteration of ways in which health educators might be expected to address relevant stem cell knowledge and research issues. Although not exhaustive, the points below highlight the importance of keeping public dialogue about this topic both vibrant and accurate.

Assessing Individual and Community Needs

Health education competencies and subcompetencies in this area include, but are not limited to, selecting valid sources of information about health needs and interests. The debate over stem cell research inevitably becomes enmeshed in moral arguments and political posturing, so it is important that scientifically accurate information and data be made prominent in the public eye. Health educators are positioned to translate technical information and make it accessible to the lay public and other interested consumers. Presently, although there are many avenues of availability for this information in the scientific and medical communities, it is far less available to the general public. What is needed are accurate sources of relevant stem cell data and other information that neither refute scientific discovery nor escalate optimism inappropriately or prematurely.

Planning, Implementing, and Administering Strategies and Programs

The highly diverse nature of the health in-

Table 1. States That Are Encouraging Stem Cell Research

State	Year	Legislation	Status	Funding
California	2004	Issuance of bonds to raise money for funding stem cell research	Passed	$3 billion+ over 10 years
Connecticut	2005	Fund for stem cell research	Passed	$100 million over 10 years
Florida	2007	Recommendation of state money for non-embryonic stem cell research (another bill proposed to provide for embryonic)	Pending	$20 million
Hawaii	2006	Study and recommendation commissioned by state for the University of Hawaii to investigate "the feasibility of encouraging stem cell research"	Pending	N/A
Illinois	2006	Illinois Regenerative Medicine Institute	Passed	$15 million
Indiana	2005	Research on fetal stem cells derived from placentas, cord blood, amniotic fluid, or fetal tissue allowed; adult stem cell research center at Indiana University	Passed	$50,000
Iowa	2007	Plan to establish Center for Regenerative Medicine; allows embryonic stem cell research	Pending	N/A
Maryland	2006	Maryland Stem Cell Research Fund (not oocytes)	Passed	$15 million (2007)
Massachusetts	2005	▪ Institute for Stem Cell Research and Regenerative Medicine at University of Massachusetts ▪ Life Sciences Investment Fund (including stem cell research)	Passed Passed	$1 million $10 million
Minnesota	2007	Currently bans embryo and fetal research; several proposals to support stem cell research using other types (and also embryo)	Pending	N/A
New Jersey	2004 2006	▪ New Jersey Stem Cell Institute ▪ Issuance of bonds for funding several stem cell–related research facilities in state (ballot-rejected proposal in 2007)	Passed	$23 million $270 million
New Mexico	2007	Proposal to fund the building of a stem cell research facility, including embryonic research; current legislation prohibits research on live fetus/embryo, but use of fertility treatment excess permitted	Pending	$10 million over three years
New York	2006 2007	▪ New York State Institute for Stem Cell Research and Regenerative Medicine ▪ The Empire State Stem Cell Trust" created for all stem cells	Passed	$300 million over two years $100 million in 2007–2008 plus $500 million in 2008–2017
Ohio	2003	Adult stem cell research only; Center for Stem Cell and Regenerative Medicine	Passed	$19.4 million plus $8 million in 2006
South Carolina	2007	Bill to allow stem cell research under institutional research board approval	Pending	N/A
Virginia	2006	Fund to support adult stem cell research	Passed	N/A
Washington	2006	Life Sciences Discovery Fund; may include funding for stem cell research	Pending	N/A
Wisconsin	2006	Funding for Stem Cell Products Inc.	Passed	$1 million

Sources: Compiled from various online reports, including www.ncsl.org/programs/health/genetics/embfet.htm, http://isscr.org/public/regions, and "Yahoo! Alerts Health News: Stem Cells" (all last accessed December 7, 2007).

Table 2. States with Legislation Relating to Embryonic Stem Cell Use

State	Legislation
Arkansas	Research prohibited except on stillborn fetuses
Louisiana	Prohibits research on embryos
Maine	Research prohibited on in vitro–fertilized embryos; a bill has been proposed for stem cell research this year
Michigan	Dead embryos and fetuses available for experimentation by consent
Missouri	Prohibits research on live fetus
Montana	Prohibits live fetal research
Nebraska	Restricted use of money for embryonic stem cell research; a ban on cloning proposed
New Hampshire	Prohibits maintenance of unfrozen fertilized embryo beyond 14 days
North Dakota	Research (after consent) on embryos from sources other than abortion
Oklahoma	Prohibits research on fetus and embryos
Pennsylvania	Prohibits research on live fetus and embryos
Rhode Island	Prohibits research on in vitro–fertilized embryos post implantation, but pending legislation for embryonic stem cell research with the consent of both parties involved in the creation of the embryo
South Dakota	Prohibits destruction of embryos
Tennessee	Allows research on aborted fetuses, but requires consent
Utah	Prohibits research on aborted fetus or post-implanted embryo

Sources: Compiled from various online reports, including www.ncsl.org/programs/health/genetics/embfet.htm, http://isscr.org/public/regions, and "Yahoo! Alerts Health News: Stem Cells" (all last accessed December 7, 2007).

formation consumer includes different levels of health literacy, disparate ethical and moral belief systems, and widely varying learning styles. Health educators are professionally prepared as a group to respond to the needs of these different audiences by identifying individuals and groups who can best benefit from knowledge about stem cell research, incorporating appropriate organizational frameworks, establishing specific learning objectives based on assessment of baseline knowledge, assigning audience-specific modes of education delivery, and developing a program delivery method that includes optimal use of learning technologies.

Health educators are able to assess both knowledge and attitude shifts through the use of well chosen surveys and other assessment instruments. Moreover, health educators can infer needed future activities and programs that build either in a linear or a spiraling fashion on past activities. Stem cell research is a pioneering endeavor, and the knowledge shifts can, therefore, be rapid; the need for recurring data and information sources suitable for general and specific audience consumption is as dynamic as the shifting sands. Health educators are prime candidates for interpreting these changes, putting them in context, and making the necessary and relevant adjustments to the public's informational needs.

Serving as an Education Resource Person

Health educators should be masters at retrieval of information that can be translated from technical to more audience-friendly language. As with their other resource functions, health educators should be able to match information needs with the appropriate retrieval systems; to select data and data systems commensurate with program needs; and to determine the relevance of various computerized health information resources, access those resources, and employ electronic technology for retrieving references. To enhance the match between information and audience, health educators should be positioned to perform readability assessments using such tools as the SMOG Test,[127] the Flesch Reading Ease Formula,[128] and other indices,[129] thereby increasing the likelihood that relevant information about stem cells will be understood.

Advocating for Education about Stem Cell Research

Health educators are expected to analyze and respond to current and future needs in health education. Particularly pertinent to stem cell research is the analysis of factors (e.g., social, demographic, political) that influence individuals who make decisions about the direction of, and restrictions on, stem cell research. Currently, the wise

course may be for health educators to be as politically neutral as possible in organizing and communicating information about stem cell research—standing neither for nor against liberalization of current research postures by the federal government and other entities. Health educators, like any other professional group, are subject to their own biases, including those emanating from personal moral philosophy, ethical principles, or other convictions. Nevertheless, they are obligated to report on stem cell matters factually. They can also serve as advocates for promoting discussions in the public sector, at professional conferences, and in their own scientific literature. Finally, practice standards support health educators' participation in continuing education on stem cell issues and their development of plans for ongoing professional development.

CONCLUSION

Stem cell research is a major area in biomedical research, one that could have a far-reaching impact on the overall health of the human race. Many people, professional and lay alike, obtain their knowledge from sources that present personal agendas or dubious interpretations of facts. In this article, we have endeavored to give a fair, balanced, and unbiased view—as much as our personal limits as scientists and individuals permit—of the potential of stem cells. We have also argued that health educators can position themselves to bring some orderliness to the debate about the merits of stem cell research and support a healthy dialogue among lay audiences as well as their own professional peers.

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