You've Come A Long Way, Dolly!

Abstract

During this activity, students construct a timeline depicting the history of cloning. They present, and then place in order, key events in cloning using the birth of Dolly the sheep as a reference point. Since students are not given the date of each event, they need to consider the relative progression of cloning techniques and the increasing complexity of cloned organisms. Once the timeline is complete and the dates are confirmed, students are asked to consider and discuss the scientific and social/political significance of the events.

Learning Objectives

- Students will understand that cloning is not a new science
- Students will understand that scientific advances are a process with one "discovery" enabling the next
- Students will think critically about the social or political impact of scientific progress
- Students will learn about the advance of cloning technologies and the current state of cloning science

Estimated time

- Class Time 70 minutes (may be extended by class discussion or assessment)
- Prep time 30 minutes

Materials

- Classroom set of Mock Newspaper Articles (cut each page in half along dotted line)
- Student handouts
- Tape
- Stickers in two colors for each student

Background

Current media attention seems to indicate that cloning is a recent scientific phenomenon. However, less-publicized studies in cloning have been carried out since 1885.

The steps leading to current cloning methods began with cloning very simple organisms by artificial embryo twinning (splitting a very early embryo in half in a Petri dish). Some of the first cloned organisms came from embryos that were split in two using a fine piece of hair as a noose. Further experiments using this technique established the fact that the nucleus directs cell growth and division.

The next step was cloning by nuclear transfer. This is the process of taking the nucleus from a donor cell and placing it in an unfertilized, enucleated egg cell. Experiments using this technique began with simple organisms and progressed to more complex mammals. Dolly the sheep was the first organism to be cloned using the nucleus from an adult somatic cell as opposed to an embryonic cell, thus indicating yet another advance in cloning technology.

Cloning technology has also been used to create transgenic organisms by placing selected genes in the nuclei of cultured adult somatic cells and then using those nuclei to create transgenic cloned embryos. When grown to maturity, these organisms can be used to produce harvestable proteins for human use. Scientists are working on using cloning techniques to harvest human stem cells for medical treatment as well.

It is important that students understand the difference between the embryo twinning and somatic cell nuclear transfer cloning techniques. Since the embryo used for embryo twinning was produced by sexual reproduction, none of the resulting clones will be genetically identical to either parent. This is also true for cloning via nuclear transfer using nuclei from embryonic donor cells. However, since the nucleus used for somatic cell nuclear transfer is taken from one of a donor's somatic cells, the clone is genetically identical to this "parent." This ability to use an adult cell eliminates the need for an embryo, enabling clones to be produced by asexual rather than sexual reproduction.

Activity Part One:

1. Begin class by discussing the significance of the birth of Dolly the sheep and the fact that Dolly's birth is just one event in the long history of cloning.

2. Tell the students that:

    - They will be using The Cloning Times newspaper articles to construct a timeline depicting the history of cloning. Each article describes a significant event in the timeline. The name of the scientist who carried out the research or a person important to that event is listed after the headlines. A sentence summarizing the event is printed in bold type at the beginning of each article.
    - As there are no dates on the articles, it is up to them to determine where to place their event along the timeline (a designated space along the wall of the classroom). Initially, they will use the birth of Dolly as a reference point.
    - To construct the timeline, they will present their article headline and summary sentence to the class, and then tape the article on the wall in the order they think it belongs relative to events already posted. They will probably make many adjustments along the way.

3. Hand out articles and student handouts. Ask the students to read the Activity Instructions and begin.

4. Next, ask the student/group whose headline reads: Hello Dolly! to read their headline and summary sentence (in boldface type) aloud to the class. Have that student tape their article in the middle of the space you have designated for timeline construction. This student must go first as their event is the reference point.

5. Call on students at random (or ask for volunteers) to read the headline and summary sentence (in boldface type) of their newspaper article aloud. After each presentation, have the student place the article along the timeline in the area they think it belongs, and ask them to explain why they are placing their event in that particular place. Students who are unsure of where to place their article may ask for input from the rest of the class.

6. When student presenters read the following three events, stop, and ask the class to write that summary sentence in the proper space on the Cloning Times Record. You will need to tell them the year of the event.

- Frogs cloned by nuclear transfer from a tadpole embryo (1952)
- Female mouse cloned by somatic cell nuclear transfer (1998)
- Human cloning might also be used to create stem cells for new medical treatments (2001)
    - This will help keep the students focused during the activity and provide additional reference points along the way. Use these events to rearrange the posted newspaper events as necessary.

7. When students have placed their newspaper articles in the proper order, the large, light letters in the background will spell out "You've Come A Long Way Dolly". Once all of the events are correctly placed, give students time to copy the headlines and summary sentences down in order on their Cloning Times Record, thus revealing the actual date of each event.

Activity Part Two:

Designate one sticker color to represent scientific significance and the other sticker color to represent political/social significance. Give the students one sticker of each color.

8. Ask students to first place the designated sticker on the timeline event they think is of the most scientific importance. Discuss these choices as a class.

9. Next, ask students to place the other sticker on the event they think has the most social or political importance. Discuss these choices as a class.

Activity Part Three:

10. Use the Questions (Part III) on the Cloning Timeline Activity Discussion and Questions student handout (S-3) in one of the following ways:

- Discuss the questions as a class.
- Ask students to choose a question and write a one-page response using information from the constructed timeline to support their answer.
- Have students chose one question to answer by drawing a mural, comic strip, or flip-book using information from the constructed timeline.
- Assign each question to a small group to discuss and present their answer to the rest of the class.

Adaptations

- This activity can be done as a whole class or within smaller groups.
- Ask students to discuss their articles in small groups and decide on an order before beginning their presentations.
- Have students use a highlighter to highlight key elements (in addition to the headline) in their newspaper article before presenting.
- Ask students in more advanced classes to present an article summary, in addition to the title and summary sentence, to the class

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The Cloning Times

Seeing Double? Sea Urchins Cloned!

Hans Adolf Edward Dreisch

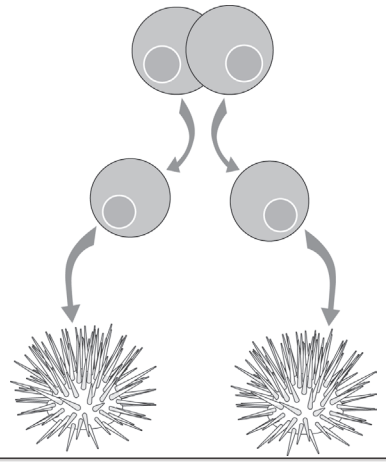
Sea urchins cloned by shaking one embryo into two separate cells.

Can the earliest embryos be split into individual cells, which go on to become separate organisms? Does each embryonic cell contain a complete set of genetic material that can direct the formation of an organism?

The sea urchin is a relatively simple organism that is useful for studying development. Dreisch showed that by merely shaking two-celled sea urchin embryos, it was possible to separate the cells. Once separated, each cell grew into a complete sea urchin.

What did this tell us? Each cell in the embryo has its own complete set of genetic instructions and can grow into a full organism. This was the first ever demonstration of cloning by embryo twinning.

Technique



Two-celled sea urchin embryo

Shake to separate cell

Two identical sea urchins

The Cloning Times

Slimy Salamanders Cloned: What's Next?

Hans Spemann

Salamander cloned by using a noose to separate the cells in an early embryo.

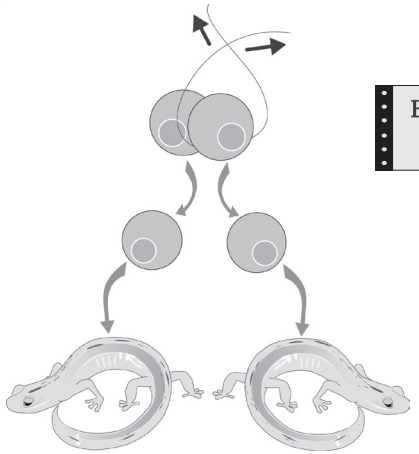
A sea urchin has successfully been cloned using embryo twinning. Now, can this be done in a more complex organism – say, something with a real backbone, like a salamander? Will the twinning approach still work?

Spemann's first challenge was to figure out how to split the two cells of an embryo much stickier than sea urchin cells. Could he tie off the two cells with a length of thread, dental floss, or even a strand of hair?

Yes! Spemann fashioned a tiny noose from a strand of baby hair and tightened it between two cells of a salamander embryo until they separated. Each cell grew into an adult salamander. Spemann also tried to divide more advanced salamander embryos using this method, but he found that cells from these embryos weren't as successful at developing into adult salamanders.

What did this tell us? Embryos from more complex organisms can also be "twinned" to form multiple organisms – but only up to a certain stage in development.

Technique



Baby hair noose separates sticky cells of two-celled embryo

Two identical salamanders

It's True: The Nucleus is in Charge

Hans Spemann

The cell nucleus controls the development of a salamander embryo.

What part of the embryonic salamander cell directs its growth and division? Is it the nucleus?

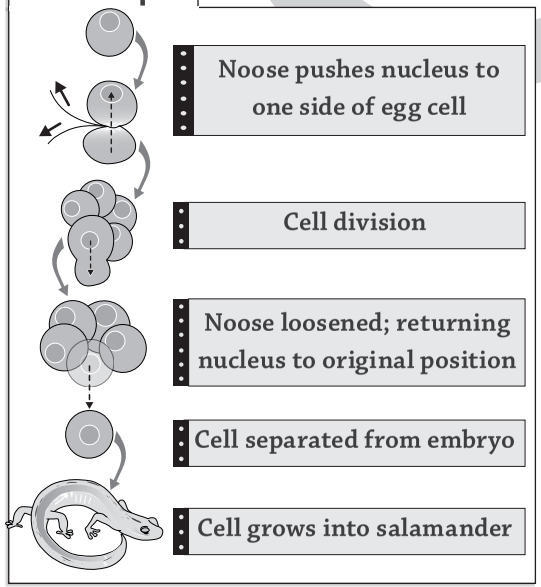
Using a high-tech gizmo – a strand of baby hair tied into a noose – Spemann temporarily squeezed a salamander's fertilized egg to push the nucleus to one side of the cytoplasm. The egg divided into more embryonic cells only on the side of the noose with the nucleus.

After a few cell divisions, Spemann loosened the noose, letting the nucleus slide back to its original position in the cell.

Spemann then used his noose to separate this "new" cell from the rest of the embryo. Since the nucleus was now in the original cytoplasm, this cell resembled a fertilized egg more than an embryonic cell. Nevertheless, this single cell grew into a new salamander embryo.

What did this tell us? The nucleus from an early embryonic cell directs the complete growth of a salamander. Essentially the first instance of nuclear transfer, this experiment showed that an embryonic cell nucleus could substitute for the nucleus in a fertilized egg cell.

Technique



Frogs Galore! Nuclear Transfer Becomes a Reality

Robert Briggs and Thomas King

Frog cloned by nuclear transfer from a tadpole embryo.

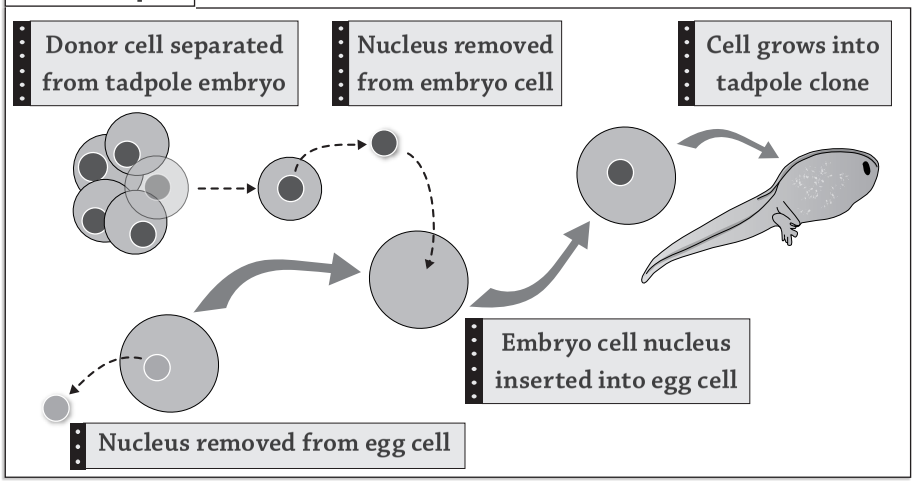
Fascinated by the idea of nuclear transfer, Briggs and King wanted to see whether they could use this technique to clone an even more complex organism: the frog.

Their first challenge was to isolate the nucleus from a donor cell: in this case, a cell from an early tadpole embryo. Next, they had to prepare a recipient frog egg cell by removing its nucleus – a process called enucleation. Last, the donor nucleus and the recipient egg cell were united. Even if all these procedures were successful, would the new "fertilized egg" develop into a tadpole?

The scientists created many normal tadpole clones using nuclei from early embryos. But just like Spemann's salamander experiments, cloning was less successful with donor nuclei from more advanced embryos: the few tadpole clones that did survive grew abnormally.

What did this tell us? Most importantly, this experiment showed that nuclear transfer was a viable cloning technique. It also reinforced two earlier observations. First, the nucleus directs cell growth and, ultimately, an organism's development. Second, embryonic cells early in development are better for cloning than cells at later stages.

Technique



The Cloning Times

For Cloning, Any Nucleus Will Do

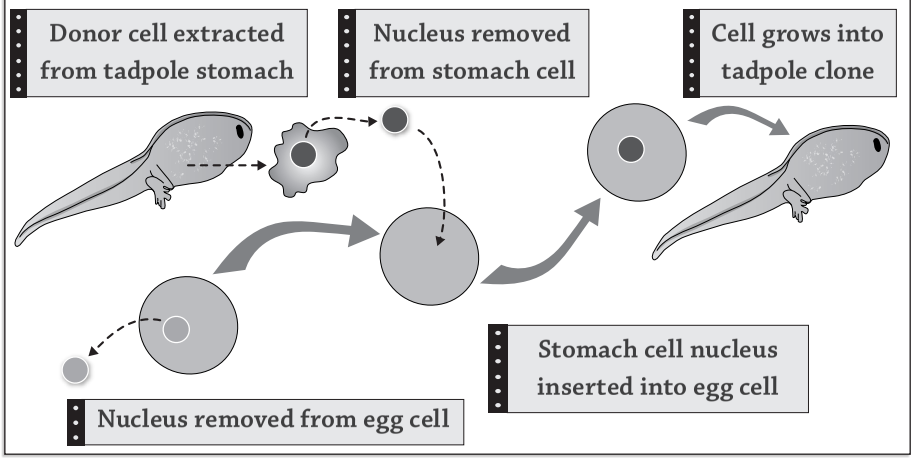
John Gurdon

Frog cloned by nuclear transfer from a differentiated tadpole cell.

Can the nucleus from an adult cell, more differentiated than an embryonic cell, serve as a donor? To find out, Gurdon transplanted the nucleus of a tadpole stomach cell into an enucleated frog egg. In this way, he created tadpoles that were genetically identical to the one from which the stomach cell was taken.

What did this tell us? Nuclei from fully differentiated somatic cells can be used for cloning. This means that that there is no loss of genetic material as cells in an organism divide and differentiate.

Technique



The Cloning Times

Cloning with a Wee Wittle Wabbit Egg

J. Derek Bromhall

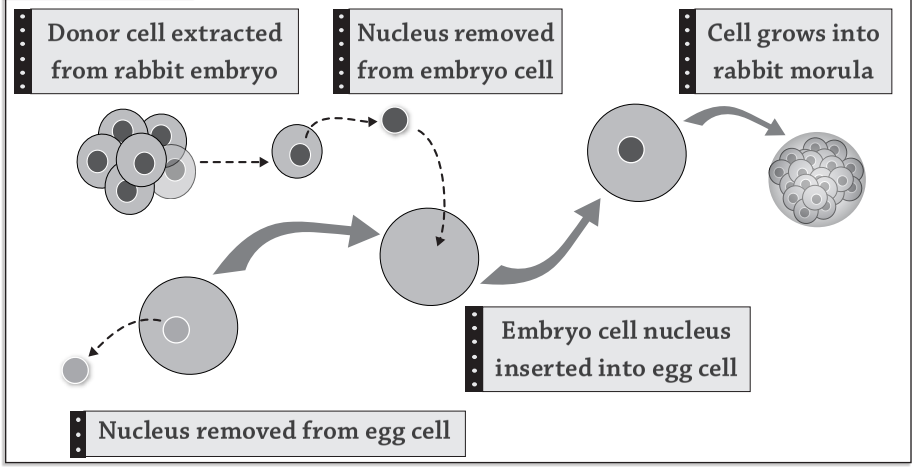
Rabbit cloned by embryonic cell nuclear transfer.

The next cloning challenge was to try nuclear transfer in a more complex mammalian organism, like the rabbit. Mammalian egg cells are much smaller than those of frogs or salamanders, so they are harder to manipulate.

Using glass pipettes as tiny straws, Bromhall transferred the nucleus from a rabbit embryo cell into an enucleated rabbit egg cell. He considered the procedure a success when a morula, or advanced embryo, developed after a couple of days.

What did this tell us? Cloning mammals using nuclear transfer is possible.

Technique



The Cloning Times

Baa-Baa from an Eartly Kind of Cell

Steen Willardsen

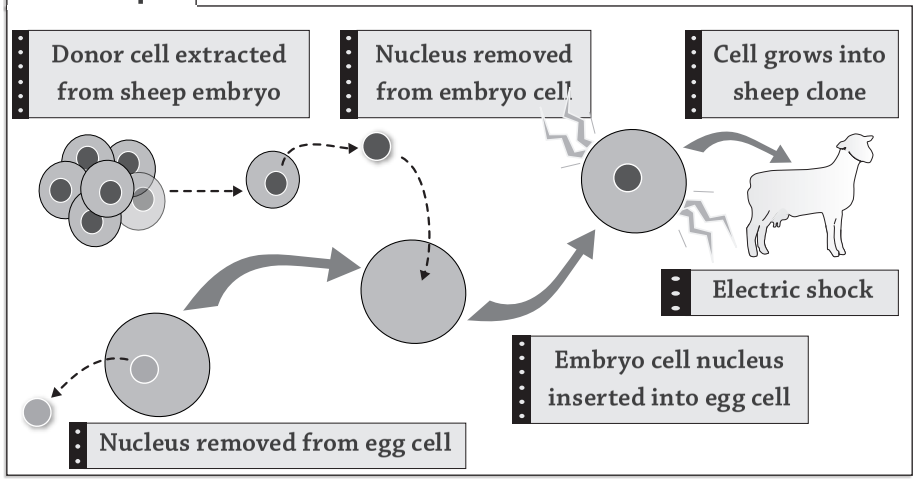
Sheep cloned by embryonic cell nuclear transfer.

Would nuclear transfer work in sheep? To find out, Willadsen chemically separated one cell from an early-stage lamb embryo and fused it to an enucleated egg cell. He then used a small electric shock to mimic fertilization by a sperm cell, causing the new cell to divide.

Finally, Willadsen placed the resulting embryo into the womb of a surrogate mother sheep to nurture it through pregnancy. This was the first large mammal to be cloned by nuclear transfer from an embryonic cell.

What did this tell us? Cloning by nuclear transfer is possible in larger mammals.

Technique



The Cloning Times

Mooove Over for Having a Cow!

Neal First, Randal Prather, and Willard Eyestone

Cow cloned by embryonic cell nuclear transfer.

Rabbits, sheep – can even larger animals, such as cattle, be cloned? First, Prather and Eyestone used a small electrical shock to fuse early-stage cow embryonic cells to enucleated egg cells. They implanted the resulting embryos into the wombs of surrogate mother cows to nurture them through pregnancy. The first two cloned calves were named Fusion and Copy.

What did this tell us? This experiment lengthened the list of mammals that could be cloned by nuclear transfer. Still, mammalian cloning was limited to using embryonic cells as nuclei donors. Cloning using nuclei from differentiated adult somatic cells wasn't thought possible.

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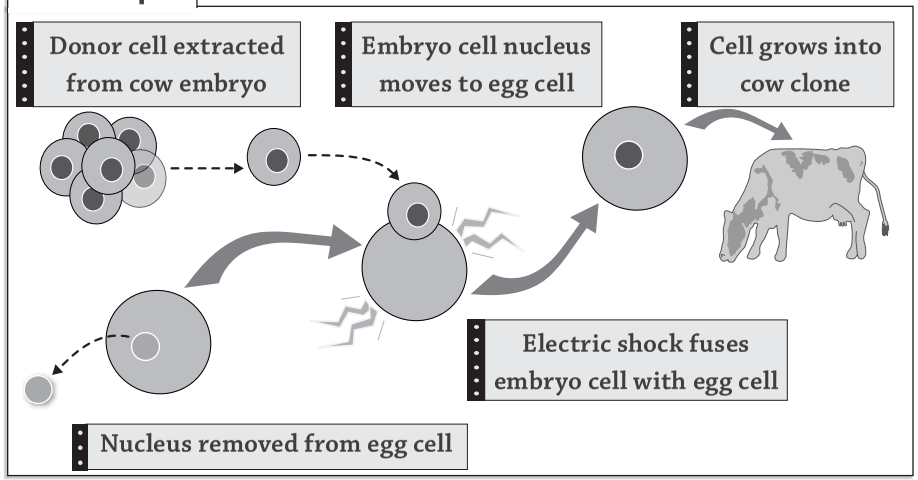
Technique



The Cloning Times

Cloning Laws Appear on the Horizon

William Jefferson Clinton

U.S. President Clinton requested legislation to protect human research subjects.

As cloning techniques improved human cloning seemed more possible, and the issue began to appear on policymakers' agendas. In 1995, President Clinton formed the National Bioethics Advisory Council (NBAC). This council, made up of scientific experts and non-scientists, evaluated ethical, religious and legal issues concerning the protection of human research subjects. This would later be relevant to the controversies surrounding human cloning.

What did this tell us? Just because something is technically possible does not mean that it is socially responsible. In a democratic society, many points of view are considered before laws are passed.

The Cloning Times

Baa-Baa Times Two from a Petri Dish Cell Zoo

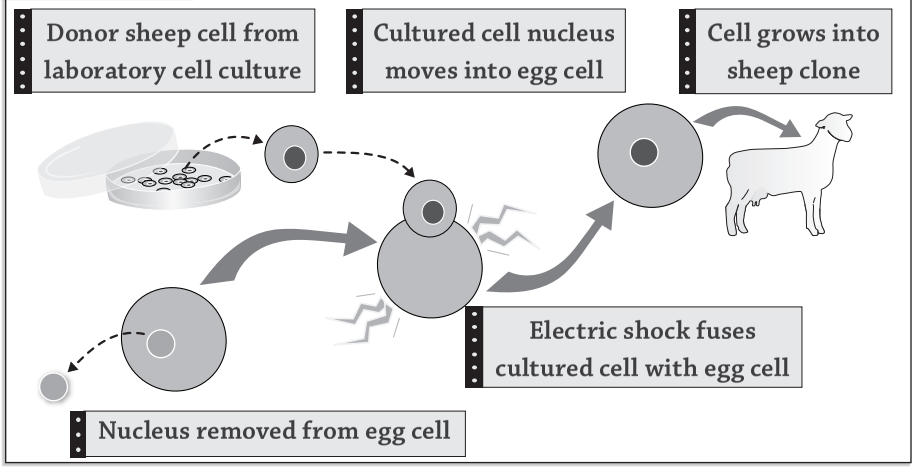
Ian Wilmut and Keith Campbell

Sheep cloned by nuclear transfer from cells grown in the laboratory.

All previous cloning experiments used donor nuclei from cells that were part of developing embryos. In their next experiment, Wilmut and Campbell used donor nuclei from a slightly different source: cultured mammalian cells, which were kept alive in the laboratory. Wilmut and Campbell transferred the nuclei from cultured cells into enucleated sheep egg cells. The lambs born from this procedure were named Megan and Molly.

What did this tell us? Cells cultured in the laboratory can also supply donor nuclei for cloning by nuclear transfer.

Technique



Hello Dolly!

Ian Wilmut and Keith Campbell

Sheep cloned by somatic cell nuclear transfer.

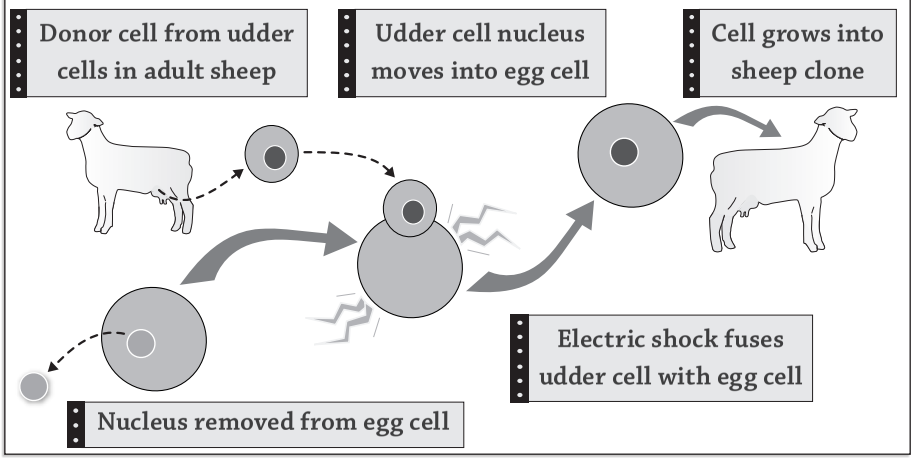
One of the biggest challenges in mammalian cloning was using a differentiated adult somatic cell as the donor. What was the big deal?

Every cell's nucleus contains a complete set of genetic information. However, the pattern of using this information differs between adult cells and embryonic cells. This means that when an adult cell nucleus is used as a donor, its genetic information must be reset, or re-booted. This allows the cell to behave like a brand-new embryonic cell rather than a differentiated adult cell.

Using the electric shock technique, Wilmut and Campbell fused enucleated sheep egg cells with udder cells from a female adult sheep. Of 277 attempts, only one produced an embryo that was carried to term in a surrogate mother. This famous lamb, named Dolly, brought cloning into the limelight.

What did this tell us? Dolly was the first mammal ever to be cloned using a donor nucleus from an adult somatic cell. Her arrival brought the potential implications for cloning, especially controversies over cloning humans and stem cell research, into the public eye.

Technique



The Cloning Times

Promises and Pitfalls of Human Cloning

William Jefferson Clinton

U.S. President Clinton blocked federal funding for human cloning research.

After Dolly the sheep was cloned in 1996, Clinton temporarily restricted the use of taxpayer funds to support research on human cloning. He also asked the National Bioethics Advisory Council (NBAC) to assess human cloning research. The NBAC concluded that any attempt to clone humans by nuclear transfer is an "irresponsible, unethical, and unprofessional act" but recommended that any laws be temporary and reviewed again in several years. While the NBAC requested that private organizations also delay cloning research, several of these went ahead with their research plans.

Based on the NBAC recommendations, Clinton encouraged Congress to pass a law banning human reproductive cloning in the United States. However, he supported cloning research that could lead to significant medical benefits including therapeutic cloning to create human embryonic stem cells for research.

What did this tell us? Cloning procedures can be used for different results. Duplicating a human using cloning creates many ethical problems. However, using cloning to create cells and tissues to treat illnesses might be beneficial.

The Cloning Times

Monkey See, Monkey Do, Monkey Monkey Cloned As Two

Li Meng, John Ely, Richard Stouffer, and Don Wolf

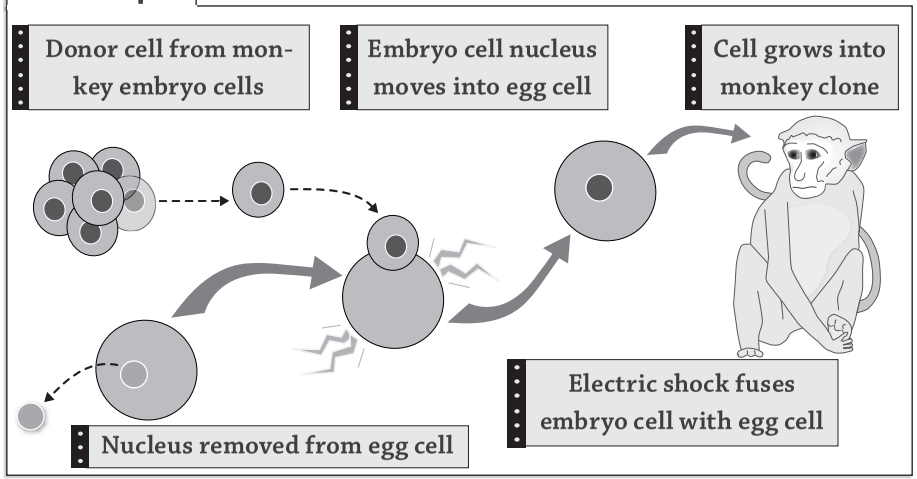
Monkeys cloned by embryonic cell nuclear transfer.

Primates are good models for studying human genetic disorders. Cloning identical primates would decrease the genetic variation and number of animals in research studies related to human genetic conditions.

Similar to previous cloning experiments, Wolf's team of scientists fused early-stage embryonic cells with enucleated monkey egg cells using a small electrical shock. The resulting embryos were then implanted into surrogate mothers. Out of 29 cloned embryos, two monkeys were born. One was a female named Neti, and the other was a male named Ditto.

What did this tell us? Primates, which are humans' closest relatives, can be cloned.

Technique



The Cloning Times

Following Dolly, Pharming Polly

Angelika Schnieke, Keith Campbell, and Ian Wilmut

Transgenic sheep clones can produce treatments for human medical disease.

How can humans benefit from cloning technology? Why would we want to do this?

Transgenic technology – the transfer of genes from one species into another – was being refined just as mammalian cloning hit the limelight. This technology makes it possible to produce transgenic animals that serve as production factories for medically useful proteins.

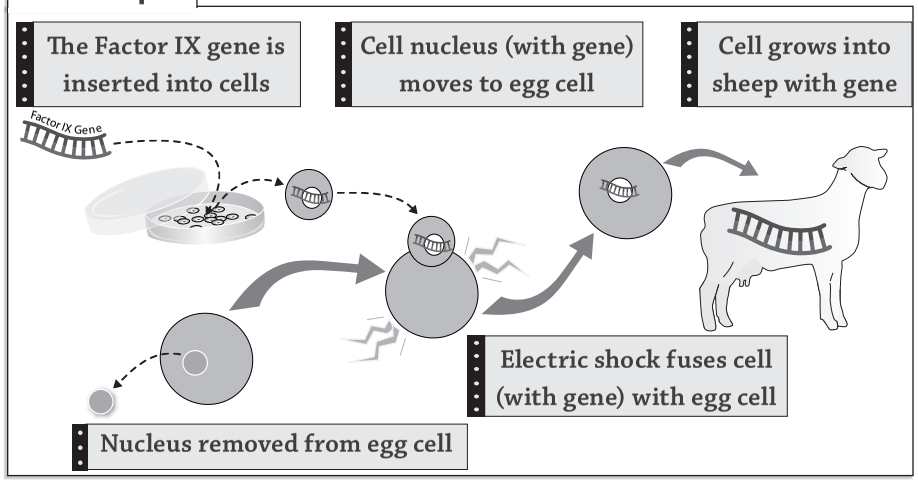
One convenient way to produce large quantities of a transgenic protein is to engineer an animal to produce the protein in its milk. Simply by milking the animals, we can collect the protein, purify it and use it for medical purposes.

Wilmut, Campbell and Schnieke set out to create cloned sheep that expressed the human gene encoding the blood clotting Factor IX ("factor nine"). This protein can be used to treat people with hemophilia, a disorder that results in the inability to stop bleeding when injured.

To create the transgenic sheep, the scientists introduced the human Factor IX gene into the nuclei of sheep skin cells grown in a laboratory dish. These nuclei were then transferred to sheep egg cells, creating transgenic cloned embryos. Polly was the first transgenic sheep produced this way.

What did this tell us? Sheep can be genetically engineered to produce therapeutic proteins for humans in their milk. The convergence of transgenic and cloning technologies resulted in a new approach to treating human diseases.

Technique



The Cloning Times

To Clone or Not to Cone?

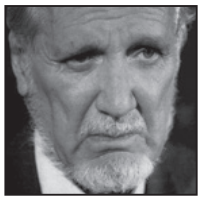
Richard Seed and Lee Bo-yeon

Perspectives on cloning humans and human cloning research.

Some people support human cloning. For example, Richard Seed is an American physicist and self-proclaimed "fertility expert." In 1998 he announced plans to clone a human being before any federal ban could be enacted. Around the same time, South Korean researcher Lee Bo-yeon claimed to have used nuclear transfer with an enucleated egg and a somatic cell from the same woman.

He reported that one of the resulting eggs began dividing. However, the Korean research team halted its development at the four-cell stage, before it could be implanted into a surrogate mother's womb. The research world rejected Bo-yeon's claim, demanding more scientific evidence.

What did this tell us? Advances in genetics are presenting the world with new choices. The potential for human cloning exists and may soon become a reality. Some people support researching this potential.



Richard Seed

Lee Bo-yeon

The Cloning Times

Dolly Shows Folks How to Clone a Mouse

Teruhiko Wakayama and Ryuzo Yanagimachi

Female mouse cloned by somatic cell nuclear transfer.

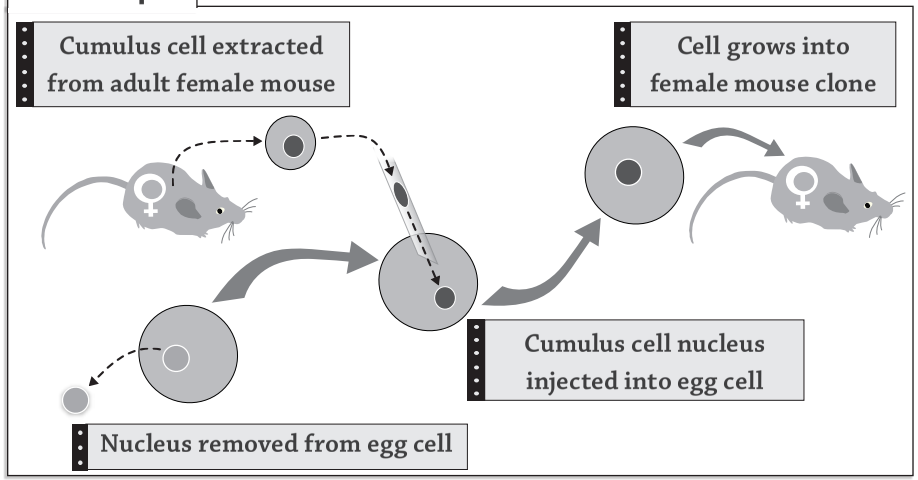
Dolly was cloned using genetic material from differentiated adult cells. Can other mammals be cloned this way?

Wakayama and Yanagimachi used mouse cumulus cells as nucleus donors. These differentiated cells nourish egg cells in female adult mice. But instead of using an electric shock to transfer the nucleus, the scientists injected the nucleus directly into the egg cell.

The new cell was chemically stimulated to divide and implanted into a surrogate mother mouse. The first cloned mouse pup, named Cumulina, was born 19 days later.

What did this tell us? Cloning using donor nuclei from adult cells can be performed in mammals other than sheep.

Technique



The Cloning Times

Fibro Brings Macho to Cumulina's Arena

Teruhiko Wakayama and Ryuzo Yanagimachi

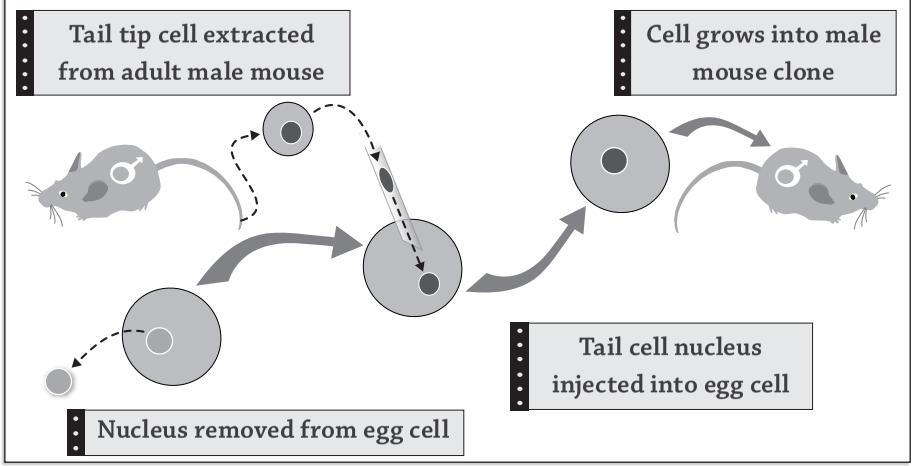
Male mouse cloned by somatic cell nuclear transfer.

Up to this point, all successful adult cell cloning attempts used cells associated with the female reproductive system.

Can a male-derived adult cell be used to generate a male mouse? Wakayama and Yanagimachi isolated donor nuclei from cells collected from the tail tips of adult male mice. After injecting these nuclei into enucleated egg cells, the scientists transferred the resulting embryos into surrogate mother mice. The single resulting male pup, named Fibro, was the only successful clone in 274 attempts.

What did this tell us? Cloning using adult somatic cells isn't restricted to females or to cells associated with the reproductive system.

Technique



The Cloning Times

Infertility Drives Cloning Research

Severino Antinori and Panayiotis Zavos

Human cloning might solve problems of couples having difficulty in becoming pregnant.

A group of reproductive experts announced their plan to clone a human within the next two years.

This international group includes Greek-American researcher Panayiotis Zavos and Italian researcher Severino Antinori. Zavos and other scientists have argued the benefits of human cloning research in front of a U.S. Congressional Committee formed to discuss issues raised by human cloning. Antinori announced that a woman would give birth to a cloned baby in January 2003, but provided no scientific details for the pregnancy. Many scientific experts are skeptical about his claim of achieving a human clone.

What did this tell us? Not being able to have a baby causes a lot of emotional pain in some people's lives. Scientists are looking at cloning as a possible solution for infertility.


Panayiotis Zavos


Severino Antinori

The Cloning Times

Human Cloning to Bolster Stem Cell Therapies?

Advanced Cell Technology

Human cloning might also be used to create stem cells for new medical treatments.

How might cloning a human benefit medical research?

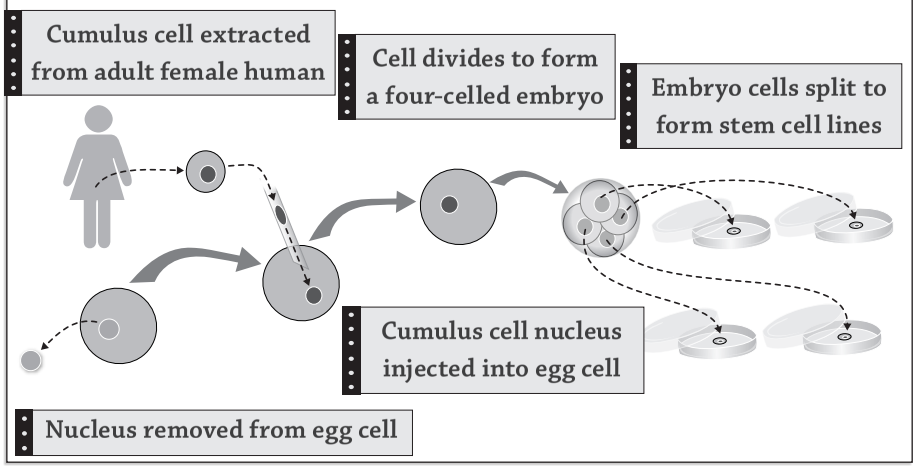
Early embryos are composed of stem cells, which can become any kind of cell in the human body. A potential approach to repairing tissue damage in a patient's body is by using the patient's genetic material to clone an early embryo that would be split into individual stem cells.

These cells would be grown in the laboratory, producing matching tissue to repair the damage. This approach, called therapeutic cloning, differs from reproductive cloning in that it aims to produce cells and tissues rather than a complete human being.

Scientists at Advanced Cell Technology, an American biotechnology company, cloned the first documented human embryo by nuclear transfer, using the nucleus from an adult cumulus cell. The cloned egg developed into a six-celled embryo before it stopped growing. This experiment showed that therapeutic cloning might be a realistic approach to producing stem cells for medical purposes.

What did this tell us? The end result of cloning isn't always a fully developed organism. Cloning might also be used to create stem cells for new medical therapies.

Technique



The Cloning Times

New President, New Policies

George Walker Bush

U.S. President Bush bans federal funding of all human cloning research.

President Bush created the President's Council on Bioethics. This group carried out a mission similar to former President Clinton's National Bioethics Advisory Council.

The Bush administration prohibited taxpayer funding to support research involving the cloning and destruction of human embryos. He also supported a federal ban on both human reproductive cloning and therapeutic cloning to create stem cells for research.

What does this tell us? Not everyone differentiates between the two types of cloning.

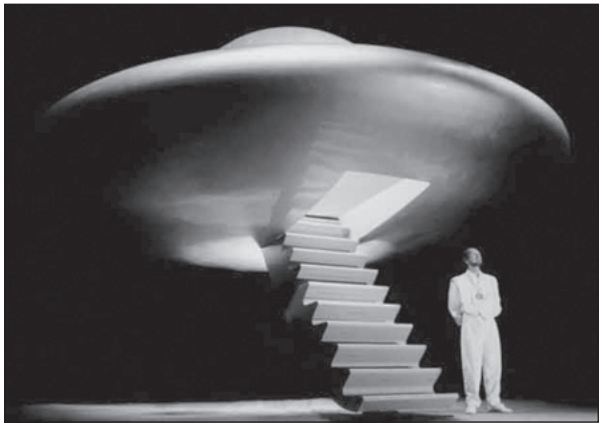
Supernatural Belief in Cloning

Human Cloning Advocates

Different perspectives on human cloning and its potential.

The Raelian Movement is a religious sect whose members believe that humans are clones created by aliens. In 1997, the Raelians organized Clonaid, "the first human cloning company." Then in 2002, the Korean office of Clonaid claimed to have a woman pregnant with a cloned embryo. However, South Korean officials found no evidence supporting the report. They rushed to enact a government ban on all human cloning in the country.

What did this tell us? Different groups of people hold different beliefs and values. It's important to analyze all sides of an issue before making your own decisions. Also, the human cloning issue extends well beyond the borders of the United States, influencing citizens of all countries.



Rael with model of alien spaceship

The Cloning Times

House Supports Cloning Ban

George Walker Bush

Human cloning bill passed in the U.S. House of Representatives.

The U.S. House of Representatives passed a ban against both reproductive and therapeutic human cloning in 2002. The bill was then sent to the Senate, the other half of Congress, for a vote.

What does this tell us? If such a bill passed, scientists funded by taxpayer money can be put in jail if they do any cloning research.