**MYP Biology: Bioethics Stem Cells -- THE STEM CELL CONTROVERSY**

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Stem cells constitute one of the most fascinating -- and controversial -- areas of biology today. Researchers, who are still learning how the body uses these cells to restore or regenerate tissue, hope to harness the power of stem cells and make them a human "repair kit." But there is also a deep division over how safe -- or how ethical -- using these cells will be. While stem cells could revolutionize medicine, they also raise profound ethical questions about what steps should be taken to restore health or save lives.

What Are Stem Cells?

Stem cells, the building blocks of the body, have two essential characteristics that make them unique. They are unspecialized cells that can renew themselves for long periods through cell division. In addition, under the right conditions, they can develop, or "differentiate" to become cells with more specialized functions. Although there are three major types of stem cells -- embryonic stem cells, embryonic "fetal" germ cells, and adult stem cells -- scientists mainly work with adult and embryonic stem cells from animals and humans. (Embryonic germ cells are found in a specific part of the embryo/fetus called the gonadal ridge; they normally develop into mature gametes -- eggs and sperm.) The labels "adult" and "embryonic" -- relate to the stem cells' place of origin.

Adult Stem Cells

Adult stem cells are unspecialized, undifferentiated cells that exist in very small numbers among specialized cells in an adult organ or tissue. Their main function is to maintain and periodically repair the tissues in which they are found. Adult stem cells are rare and hard to detect, but so far researchers have found them in a number of places, including the brain, the bone marrow, peripheral blood, blood vessels, skeletal muscle, skin, and liver. One adult stem cell, the hematopoietic stem cell, has been used for decades to treat diseases, including leukemia, lymphoma, and inherited blood disorders, and to replace cells destroyed by cancer chemotherapy. Researchers are investigating whether it is possible to expand adult stem cells, increasing their numbers in either a cell culture or within the body so that more diseases might be treated.

Researchers long assumed that adult stem cells could yield only those specialized cells of the tissue or organ where they were located -- for example a skin stem cell could only give rise to a skin cell. But the last few years has brought provocative evidence that some adult stem cells may have "plasticity" and may be able to transform into different cell types, a process known as transdifferentiation.

Embryonic Stem Cells

Embryonic stem cells, as their name implies, are taken from embryos. These cells are "pluripotent," or capable of differentiating into any cell type derived from the three embryonic germ layers (the three initial tissue layers arising in an embryo) -- mesoderm, endoderm, and ectoderm. Under the right conditions, human embryonic stem cells will proliferate indefinitely without specializing or differentiating into specific cell types, to form an embryonic stem cell line. Embryonic stem cells were first isolated in mice more than 20 years ago, but it was not until 1998 that James Thomson of the University of Wisconsin managed to derive and grow the first stable line of human cells.

The embryos from which these stem cells are derived form under two different conditions. Until very recently, these cells were always taken from surplus eggs left over from in vitro fertilization procedures and contributed with the informed consent of the donors. In vitro fertilization is a technique used to assist women who are experiencing difficulty in conceiving a child. A woman's eggs are removed from her ovary and then fertilized in a laboratory culture dish. The fertilized eggs are maintained in a laboratory dish and allowed to develop into pre-implantation embryos, or pre-embryos. A little over two days later, they are delivered to a healthy uterus to continue development.

Many times, surplus embryos remain after the in vitro procedure. These can be donated to other couples or discarded, but they can also be frozen and stored for future IVF attempts or donated for research. The best estimate, by the RAND Institute in May 2003, is that nearly 400,000 embryos are frozen and stored in the U.S. alone, with about 11,000 such embryos designated for research.

In February 2004, scientists in South Korea became the first to derive human stem cells from embryos using a second method called somatic cell nuclear transfer (SCNT) -- a procedure often referred to as therapeutic cloning. [See the Stem Cell Challenge for a detailed description of both the SCNT and IVF methods of obtaining stem cells.]

Whether the embryonic stem cells are isolated from surplus IVF embryos or through SCNT, the embryo is destroyed in the process. This fact is the root of the controversy over using these cells in research.

Researchers think human embryonic stem cells could be a boon to medical research and treatment. "Embryonic stem cells could serve as replacement cells for those that have been lost or destroyed because of disease," says Robert Goldstein, Chief Scientific Officer of the Juvenile Diabetes Research Foundation. "If we can discover the biological cues that make an embryonic stem cell develop into a specialized cell -- like an insulin-secreting cell in the pancreas -- we could try to reproduce these signals in the lab and create a source of replacement cells for many afflictions."

Embryonic stem cells have other potential uses: as tools for studying early events in human development (shedding light on birth defects), as test systems for new drug therapies, to screen potential toxins, and as vehicles or "vectors" to deliver genes that could correct defects. These applications remain theoretical -- the field is too new for any of these treatments to have reached human stages. But various animal studies have demonstrated "proof of principle" that these approaches can work. For example, mouse embryonic stem cells have been converted into specialized cell types and transplanted into animals to relieve symptoms of spinal cord injury and Parkinson's disease.

The Controversy

The isolation of human embryonic stem cells in 1998 thrust stem cell research into a volatile national debate tied to the fight over abortion. Deriving embryonic stem cells, and destroying an embryo in the process, raised profound ethical questions. Most revolve around the question of when life begins. Is an embryo a person? Should we forego embryonic stem cell research to protect the embryo? Is it right to negate a potential life for benefits that are unproven? Should researchers avoid this ethical minefield and redouble their efforts with adult stem cells?

The Case Against Using Embryonic Stem Cells

Objections to deriving human embryonic stem cells arise from the contention that human embryos are nothing less than individual beings in the earliest stages of life. As some members of a bioethics council appointed by President Bush put it in 2002, "We find it disquieting, even somewhat ignoble, to treat what are in fact the seeds of the next generation as mere raw material for satisfying the needs of our own."

Those opposed to using embryonic stem cells contend that the benefits from the cells are speculative today, while the medical applications of adult stem cells have been shown for years. "Embryonic stem cells have not helped a single human patient or demonstrated any therapeutic benefit," reads a statement by the United States Conference of Catholic Bishops. "By contrast, adult stem cells and other ethically acceptable alternatives have already helped hundreds of thousands of patients, and new clinical uses expand almost weekly."

Many on this side of the argument cite the recent studies suggesting that adult stem cells can change type, or transdifferentiate. If researchers could isolate enough adult stem cells, couldn't they, instead of embryonic stem cells, be used as replacement tissue? Some scientists even think it might be possible to "reprogram" adult stem cells back to an embryonic-cell-like state -- again providing a source for replacement tissue without the moral objections. An added benefit of this technique would be that the cells come from the patient's own body and thus are less likely to be rejected.

Another issue with using embryonic stem cells concerns their ability to divide indefinitely. Studies in animals have shown that embryonic stem cells sometimes form tumors called "teratomas" or develop into a mixed collection of partially formed tissue. This could make injecting them into human patients risky. Adult stem cells, on the other hand, are not thought to pose such risks.

The Case for Using Embyronic Stem Cells

Many scientists do not think adult stem cells offer the same therapeutic and research potential as embryonic stem cells. Adult stem cells are difficult to isolate, and they do not proliferate well in culture. There's little proof, researchers argue, of a wide array of human adult stem cells that can differentiate into multiple tissue types. Some studies that appeared to show adult stem cells transforming into other cell types have been called into question by more recent findings, and evidence seems to indicate that adult stem cells may not possess the same capacity to give rise to any cell type as embryonic stem cells do.

But despite the questions, the consensus among most scientists is that research on both stem cell types should continue on parallel tracks. Even those who have made their mark working with adult stem cells, such as Catherine Verfaillie of the University of Minnesota, hold this view. "We will not know which stem cells, adult or embryonic, are most useful in treating a particular disease without side by side comparison of adult and embryonic stem cells," Verfaillie wrote on February 4, 2002 in a letter submitted to Pennsylvania Senator Arlen Specter.

And in 2001, a letter from 40 Nobel Laureates to President Bush stated: "It is premature to conclude that adult stem cells have the same potential as embryonic stem cells -- and that potential will almost certainly vary from disease to disease ... Therefore, for disorders that prove not to be treatable with adult stem cells, impeding human pluripotent stem cell research risks unnecessary delay for millions of patients who may die or endure needless suffering while the effectiveness of adult stem cells is evaluated."

Many disease sufferers consider embryonic stem cells to be their only lifeline. Karen Miner, 52, has been paralyzed from the shoulders down after her car went into a ravine during a rainstorm 11 years ago. In 1998, she co-founded Californians for Cure, which advocates for spinal cord and embryonic stem cell research in California. Miner doesn't understand why "pro-life" forces are aligned against her cause.

"They really don't understand that it's not destroying a life, it's saving a life," she says. "I do not believe these cells are children. Blood cells are alive, and so are skin cells. We cut into them during surgery, but no one considers that murder. They make it sound like there are people growing out in warehouses that we take body parts from."

Finally, in answer to those who consider destruction of an embryo unjustified even if it saves a life, those favoring embryonic stem cell research point out that IVF-created embryos often get discarded, so they should be put to use rather than wasted.

Current U.S. Policy

On August 9, 2001, the Bush Administration announced that U.S. federal funds could be used to support research using selected human embryonic stem cell lines. This policy had one major sticking point: The lines had to already be in existence -- federal funds could not go to research on stem cells derived after the day of the announcement. At the time, President Bush claimed there were about 60 embryonic stem cell lines eligible for funding, and soon after the estimate went up to 78.

Stem cell researchers, however, were skeptical of the claim from the beginning, arguing that the number of lines actually available was far lower. The skepticism has been borne out -- as of March 2004, the official NIH Human Embryonic Stem Cell Registry lists just 15 eligible lines as being available for distribution to researchers, who say such a small number of lines is severely restricting many areas of medical science and delaying any therapeutic benefits that could result.

Researchers also say the current guidelines are driving top investigators to greener pastures in other countries and causing scientists to shy away from the field altogether. For example, soon after President Bush announced the stem cell policy in 2001, one major stem cell researcher, Roger Pederson, decamped from the University of California, San Francisco to Cambridge University in the United Kingdom, which has a more supportive environment. He readily acknowledges that the U.S. policy compelled him to leave.

Cloning

Creating cells through therapeutic cloning raises even more troubling questions because it involves creating embryos for medical or research purposes. After the report of the therapeutic cloning success in South Korea, Leon Kass, Chairman of the President's Council on Bioethics, voiced the fears of many when he told THE NEW YORK TIMES: "The age of human cloning has apparently arrived: today cloned blastocysts for research, tomorrow cloned blastocysts for baby making."

No stem cells have been created through this method in the U.S., at least none that have been reported and verified, but no law forbids such an act either. The political fight, however, has been under way for several years. The House of Representatives twice passed bills that would ban all forms of cloning, but the Senate is deadlocked on the issue. Two competing Senate bills have had roughly equal support -- one that bans all forms of cloning, and one that bans reproductive cloning but allows therapeutic cloning. (Reproductive cloning uses somatic cell nuclear transfer to make an embryo that is placed in the womb and allowed to progress toward birth. It was used to produce Dolly the sheep in 1996. In therapeutic cloning, the embryo is not placed in a womb but used for the derivation of stem cells.) The legislative outcome is not expected to be resolved anytime soon.

Most scientists favor a ban on reproductive cloning but think therapeutic cloning should be allowed. A number of scientific organizations, notably the National Academy of Sciences, and the American Association for the Advancement of Sciences, have taken this position. Some researchers contend that the therapeutic cloning achievement in South Korea is a sign that research momentum relating to stem cells has shifted overseas.

The Impact

Karen Miner, hoping to overcome her paralysis, is frustrated at the delays due to the political fight over stem cells, especially when she sees promising results from animal studies. "I was able to go down to the University of California at Irvine and see [previously paralyzed] rats walking," she said. "That was a year and a half ago, and it's still just the rats walking. If they delay it another four years, that's a lifetime sentence to my chair. I'm 52. I just can't keep going like this, sitting in a chair 17 hours a day, and expect to recover when they do find a cure. This is my window of opportunity."

Don Reed, co-founder of Californians for Cure, has a son, Roman, who was paralyzed 10 years ago in a football game. "Every scientist I talk to says this stem cell research must go forward," Reed said. "Millions of people will suffer if [Bush] wins and keeps restricting it. It's sad that the leader of the country is going against the best interest of American families."

Both sides have become entrenched. A telling sign of the depth of the divide came last month when the President's Council on Bioethics released a long-awaited report on embryonic stem cells. At the end of 417 pages, the council made no recommendations and took no particular ethical or policy position.

In the end, the easy answer everyone wants is simply not there. As John Civin, a professor of oncology at the Johns Hopkins Kimmel Cancer Center, has remarked, "People always ask if the new finding -- whatever it is -- means that scientific and medical goals could be accomplished by researching only 'adult' stem cells to avoid the ethical debate. The bottom line is that we don't know enough to answer that question, and we won't for some time."

Indeed, if there's one point on which virtually all stem cell scientists agree, it is that much more needs to be learned about how stem cells work in order to use them safely and effectively. Researchers have only begun to understand how the body grows and repairs itself, and increasing their knowledge is necessary before the full potential of stem cells can be determined