Therapeutic Cloning of a Human Embryo

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Abstract

The definition of cloning varies with its purpose. This report clarifies the distinctions between the different types of cloning and explains the medical incentive behind therapeutic cloning. The report also describes the process of therapeutic cloning of human embryos for embryonic stem cells.

Figure 1. "Dolly." BBC News

Defining Cloning

"The term *cloning* is used by scientists to describe many different processes that involve making duplicates of biological material. In most cases, isolated genes or cells are duplicated for scientific study, and no new animal results. The experiment that led to the cloning of Dolly the sheep in 1997 was different: It used a cloning technique called *somatic cell nuclear transfer* and resulted in an animal that was a genetic twin — although delayed in time — of an adult sheep. This technique can also be used to produce an embryo from which cells called *embryonic stem* (ES) *cells* could be extracted to use in research into potential therapies for a wide variety of diseases.

Thus, in the past five years, much of the scientific and ethical debate about somatic cell nuclear transfer has focused on its two potential applications: 1) for reproductive purposes, i.e., to produce a child, or 2) for producing a source of ES cells for research."[1]

Cloning: *making duplicate copies of genetic material.*

Somatic cell: *any cell in the body other than the gametes (egg and sperm) cells.*

Embryonic Stem Cells (ES): *unique cells found in embryos that have the potential to grow into various types of cells or tissues.*

Reproductive Cloning

Cloning a human embryo for the purposes of reproduction is illegal in most countries, and to date has not been accomplished. However, because *somatic cell nuclear transfer* has made cloning an organism possible—as in the case of Dolly, the sheep—this type of cloning has become a controversial topic.

The reproductive cloning procedure would be similar to that of in vitro fertilization, where a laboratory fertilizes eggs, grows embryos to a viable stage, and implants them in a human uterus. 40 to 60 percent of these embryos end up as babies.[2] These babies are a product of both parents' genetic material.

Somatic Cell Nuclear Transfer: *A procedure in which a cell's nucleus is removed and placed into an egg with its own nucleus removed so the genetic information from the donor nucleus controls the resulting cell.*[3]

However, reproductive cloning is a form of asexual reproduction, in which the egg is not fertilized, but receives half its genetic material via nuclear transfer, and is stimulated through chemical and electrical processes to perform cell division and develop into an embryo.

A mature egg contains only half the genetic material necessary to reproduce. For reproduction to occur, the egg must be furnished with the second half of the genetic material, either through fertilization or nuclear transfer.

The resulting organism would be a genetic copy of one parent, as opposed to an organism created through sexual reproduction, in which the result is a product of the genetic combination of two parents.

Therapeutic Cloning

Both reproductive cloning and therapeutic cloning of human embryos involve the same laboratory procedures. However, therapeutic cloning is, by definition, performed for the purposes of extracting embryonic stem cells (ES) for medical purposes. In therapeutic cloning, the embryo is never implanted in a uterus or grown into a human being.

The Incentive for Therapeutic Cloning

The goal of therapeutic cloning is the extraction of embryonic stem cells. "Stem cells have two important characteristics that distinguish them from other types of cells. First, they are unspecialized cells that renew themselves for long periods through cell division. The second is that under certain physiologic or experimental conditions, they can be induced to become cells with special functions such as the beating cells of the heart muscle or the insulin-producing cells of the pancreas.

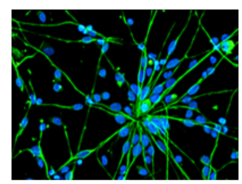


Figure 2. Human Embryonic Stem Cells, "Stem Cells and Cloning," The Royal Society, London, England

Serving as a sort of repair system for the body, they can theoretically divide without limit to replenish other cells as long as the person or animal is still alive. When a stem cell divides, each new cell has the potential to either remain a stem cell or become another type of cell with a more specialized function, such as a muscle cell, a red blood cell, or a brain cell."[4]

"It is what patients with diseases like Parkinson's and diabetes have been waiting for, the start of so-called therapeutic cloning. The idea is to clone a patient's cells to make embryonic stem cells that are an exact genetic match of the patient. Then those cells, patients hope, could be turned into replacement tissue to treat or cure their disease without provoking rejection from the body's immune system."[5]

[1] Hanna, Kathi E., M.S., Ph.D. "Ethical Boundaries Workshop: Cloning/Embryonic Stem Cells." National Human Genome Research Institute online. March 2004. <http://www.genome.gov/10004765>.

[2] Kolata, Gina. "Cloning Creates Human Embryos." New York Times online. February 12, 2004. <http://www.nytimes.com>.

[3] The Department of Energy. Human Genome Project Information online. March 2004. >http://www.ornl.gov/sci/techresources/Human_Genome/glossary/glossary_n.shtml>.

[4] National Institutes of Health online. "Stem Cell Information." <http://stemcells.nih.gov/stemcell/whatAreStemCells.asp>.

[5] Kolata, Gina. "Cloning Creates Human Embryos."

The Process of Cloning: Somatic Cell Nuclear Transfer

An embryo can be created in three ways: sexual reproduction, cloning, and *parthenogenesis*. Cloning of a human embryo was achieved by scientists in late 2001, but only recently have scientists successfully extracted embryonic stem cells from a cloned human embryo.

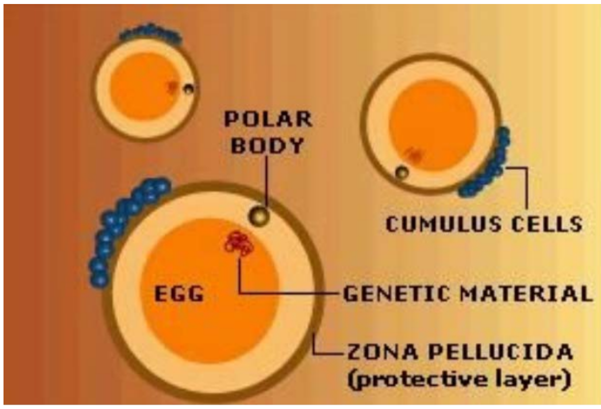
Parthenogenesis: *the process in which an unfertilized egg develops into an organism.*

Therapeutic Cloning: How It's Done[6]

Somatic cell nuclear transfer begins with an unfertilized egg, which is provided by a donor. An egg is coaxed to mature in a culture dish. Each egg has a remnant egg cell inside of it called the polar body and *cumulus cells* from the ovary clinging to the outside of it.

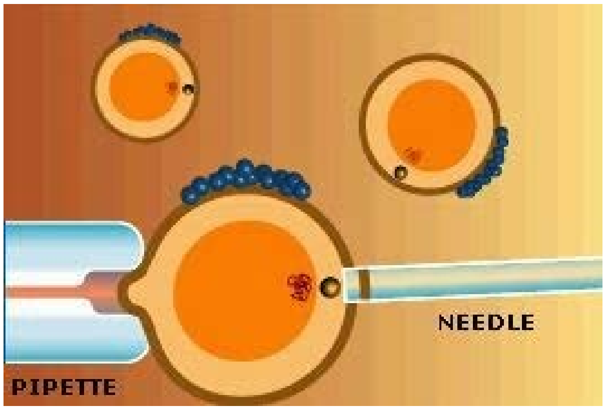
Cumulus cells: *tiny cells from the ovary that are small enough to be inserted inside the nucleus of an egg cell.*

"The normal function of cumulus cells is to nourish eggs in the ovaries, but like other body cells, they also contain a person's complete genetic information."[7]



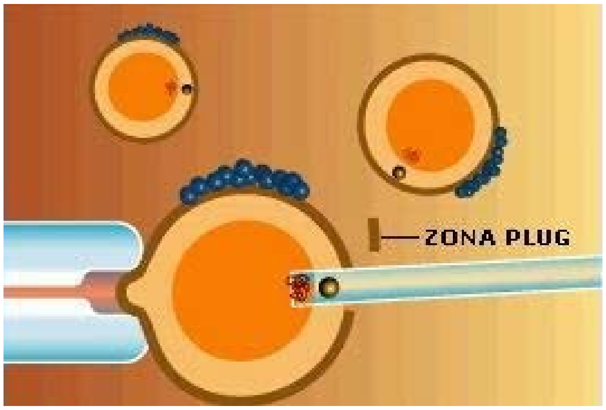
While an egg is held still with a pipette, a needle is used to drill through the zona pellucida, removing a plug.

Zona pellucida: *protective layer surrounding the egg cell.*

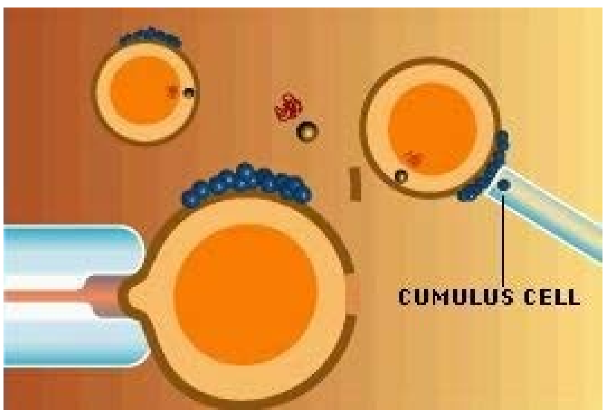


After ejecting the zona plug, the needle is reinserted back in the egg to withdraw and discard the polar body and the egg's genetic material.

The egg's nucleus contains half the necessary genetic material, so it must be supplemented with the second half of the genetic material or removed to make room for a full copy of the donor's DNA.

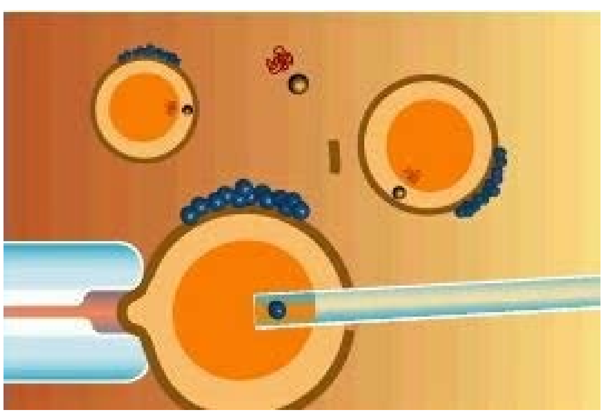


A cumulus cell from another egg is taken up into the needle.



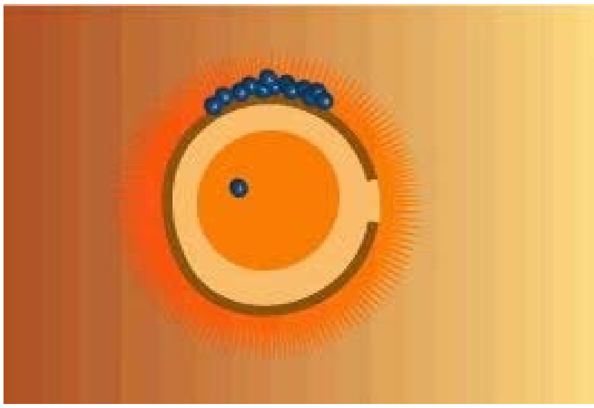
The cumulus cell is injected deep into the egg that has been stripped of its genetic material.

Cumulus cells have been found to work better than larger cells or their nuclei.



The injected egg is exposed to a mixture of chemicals and growth factors designed to activate it to divide.

This process is called "activation" It is designed to "trick" the egg into dividing as if it had been fertilized normally.[8]



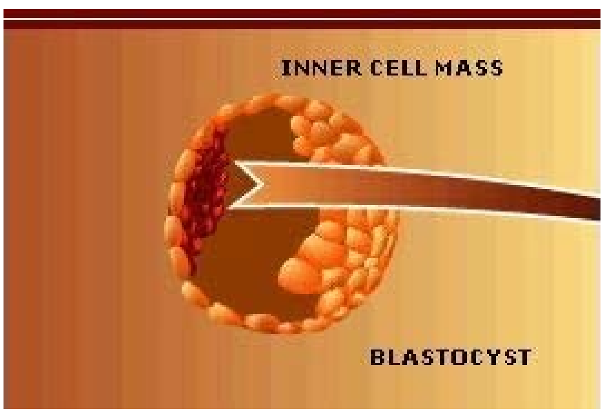
After roughly 24 hours, the activated egg begins dividing. The cells contain genetic material only from the injected cumulus cell.

After three days, the embryo typically has four to eight cells, and after five, sixteen cells. At this point, the embryo is called a morula, and stem cells can be derived, according to animal studies.

If the embryo progresses to a blastocyst, stem cells can be more readily obtained.[9]

By the fourth or fifth day, a hollow ball of roughly 100 cells has formed. It holds a clump of cells called the inner cell mass that contains stem cells.

***Blastocyst:** a preimplantation embryo of about 150 cells. The blastocyst consists of a sphere made up of an outer layer of cells, a fluid-filled cavity, and a cluster of cells on the interior (inner cell mass).[10]*



The blastocyst is broken open, and the inner cell mass is grown in a culture dish to yield stem cells.

On February 12, 2004, Korean scientists announced that they have created human embryos through cloning and extracted embryonic stem cells.[11]

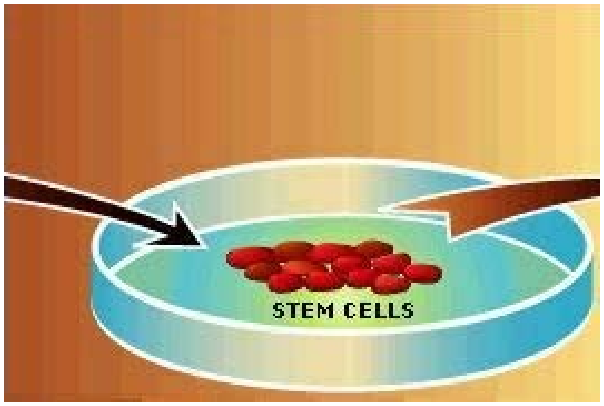
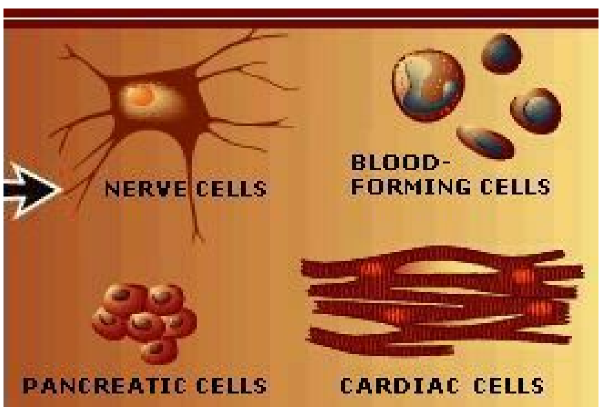


Figure 3

The stem cells, in turn, can be coaxed to grow into a variety of cells that might one day be injected into patients.



"As long as the embryonic stem cells in culture are grown under certain conditions, they can remain undifferentiated (unspecialized). But if cells are allowed to clump together to form embryoid bodies, they begin to differentiate spontaneously. They can form muscle cells, nerve cells, and many other cell types. Although spontaneous differentiation is a good indication that a culture of embryonic stem cells is healthy, it is not an efficient way to produce cultures of specific cell types.

So, to generate cultures of specific types of differentiated cells — heart muscle cells, blood cells, or nerve cells, for example — scientists try to control the differentiation of embryonic stem cells. They change the chemical composition of the culture medium, alter the surface of the culture dish, or modify the cells by inserting specific genes. Through years of experimentation scientists have established some basic protocols or "recipes" for the directed differentiation of embryonic stem cells into some specific cell types

If scientists can reliably direct the differentiation of embryonic stem cells into specific cell types, they may be able to use the resulting, differentiated cells to treat certain diseases at some point in the future. Diseases that might be treated by transplanting cells generated from human embryonic stem cells include Parkinson's disease, diabetes, traumatic spinal cord injury, Purkinje cell degeneration, Duchenne's muscular dystrophy, heart disease, and vision and hearing loss."[12]

Summary

The term "cloning" often engenders confusion and controversy. This report has explained how "cloning" can be as simple as making copies of one cell, or as complicated as creating a human embryo. The therapeutic cloning process, as described above, offers the potential for great achievements in the treatment of medical conditions and diseases. Reproductive cloning, although accomplished with animals—such as Dolly, the sheep—is still unpredictable and unreliable. As the cloning process and its results are refined, closer scrutiny will become necessary to ensure that scientists everywhere are adhering to generally agreed upon ethical standards.

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[8] Rohm, Wendy Goldman. “Seven Days of Creation.”

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[10] Rohm, Wendy Goldman. “Seven Days of Creation.”

[11] Kolata, Gina. “Cloning Creates Human Embryos.”

[12] National Institutes of Health. “Stem Cell Information.”