

# Lesson

# 2

## Techniques for Obtaining Stem Cells

### Objectives

Students will be able to:

- Describe scientific techniques (IVF, therapeutic cloning, using cord blood and bone marrow, inducing pluripotent stem cells) used for producing stem cells.
- Identify the type of stem cell (adult, embryonic) each technique yields.
- Provide an example of each technique.
- Describe how stem cells are currently used in research.

### Class Time

One class period; homework assignment may be done in class if periods are longer.

### Prior Knowledge Needed

- Definition and significance of stem cells.
- Sources of stem cells.
- Embryonic development.
- Potencies of stem cells from different sources.

### Common Misconceptions

- The foremost purpose of cloning (SCNT) is to create genetically identical individuals, such as for reproductive use.
- New techniques using adult stem cells indicate embryonic stem cells are no longer needed in research.
- Embryos look like little tiny fetuses.

### Introduction

In this lesson students learn about the variety of techniques used for obtaining stem cells, and find out if a given technique produces embryonic (pluripotent) or adult (multipotent) stem cells.

Background news articles are included for each of the following techniques: *In Vitro* Fertilization (IVF), “Therapeutic Cloning”, utilizing Umbilical Cord Blood and Bone Marrow, and inducing Pluripotent Stem Cells.

### Key Concepts

- There are a number of methods for obtaining stem cells.
- Different techniques produce different types of stem cells— IVF procedures and ‘Therapeutic Cloning’ produce embryonic stem cells, umbilical cord blood and bone marrow produce adult stem cells, and the iPS technique produces pluripotent cells that behave like embryonic stem cells.
- The uses of these techniques have societal implications.
- Stem cells are currently being used for
  - regenerative medicine
  - drug development and testing
  - illustrating early growth and differentiation
  - understanding development of diseases.

### Materials

Student Handouts:

2.1 – *What is IVF?*

2.2 – *What is “Therapeutic Cloning”?*

2.3 – *How are Umbilical Cord Blood and Bone Marrow Used?*

2.4 – *How do Differentiated Adult Cells become induced Pluripotent Stem Cells (iPS)?*

2.5 – *Summary of Newsflash! Information*

2.6 – *Overview: How Do We Get Stem Cells?*

2.7 – *How are Embryonic Stem Cells used?*

2.8 – *Current Stem Cell Research Article Review*

*An embryonic stem cell line can be made from the inner cell mass of the blastula. These cells are transferred into a plastic laboratory culture dish and grown in a medium that provides support and nutrients.*

*When kept in this way, the inner cell mass (or embryonic stem cells) can continue to divide and proliferate for long periods of time without differentiating or losing pluripotency. When coaxed to differentiate, they can then become any cell in the body.*

## Internet Resources

An animated tutorial showing some stem cell techniques from the University of Michigan can be found at: <http://www.lifesciences.umich.edu/research/featured/tutorial.html>

The 15-minute video “The Cloning Process” from NOVA ScienceNOW reviews stem cells and touches upon different techniques. The video can be found at: [www.pbs.org/wgbh/nova/sciencenow/3209/04.html](http://www.pbs.org/wgbh/nova/sciencenow/3209/04.html)

Student Handout 2.7 directs students to these two websites:

[http://www.isscr.org/public/selected\\_topics.htm](http://www.isscr.org/public/selected_topics.htm)

<http://www.pbs.org/wgbh/nova/sciencenow/3209/04-related.html>

## Procedure

Begin by asking students: “How do you think scientists get different types of stem cells for research and medical therapies?”, and “Are scientists now using stem cells for therapies?”

- Brainstorm any ideas students have about obtaining stem cells.
- Tell students that they will read about some of the major techniques currently used for both adult and embryonic stem cell research and potential therapies.

## News Flash! – Jigsaw activity

1. Students count off by fours, and then break into groups based on their number. Distribute copies of Student Handouts 2.1-2.4 to groups, so that each group is reading one article. Each two-sided handout has a description and a diagram of a technique used for obtaining stem cells on one side, and a news story about that technique on the other side.
2. Student should read quietly for approximately 7 minutes, until all members of their group are finished. Students use Student Handout 2.5 to summarize the information.
3. Once everyone has finished reading, the group should discuss the article and each student should take notes on his or her summary sheet.
4. Rearrange groups, so that there are groups of four with a student who has read each article. Each student should spend 2-3 minutes sharing the information in his or her article with the students who read a different article. Students should summarize the story they read and the answers to the questions from Handout 2.5.

*“Therapeutic Cloning” is also referred to as Somatic Cell Nuclear Transfer, or SCNT.*

5. Distribute Student Handout 2.6 “Overview: How Do We Get Stem Cells?” to each student.
  - Students work in groups to complete the table using information from the articles.
  - Students should diagram/flowchart the basic ideas from each technique on the back of this handout.

### **Discussion**

1. Review tables with entire class. Students should fill in any missing information and correct any errors as you proceed.
2. Make sure students are clear about how embryonic versus adult stem cells are derived.
3. Of the four techniques described, reinforce to students that the clinical applications of “Therapeutic Cloning” and using iPS (induced pluripotent stem cells) have not yet been realized in humans.
4. Many animals have been cloned using the technique of “Therapeutic Cloning” (including Dolly the sheep) even though there have not yet been any human clinical applications. Therapeutic cloning remains the most controversial of the techniques.

### **How are Embryonic Stem Cells used?**

1. Ask students: “When scientists get stem cells through one of these techniques, how are those stem cells used?”
2. Brainstorm any ideas that students may have.
3. Distribute Student Handout 2.7 “How are Embryonic Stem Cells Used?” to each student.
4. Give students enough time to read about the uses of stem cells detailed on the handout.
5. Discuss the handout. Pose questions such as:
  - Which of these uses might be the most beneficial? Why?
  - Do any of these uses seem problematic? Why?

### **Homework**

#### **Student Handout 2.8**

Students are directed to the following two websites and asked to find articles about stem cells. Handout 2.8 provides questions about stem cell research to help students summarize their findings.

[http://www.isscr.org/public/selected\\_topics.htm](http://www.isscr.org/public/selected_topics.htm)

<http://www.pbs.org/wgbh/nova/sciencenow/3209/04-related.html>

The case study from Lesson 3 (Student Handout 3.1) can be given as homework the night before beginning Lesson 3.

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### **Extensions**

- Create a timeline with the major advances in stem cell technology. Students can use *Key moments in the Stem Cell Debate* from Lesson 5 (Student Handout 5.1) as a reference.
- Read the article “A Law’s Fetal Flaw” by Nell Boyce from US News and World Report aloud to the class while students read along and discuss the issues raised by the story. It can be found at: <http://health.usnews.com/usnews/health/articles/030721/21cure.htm>.
- Brainstorm other diseases that involve the degeneration or irreparable damage of cells. Possible ideas include Parkinson’s Disease, Diabetes Type 1, Alzheimer’s Disease, spinal cord injuries, heart disease, organ transplants, and blindness.
- Have students look for news articles that illustrate one or more of the embryonic stem cell uses described in Student Handout 2.7. Students can also research other ways in which embryonic stem cells are being used.

### **Adaptations**

After learning the four techniques introduced in this lesson, students could do their own internet search to find current articles to summarize. The table on handout 2.6 could be completed as a class.

### **Assessment Suggestions**

- Check for accuracy on handouts
- Students reasoning on whether techniques should be used for different purposes
- Class discussion

### **Source Information for Federal Policies**

- National Institutes of Health Guidelines on Human Stem Cell Research, 2009. <http://stemcells.nih.gov/policy/2009guidelines.html>

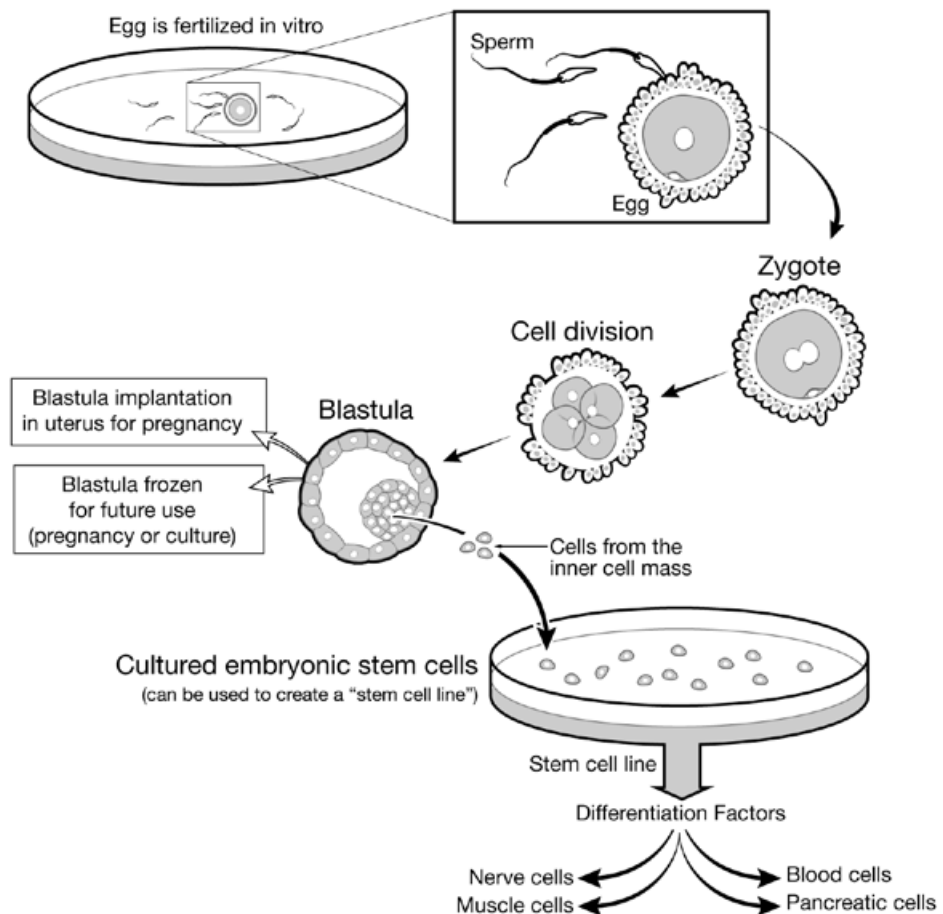
## What is *In vitro* Fertilization (IVF)?

*Vitro* is Latin for "glass". *In vitro* means "in glass" referring to a test tube or Petri dish.

*In Vitro* Fertilization is a technique that has been used for nearly thirty years for fertility purposes. A woman is given fertility medications designed to trigger the release several mature eggs from the ovaries which are collected and fertilized with sperm "*in vitro*" or in a lab, outside of her body. The fertilized eggs, or embryos, are then grown to the blastula stage. Some are placed into her uterus and if successful, will result in a healthy pregnancy. The remaining embryos are frozen for later use if she chooses to attempt another pregnancy. Embryos for which she no longer has use will remain frozen. There are currently over 400,000 embryos stored in the U.S. by IVF clinics, the majority of which will never be used for reproduction.

To be used for stem cell research, the frozen embryos are thawed and cells from the pluripotent inner cell mass is removed and grown in a Petri dish in a research laboratory. Under the right conditions, these embryonic stem cells can self-renew (make more of themselves by dividing) indefinitely. By differentiating the embryonic cell lines into various cell and tissue types, researchers can generate new tissue to repair or replace damaged tissue, or investigate diseases such as diabetes, Parkinson's, Alzheimer's and others. Embryos created for IVF are the source of all embryonic stem cell lines currently used in federally funded research in the U.S. As of July 2009, federal funds cannot be used for research in which an embryo is created only to be destroyed for research purposes.

Pluripotent cells from the inner cell mass of the blastula are referred to as "embryonic" stem cells.



## Stem Cell Research May Benefit Couples Using IVF

The origins of embryonic stem cells used in research are the IVF clinics that derive them for reproductive uses. Many couples chose to donate their unused embryos for research after a team of researchers in Wisconsin first isolated stem cells from embryos in 1998. Now this research is producing information that may ultimately result in more successful IVF pregnancies using fewer embryos. Fertility specialists are partnering with stem cell scientists in the hope that a clearer understanding of human development in these early stages will improve IVF rates. "If we can find the best way to grow embryos to get stem cells, and understand the best techniques to nurture them, then we can do studies to see if it might make a difference in our standard culture lines for things we are indeed going to place into patients," said Dr. David Smotrich, medical director and founder of La Jolla IVF.

Smotrich has teamed up with Evan Snyder, a biologist at the Burnham Institute in San Diego. The two are working on improving embryo handling methods such as freezing and thawing embryos to decrease damage. IVF methods are much more successful than they were in 1978 when the first *in vitro* baby was born, but many couples still fail to conceive after multiple attempts and it isn't always clear why. "You are dealing with a biological system whose signals we just don't understand, by and large," Snyder said.

Another example of how stem cell research has benefited couples hoping to conceive comes from Susan Fisher at UCSF. Dr. Fisher has been growing embryonic stem cells on a bed of human placental cells instead of the usual feeder mouse cell layer to reduce contamination by non-human proteins. This approach is now being experimented with at IVF clinics for use with the more difficult infertility cases. IVF clinics usually use a nutrient media that works well enough to keep embryos healthy enough to implant, but in some cases, embryos need the extra rich nutrients placental cells provide.

Many people disapprove of embryonic stem cell research because it destroys the human embryo. This research is showing that some of the first results of stem cell studies may improve IVF, reducing the number of embryos necessary to produce a successful pregnancy and ultimately increasing the number of babies born.

Adapted from:

Stem cell research may be boon to fertility clinics by Carl T. Hall *San Francisco Chronicle*, February 21, 2005

Reduce multiple IVF births, experts urge by Patricia Reaney, *Reuters.com* Jun 18, 2006



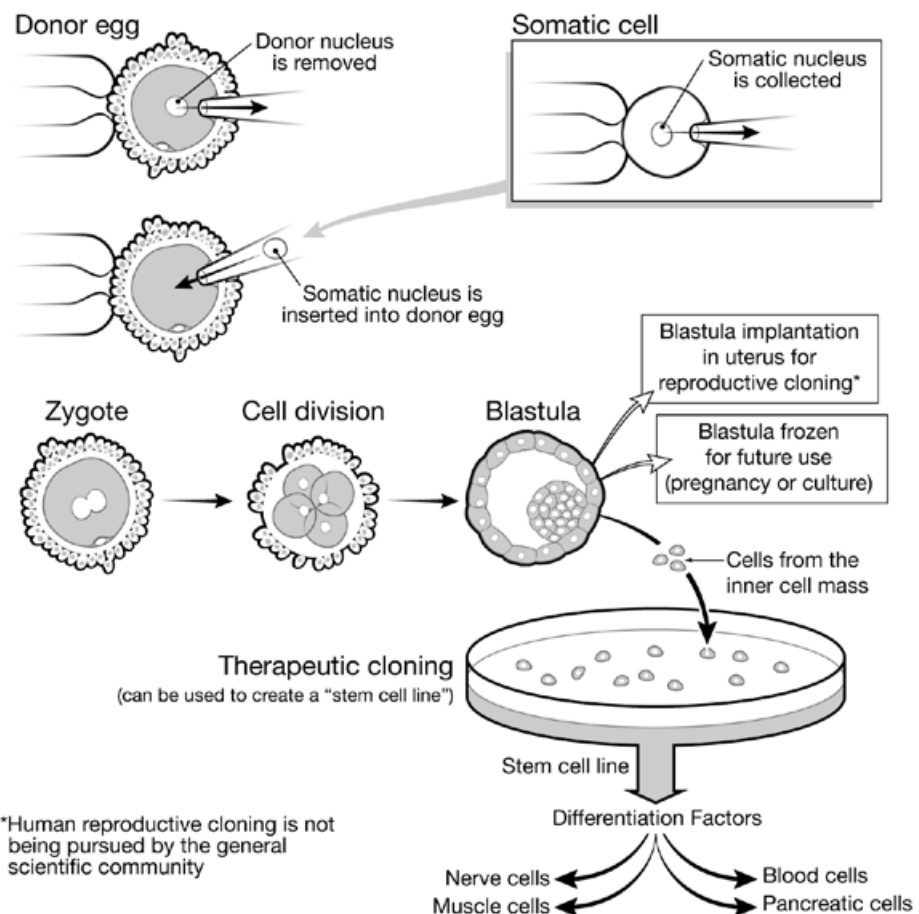
## Therapeutic Cloning

“Therapeutic Cloning” is a technique used to create stem cells that are a genetic match to a donor. It has been used to clone non-human animals, the most famous being the sheep Dolly. Therapeutic cloning has been negatively associated with the idea of human reproductive cloning but the majority of scientists do not support the reproductive uses of this procedure in humans.

A somatic cell is any cell in the body not involved in gamete production or the gametes. Skin cells, bone cells, liver cells or cheek cells are all examples of somatic cells. In therapeutic cloning, the nucleus of a donated egg cell is removed and the nucleus from a patient’s somatic cell is inserted. After receiving electric and chemical signals to stimulate it, the egg then behaves as if it has been fertilized and it begins to mitotically divide through the stages of zygote, morula, and blastula. In the center of the blastocyst, is an inner mass of cells. This inner mass is removed and grown in the lab in a Petri dish. These pluripotent embryonic stem cells (ESC) are genetically identical to the original somatic cell from the patient. This means that ESCs derived from the therapeutic cloning method may be used in treatments *without the risk of rejection by the patient’s immune response*.

Another potential use for these ESCs is in the research of specific diseases. ESCs made from a patient with a specific disease could be used to follow the disease mechanisms in the search for possible treatments. Therapeutic cloning is also known as *somatic cell nuclear transfer (SCNT)* or *patient specific stem cells* because of these uses. As of July 2009, no human stem cell lines have been produced using this technique, and the federal government will not fund research that uses therapeutic cloning to derive stem cell lines.

*Pluripotent cells from the inner cell mass of the blastula are referred to as “embryonic” stem cells.*



## **Harvard Recruiting Egg Donors For Stem Cell Research**

Harvard Stem Cell Institute (HSCI) became the second academic institute in the country to begin work on human therapeutic cloning when it announced Tuesday that HSCI will recruit women as egg donors. Therapeutic cloning, also referred to as somatic cell nuclear transfer, can be used to create stem cell lines which are genetically identical to patients. Experts believe such stem cell lines could be very valuable tools for studying diseases such as Alzheimer's and Parkinson's. However, the process of creating then destroying an embryo is controversial and opposed by some. South Korean scientists claimed to have created almost a dozen stem cell lines using therapeutic cloning but this year admitted that their results were made up.

The procedure for recruiting egg donors required significant thought and consideration. Because women will not be paid, aside for expenses associated with the donation process (travel, hotel, etc.), they are considered "compassionate" donors. The expenses that are paid, like all funding for the projects, must come from private donations because of the federal ban of such research. In order to harvest eggs, women are given hormones which stimulate them to release more eggs. In South Korea, this caused considerable health problems for donors. As a result, Harvard researchers will limit the amount of hormonal stimulation and the number of eggs harvested from each woman. Finally, women who agree to donate will sign a detailed informed consent form.

One project that has been given the go-ahead requires scientists to remove the nuclei of skin cells taken from diabetes patients. These would then be inserted into donated eggs to create disease-specific stem cell lines. "We're excited using SCNT [Somatic Cell Nuclear Transfer, or "Therapeutic Cloning"] as a way forward where in essence we can move the study of disease from patients to Petri dish," said Douglas Melton, co-director of the Harvard Stem Cell Institute. Melton's son has been diagnosed with juvenile diabetes.

Adapted from:

Harvard Embarks on Research Cloning by Constance Holden *ScienceNOW* Daily News 6 June 2006

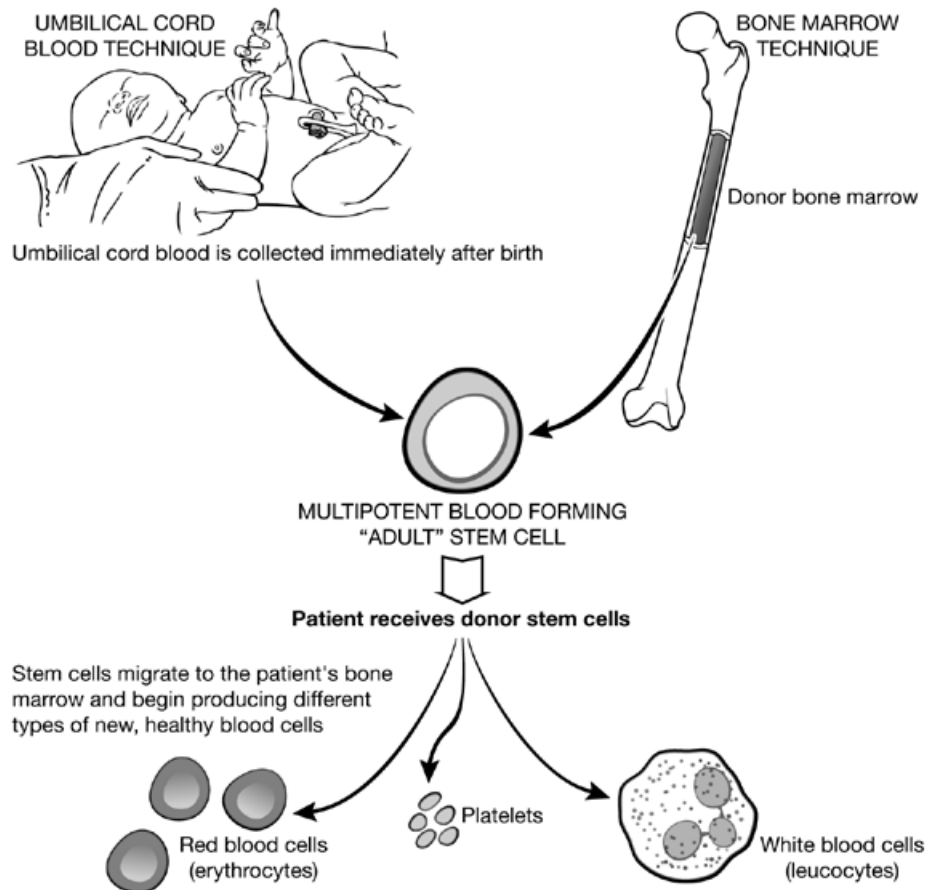
Why Harvard is recruiting stem cell donors by Alice Park *Time* June 6, 2006



## How are Umbilical Cord Blood and Bone Marrow Used?

There are three main types of blood cells; erythrocytes (red blood cells), leucocytes (white blood cells) and platelets. Each cell type has specific functions related to oxygen exchange, the immune system and clotting and requires constant replenishment as cells age or are destroyed as part of the immune response. New blood cells are produced in the bone marrow by multipotent blood forming adult stem cells. These adult stem cells can also be found in umbilical cord blood and in small amounts in the blood stream. Both umbilical cord blood and bone marrow transplant procedures are used to treat blood cancers such as leukemia and genetic blood disorders such as sickle cell anemia. First, a patient's diseased cells are usually destroyed and removed through chemotherapy and radiation. Healthy cells from either a genetically matched bone marrow donor or an umbilical cord blood donor are then given through the central venous catheter into the bloodstream. The stem cells make their way to the patient's own bone marrow and if the procedure is successful, begin making healthy new blood cells.

A bone marrow transplant is the best-known and oldest stem cell therapy, with the first successful transplant (between identical twins) taking place in 1956. Cord blood transplantation is still relatively new and the umbilical cord has typically been thrown away after birth. However, doctors now commonly ask parents if they would like to preserve it. Rejection is less common with umbilical cord blood transplants, because the cells have not developed features that the patient's immune system might recognize as foreign.



*The multipotent cells found in umbilical cord blood and bone marrow are already committed to only making different types of blood cells. They are considered "adult" stem cells.*

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Source: Genetic Science Learning Center

## **Saving Blood Saves Lives**

Susan Orr was six months pregnant when her 2 year old son Brandyn was diagnosed with leukemia. She and her then-husband, Bob, had never heard of cord blood when an oncologist suggested they save the umbilical cord blood from the birth of their second son, Kaelyn. Willing to do anything that might help Brandyn, they agreed without even thinking about the cost.

The blood remaining in the umbilical cord and placenta after a woman gives birth is rich in adult stem cells that have the ability to develop into many types of blood cells. Beginning in 1988, cord-blood transplants have been used to treat blood disorders and regenerate immune cells following chemotherapy. The Orrs signed on with a private cord-blood bank and paid a \$1,000 fee to have the blood collected and stored. They did the same when two more sons, Devyn and Jadyn were born in the next few years.

Meanwhile, Brandyn continued treatment, and after three difficult years, his cancer went into remission. It seemed the cord blood wasn't needed after all.

Brandyn's parents didn't think much of his complaints about feeling tired and sore during a family vacation to Florida. But when he fell down on the playground and couldn't get up, they rushed him to the hospital. Their worst fear was confirmed – the leukemia had returned. The only hope this time was a transplant, and there was not time to wait for a donor. They asked to have the banked cord-blood tested. Kaelyn's blood was not a match, but to everyone's relief, Devyn's was.

Before the transplant could be performed, 6-year-old Brandyn had to endure weeks of radiation and chemotherapy in order to destroy the cancerous cells. After the treatment, a syringe containing his brother's cord blood cells was pushed into an intravenous tube. The transplant took five minutes. Brandyn was required to stay in the hospital for five weeks after the procedure, then return for weekly check ups and treatments.

Today, Brandyn has been cancer free for nearly 6 years. He plans to be a computer programmer, or a repairman, or even an artist. Since his parent's divorce, he's the man of the house and helps out by doing everything from installing a new ceiling fan to fixing the VCR. He's glad his past with leukemia is over and now spends his time dreaming about the future.

Adapted from:

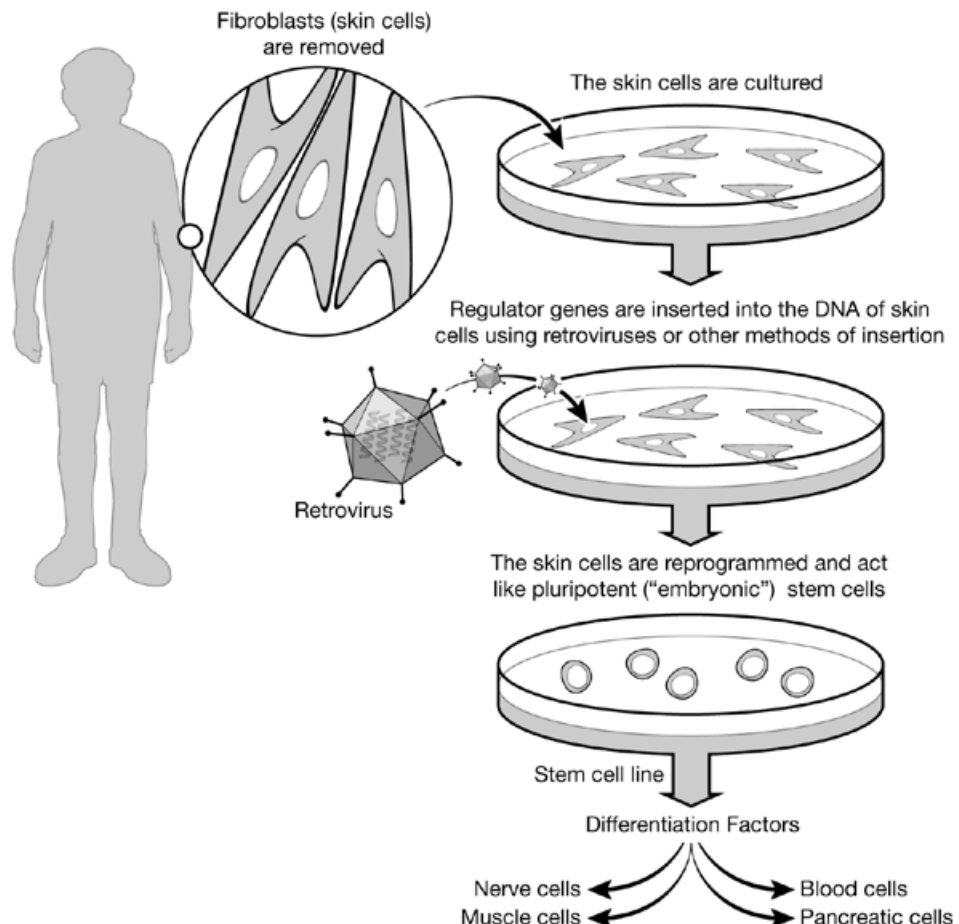
**"Umbilical cord blood provides a lifesaving solution"** Christina Vanoverbeke, East Valley Tribune, June 25, 2006

## How do Differentiated Adult Cells become induced Pluripotent Stem Cells (iPS)?

*Although each team of researchers inserted four master regulator genes into skin cells, the teams used different combinations of genes; only two of the four genes were the same in both groups.*

Scientists have shown that differentiated adult cells can be reprogrammed to behave like undifferentiated human embryonic stem cells, producing *induced pluripotent stem cells*, or iPS cells. Pluripotent cells are able to develop into any of the hundreds of cell types in the human body, such as muscle, nerves, cartilage, blood or bone. To make iPS cells, four or more master regulator genes are inserted into the DNA of an adult cell such as a fibroblast skin cell. These regulator genes act like a reset button, returning the cell to a 'blank' state. This reprogramming allows the former skin cell to behave like an embryonic (pluripotent) stem cell, and give rise to different types of tissue. Though promising, this new technique is not yet ready to be used to treat diseases in humans. Researchers are working to find the best way to insert the master regulator genes into the DNA of the adult cell. Retroviruses have been used but are problematic because the inserted genes are spliced into the DNA at random places and can cause tumors. Recent work using transposons ('jumping genes') to insert the master regulators genes shows potential, but requires further study.

Using skin cells or other adult tissue to produce iPS cells is less ethically objectionable to some people since no embryos are destroyed in the process. Most scientists believe that it will be necessary to continue studying embryonic stem cells through traditional means, as they serve as the "gold standard" and as a basis for evaluation and comparison. Earlier studies on embryonic stem cells also identified the genes chosen to reprogram the skin cells.



**Skin Cells fix Sickle Cell Anemia in Mice**

Using a new technique to turn skin cells into stem cells, scientists have corrected sickle cell anemia in mice. The advance provides “proof of principle” that stem cells made without embryos can treat disease, at least in lab animals, says Rudolf Jaenisch, the biologist who led the work at the Whitehead Institute for Biomedical Research in Cambridge, Mass. Jaenisch and his team caution, however, that the technique is not yet suitable for use in humans because it may cause tumors.

Still, Jaenisch says that embryofree stem cells now “have the same potential for therapy as embryonic stem cells, without the ethical and practical issues.” Embryonic stem cells are difficult to obtain, and some people oppose such research because it destroys discarded embryos.

The Whitehead researchers obtained mice engineered to carry a defective version of the human hemoglobin gene. That flaw distorts red blood cells into the characteristic sickle shape. To fix the flaw, the researchers induced skin cells plucked from the tails of the mice to become iPS [induced pluripotent stem] cells, and corrected the genetic defect.

Next, the Whitehead team prodded the corrected cells into becoming blood stem cells, which can produce red and white blood cells. The team used a recipe originally developed for embryonic stem cells and found that it also made iPS cells grow into blood stem cells.

“We wanted to compare the embryonic stem cells versus the iPS cells,” says Whitehead researcher Jacob Hanna. “They behaved similarly.”

Finally, the researchers performed a procedure akin to a bone marrow transplant. They transfused a million of the corrected blood stem cells into each of three mice whose bone marrow—which harbored the mice’s original defective blood stem cells—had been obliterated by radiation. The corrected blood stem cells soon began producing healthy red blood cells. Because the same animal was both donor and recipient, the infused cells were not rejected, as commonly occurs in human bone marrow transplants. After this treatment, the formerly lethargic mice made swift recoveries. “The improvement was profound,” says Hanna. “There was a clear sign of reduction of destruction of red blood cells, which is actually the main problem in sickle cell anemia.”

Mark Walters, a bone marrow transplant specialist at Children’s Hospital and Research Center in Oakland, Calif., says the procedure surmounts the biggest obstacle in performing such transplants in children—finding a genetically matched donor. Worldwide, only 300 to 400 children with sickle cell anemia have received bone marrow transplants because matched siblings are rare. “But the results are outstanding, with a cure rate between 85 and 90 percent,” Walters says.

Before the procedure can advance to human trials, though, researchers must find a more benign way to make iPS cells, because the viruses currently used can trigger cancer. “We’d have to have some information that these are not preleukemic or premalignant cells, that they’re safe in the long term,” says Walters.

Source: Brian Vastag, From *Science News*, Vol. 172, No. 23, Dec. 8, 2007, p. 355.







**Overview: How do we get stem cells?**

Technique	How is it done?	Origin of stem cell (adult or embryonic?)	Points of controversy
<p><b>“Therapeutic Cloning”</b></p>			
<p><b><i>In vitro</i> fertilization (IVF)</b></p>			
<p><b>Umbilical Cord Blood/ Bone Marrow Transplantation</b></p>			
<p><b>Induced Pluripotent Stem Cells (iPS)</b></p>			

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**Diagram the technique in each space below.**

<p><i>“Therapeutic Cloning”</i></p>	<p><i>In vitro Fertilization (IVF)</i></p>
<p><i>Umbilical Cord Blood/Bone Marrow Transplant</i></p>	<p><i>Induced Pluripotent Stem Cells (iPS)</i></p>

### Overview: How do we get stem cells?

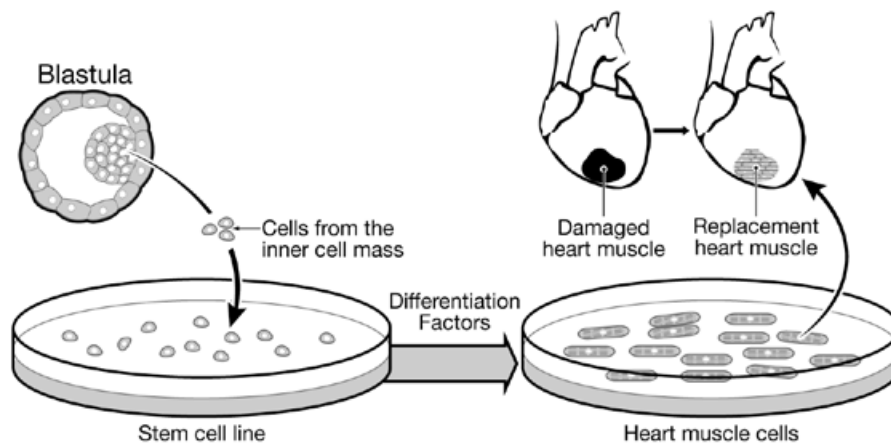
Technique	How is it done?	Origin of stem cell (adult or embryonic?)	Points of controversy
<b>“Therapeutic Cloning”</b>	The nucleus of a donated egg cell is removed and replaced with the nucleus from a patient’s somatic cell, such as a skin cell or liver cell. The egg, now having a full set of chromosomes, is stimulated to divide. At the blastula stage, the inner cell mass is cultured and coaxed into eventually becoming the type of tissue the patient needs, such as insulin-producing cells to treat diabetics.	Embryonic	<p>Could this lead to reproductive cloning?</p> <p>Should women be paid for donating eggs?</p> <p>Is it better to use cells from a blastula that was never intended to become a baby?</p>
<b><i>In vitro</i> fertilization (IVF)</b>	Several eggs are fertilized with sperm <i>in vitro</i> . At the blastula stage, some of the fertilized eggs are implanted into the uterus. If successful, pregnancy results. The remaining embryos are frozen for future use by the couple, if needed. The inner cell mass from the “leftover” blastulas can be cultured and coaxed into eventually becoming the type of tissue the patient needs, such as insulin-producing cells to treat diabetics.	Embryonic	<p>The blastula was originally created by an infertile couple wanting to have children—does the original purpose for creating the blastula matter?</p> <p>Should “leftover” embryos from IVF be used in this way? How else might they be used?</p> <p>Should donor have to give consent to donate their blastulas?</p>
<b>Umbilical Cord Blood/ Bone Marrow Transplantation</b>	Patients with blood cancers (such as leukemia) have their diseased blood cells destroyed and replaced with healthy, genetically-matched cord blood or bone marrow donor cells. The multipotent stem cells from the cord blood or the bone marrow can develop into any type of blood cell.	Adult	<p>Should a couple with a child with leukemia try to have another baby, in hopes of being able to use the cord blood to help the older child?</p> <p>Who should pay for saved cord blood?</p> <p>Should bone marrow donors be paid?</p>
<b>Induced Pluripotent Stem Cells (iPS)</b>	With the introduction of 4 ‘master regulator genes’, an adult fibroblast skin cell can be coaxed into reverting to a pluripotent state, thus having the ability to become any type of cell in the body.	Adult	<p>Does this mean blastulas are not needed as sources of embryonic (pluripotent) stem cells?</p> <p>Does this really sidestep the controversy of using embryonic stem cells from other sources?</p>



## How are Embryonic Stem Cells used?

**Regenerative medicine.** Regenerative medicine uses stem cells to regenerate, or re-grow, new cells, tissues or organs in order to repair or replace diseased tissues and organs. Human embryonic stem cells can be directed to develop into any of the hundreds of specific cell types in the body. For a person with Type I Diabetes, for example, this could mean re-growing the insulin-producing cells that the body has lost over time. For a person living with heart disease or who has had a heart-attack, this could mean growing a patch of heart muscle that would replace damaged tissue. Future therapies will likely include using stem cells to grow an entire organ for transplantation that would be genetically matched with a patient. This type of medicine offers the possibility of growing cells and tissues to treat diseases such as Parkinson's and Alzheimer's disease, spinal cord injury, stroke, burns, and arthritis. See figure 1.

Figure 1 – Using embryonic stem cells for regenerative medicine



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**Early Human Development.** This research uses cells from the inner cell mass of the blastocyst (blastula) embryo to grow human embryonic stem cells in cultures. Because the cells can mimic normal development even though they are outside of the body, scientists are better able to understand the complex events that unfold as undifferentiated stem cells become differentiated cells and tissues. What genes are central to this process? What signals turn those genes on and off? When this process goes awry and cells divide abnormally or do not differentiate correctly, loss of pregnancy and serious medical conditions such as cancer and birth defects can result. Many cancers, for example, result from uncontrolled cell division. Using human embryonic stem cell cultures to better understand the factors that control early cell division and differentiation will eventually allow researchers to devise better treatments and therapies.

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### Sources:

Stem Cell Basics, National Institutes of Health. <http://stemcells.nih.gov/staticresources/info/basics/SCprimer2009.pdf>

Wadman, Meredith, "New Tools for Drug Screening" Science Magazine, December 20, 2007.

<http://www.nature.com/stemcells/2007/0712/071220/full/stemcells.2007.130.html>

Colen, B.D., "Daley and colleagues create 20 disease-specific stem cell lines" Harvard Science, August 7, 2008. <http://www.harvardscience.harvard.edu/foundations/articles/daley-and-colleagues-create-20-disease-specific-stem-cell-lines>

**Drug Development and Testing.** Getting a new drug into the marketplace can cost billions of dollars and require decades of research. In early rounds of drug development, chemical compounds are tested on various cell types in the laboratory. In later rounds of safety testing, before any tests with human subjects, drugs are tested on more specific tissues types that may be affected by the drug. The liver, for example, can be harmed by the drugs it breaks down; liver tissue is therefore an important component for many drug safety studies. Currently, scientists rely on animal tissues, animal toxicity studies and scarce, often diseased, human liver tissue samples for safety testing. Human embryonic stem cells that have been coaxed to make liver tissue would offer tremendous advantage to the drug development and testing process. Likewise, stem cells that have differentiated into heart, nerve or other tissue types could be used in the same way. This use of stem cells could also eventually reduce the need for animals in research.

**Understanding Disease.** Creating disease-specific stem cell lines allows researchers to watch the development of a disease in a Petri dish, outside of the human body. Cell lines have been made from embryonic stem cells carrying the mutation that causes cystic fibrosis, for example. Using the Induced Pluripotent Stem Cell (iPS) technique, researchers have also created cell lines that carry the version of the genes (or genetic components) that cause Parkinson’s disease, Type I Diabetes, Down syndrome, Huntington’s disease, two forms of Muscular Dystrophy, and others. Although in the early stages of research, these cell lines will likely be valuable tools for understanding the development of disease. They will also aid in creating treatments, therapies, and new drugs that would attack the root cause of the disease. See Figure 2

Figure 2 – Using embryonic stem cells to better understand disease

