

Teacher Guide: You've Come A Long Way Dolly!

ACTIVITY OVERVIEW

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.

Module:

Cloning in Focus

Key Concepts:

The importance of the nucleus; cell differentiation; enucleation; various cloning techniques, including embryo twinning and nuclear transfer; relative complexity of organisms; the long history of cloning; the social significance of cloning

Prior Knowledge Needed:

Knowledge of basic cell structure; a basic understanding that cells differentiate throughout development; knowledge of the birth of Dolly the sheep as the first mammal cloned from an adult cell (not an embryo)

Materials:

Mock newspaper articles, student handouts, tape, stickers in two colors

Appropriate For:

Ages: 12 - 18
USA grades: 7 - 12

Prep Time:

30 minutes (copying and review)

Class Time:

70 minutes (may be extended by class discussion and/or assessment)

Activity Overview Web Address:

<http://gslc.genetics.utah.edu/teachers/tindex/overview.cfm?id=dolly>

Other activities in the *Cloning in Focus* module can be found at:

<http://gslc.genetics.utah.edu/teachers/tindex/>

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I. PEDAGOGY

A. 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

B. Background Information

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

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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.

For additional information, see *What is Cloning?*, available on the Genetic Science Learning Center website at <http://gslc.genetics.utah.edu/units/cloning>.

C. Teaching Strategies

1. Timeline

- Day before activity:
 - Make photocopies of *The Cloning Times* newspaper articles - one set per class.
 - Make photocopies of the student handouts, including the Cloning Timeline Activity Instructions (S-1) and *The Cloning Times* Record (S-2).
 - Determine where in the room you will construct the timeline; students do so by taping up their newspaper articles, so be sure to have plenty of room.
 - Select stickers in two colors
- Day of activity:
 - Hand out *The Cloning Times* newspaper articles to individuals or small groups.
 - Hand out the Activity Instructions and blank *Cloning Times* Record sheets to each student.
 - Have students carry out the timeline activity.

2. Classroom Implementation

Activity Part One:

- Hand *The Cloning Times* articles and the student handouts to students as they enter the class.
- 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.
- 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).

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- 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.

NOTE: The completed timeline is available for your reference. See Teacher Resource (Page 9).

- Ask the students to read the Activity Instructions and begin.
 - Students will first silently read the newspaper article you gave them and think about whether their event might have occurred before or after Dolly's birth. Have them write at least one reason for their decision in the space provided (Step 1 in the Activity Instructions).
 - If students are working in small groups, have them first silently read the newspaper article. Then have them discuss the event as a group and decide when it might have occurred relative to Dolly's birth.
- 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.
- 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.
- 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.

NOTE: These key events are indicated in bold italics on the completed timeline for your reference. See Teacher Resource on Page 9.

- 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".

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- 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.
- 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.
- 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:

- 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 choose 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.

3. 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

4. Assessment Suggestions

- See Activity Part Three, above.

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II. ADDITIONAL RESOURCES

A. Activity Resources - linked from the online Activity Overview:

<http://gslc.genetics.utah.edu/teachers/tindex/overview.cfm?id=dolly>

- Website: For more information on the events in the timeline, see Additional Resources for the Cloning in Focus module at <http://gslc.genetics.utah.edu/units/cloning/cloningresources/>
- Website: For animations of the cloning techniques described in the timeline see *The Clone Zone* in the Cloning in Focus module at <http://gslc.genetics.utah.edu/units/cloning/clonezone/>

III. MATERIALS

A. Detailed Materials List

- Copies of *The Cloning Times* newspaper articles (cut each page in half along the dotted line) – one set per class
- Copies of the Cloning Timeline Activity Instructions (S-1), *Cloning Times* Record (S-2) and Cloning Timeline Activity Discussion and Questions (S-3) – one for each student
- Stickers in two different colors – one of each color per student
- Transparent (“Scotch”) tape or masking tape
- Highlighters (optional – see Adaptations)

IV. STANDARDS

A. U.S. National Science Education Standards

Grades 5-8:

- Content Standard C: Life Science - Structure and Function in Living Systems; all organisms are composed of cells that grow, divide and differentiate to form tissue
- Content Standard C: Life Science - Reproduction and Heredity; hereditary information is located in genes that are responsible for specifying traits
- Content Standard E: Science and Technology; technologies enable scientific discovery; scientific discovery progresses with technology
- Content Standard G: History and Nature of Science - Science is a Human Endeavor
- Content Standard G: History and Nature of Science - Nature of Science; scientists test explanations of nature through experiments

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- Content Standard G: History and Nature of Science - History of Science; many individuals have contributed to scientific ideas and realities

Grades 9-12:

- Content Standard A: Science as Inquiry - Understandings About Scientific Inquiry; scientists inquire about how living systems function and conduct investigations to discover new aspects of those systems; new techniques and tools guide inquiry and contribute to the advance of science
- Content Standard C: Life Science - The Cell; the nucleus guides cell division and development
- Content Standard C: Life Science - Molecular Basis of Heredity; instructions for specifying characteristics of organisms are carried in DNA
- Content Standard E: Science and Technology - Understandings About Science and Technology; technologies enable scientific discovery; scientific discovery progresses with technology
- Content Standard F: Science in Personal and Social Perspectives - Science and Technology in Local, National and Global Challenges; progress in science and technology can affect and is affected by social issues and challenges
- Content Standard G: History and Nature of Science - Science is a Human Endeavor
- Content Standard G: History and Nature of Science - Nature of Scientific Knowledge; scientists test explanations of nature through experiments
- Content Standard G: History and Nature of Science - Historical Perspectives; many individuals have contributed to scientific ideas and realities; changes in science occur as small modifications in extant knowledge

B. AAAS Benchmarks for Science Literacy

Grades 6-8:

- The Nature of Science: Scientific Inquiry - scientific knowledge is subject to modification as new information challenges prevailing theories
- The Living Environment: Heredity - an egg multiplies to form a complete organism
- The Living Environment: Cells - cells repeatedly divide to create an organism
- The Nature of Technology: Science and Technology - technology is essential to science

Grades 9-12:

- Nature of Science: Scientific Inquiry - changes that take place in the body of scientific knowledge are small modifications to prior knowledge and the testing, revising and occasional discarding of theories never ends
- The Nature of Science: The Scientific Enterprise - progress in science and invention depends heavily on what else is happening in society

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- The Living Environment: Heredity - information passed from parent to offspring is coded in DNA; genes can be inserted to produce desirable traits
- The Living Environment: Cells - cells have specialized parts
- The Nature of Technology: Science and Technology - technology makes it possible for scientists to extend their research
- The Nature of Technology: Issues in Technology - social forces strongly influence which technologies will be developed and used

C. Utah Core Curriculum

Intended Learning Outcomes for the Utah Secondary Core Curriculum in Science:

Students will:

4. Demonstrate awareness of the Social and Historical Aspects of Science
 - a) Understand that social and cultural forces have influenced the historical development of science.
 - b) Understand how technological advances have influenced the progress of science, and how science has influenced developments in technology.
 - c) Appreciate the challenges faced by scientists in the past and respect the contributions these men and women have made to advancing science and technology.
 - d) Recognize the personal relevance of science in daily life.
 - e) Respect the contributions of science to the quality of human life.
 - f) Recognize the interdependence of science, technology, and society.
 - h) Respect the contributions scientists make to informing public policy debates, but acknowledge that policy issues cannot be resolved by science alone because value issues must also be considered.

Biology (9-12):

- Standard 2: Students will understand the classification and function of cells
Objective 1: Investigate the structure and function of cells
 - Report the role technology plays, past and present, in the understanding of cells
- Standard 4: Students will analyze how genetic information is passed from one cell to another.
Objective 3: Research and analyze perspectives on issues related to genetic technologies
 - Evaluate applications of genetic technologies

Biology: Human Biology (9-12)

- Standard 2: Students will understand the classification and function of cells
Objective 1: Investigate the structure and function of cells
 - Report the role technology plays, past and present, in the understanding of cells

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- Standard 3: Students will analyze how genetic information is passed from one cell to another.
Objective 3: Describe the significance and impact of genetic alteration on living things
 - Describe applications of genetic technologies

V. CREDITS

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Harmony Starr, Genetic Science Learning Center (illustrations)

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A. Cloning Timeline Events

YEAR	SUMMARY SENTENCE
1885	Sea urchins cloned by shaking one embryo into two separate cells.
1902	Salamander cloned by using a noose to separate cells from an early embryo.
1928	The nucleus of cells controls the development of a salamander embryo.
1952	<i>Frog cloned by nuclear transfer from a tadpole embryo.</i>
1968	Frog cloned by nuclear transfer from a differentiated tadpole cell.
1975	Rabbit cloned by embryonic cell nuclear transfer.
1986	Sheep cloned by embryonic cell nuclear transfer.
1987	Cow cloned by embryonic cell nuclear transfer.
1995	U.S. President Clinton requested legislation to protect human research subjects.
1996	Sheep cloned by nuclear transfer from cells grown in the laboratory.
1996	<i>Sheep cloned by somatic cell nuclear transfer.</i>
1997	U.S. President Clinton blocked federal funding on human cloning research.
1997	Monkeys cloned by embryonic cell nuclear transfer.
1997	Transgenic sheep clones can produce treatments for human medical disease.
1998	Perspectives on cloning humans and human cloning research.
1998	<i>Female mouse cloned by somatic cell nuclear transfer.</i>
1999	Male mouse cloned by somatic cell nuclear transfer.
2001	Human cloning might solve problems of couples having difficulty in becoming pregnant.
2001	<i>Human cloning might also be used to create stem cells for new medical treatments.</i>
2001	U.S. President Bush bans federal funding of all human cloning research.
2002	Different perspectives on human cloning and its possibility.
2002	Human cloning bill passed in the U.S. House of Representatives.



CLONING TIMELINE ACTIVITY INSTRUCTIONS

Introduction

During the 1990's, cloning stole the limelight. Dinosaurs came back to life in the *Jurassic Park* movies, Dolly the sheep burst onto the scene, and suddenly we faced the possibility that humans too could be cloned.

Less obvious in the midst of all the buzz was the fact that cloning is nothing new: its rich scientific history spans the past 100 years, and continues to progress quite rapidly. In this activity, you and your classmates will construct a timeline on the history of cloning.

PART I – Activity Instructions

1. Silently read through your *Cloning Times* newspaper article. Think about whether your event might have occurred before or after the cloning of Dolly the sheep in 1996. Write at least one reason for your decision below.
2. When called upon, present the headline and summary sentences (in boldface type) of your newspaper article to the class. Then, place the article on the timeline where you think the event might have happened relative to those that are already posted. Explain why you placed it where you did.
3. As you listen to other students present their events, think of where your event might have occurred relative to theirs on the timeline. Does your event seem less or more advanced than what has been presented? Be prepared to explain your reasoning.
4. Your teacher will instruct you to fill out a few significant headlines in the correct place on your *Cloning Times* Record (page S-2) when your classmates present them.
5. After all of the events are in the correct order, you will be given time to add the rest of the summary sentences to your *Cloning Times* Record.

The Cloning Times Record

1885

1902

1928

1952

1968

1975

1986

1987

1995

1996

1996 - - - Sheep cloned by somatic cell nuclear transfer.

1997

1997

1997

1998

1998

1999

2001

2001

2001

2002

2002

What does the timeline spell out? _____



PART II – Discussion

1. Which *scientific event* do you think is the most significant in the history of cloning? Place a sticker on that event on the timeline. Be prepared to discuss and defend why you think that discovery had a large impact on scientific research.
2. What *social or political event* do you think is the most significant in the history of cloning? Place a different sticker on that event on the timeline. Be prepared to discuss and defend why you think that event was important.

PART III – Questions

1. Outline a brief history of cloning, highlighting breakthrough events that show different techniques.
2. What do you notice about the progression of organisms that have been cloned? What factors might influence the ease of cloning a particular organism?
3. Describe how cloning techniques have changed through time. Which techniques or principles have endured?
4. Explain the difference between using embryonic cells and differentiated adult somatic cells for cloning. What characteristics of embryonic cells led scientists to use them for the first cloning experiments? What characteristics of differentiated adult somatic cells made them more difficult to use for cloning?
5. Throughout the history of cloning, have there been periods of low or high scientific activity? Why do you think this has or has not happened?
6. Explain why the cloning of Dolly the sheep was such a major scientific breakthrough.
7. Are scientists as close to cloning humans as you thought? Support your answer with timeline entries.

SEEING DOUBLE? SEA URCHINS CLONED!

HANS ADOLF EDWARD DREISCH

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

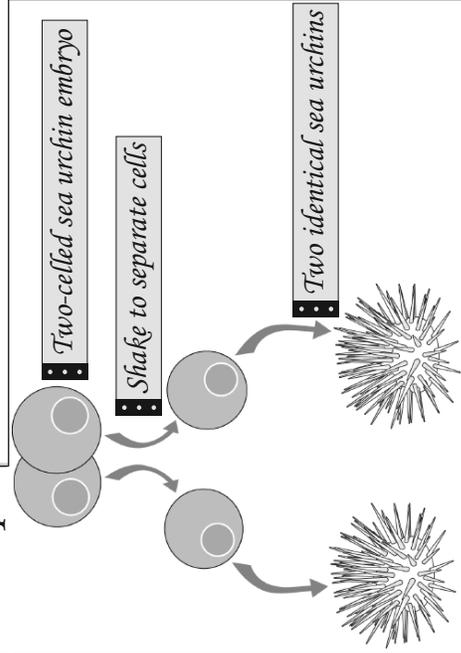
Can the earliest embryos be split into individual cells, which go on to become separate organisms? Does each embryonic cell contain a complete set of genetic material that can direct the formation of an organism?

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



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?

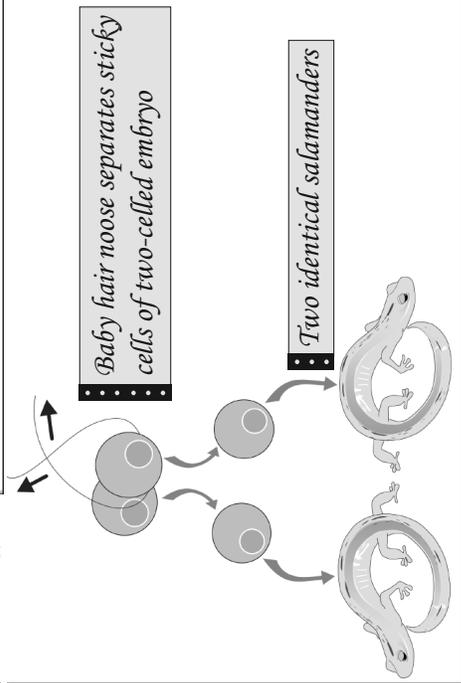
Spemann's first challenge was to figure out how to split the two cells of an embryo much stickier than sea urchin cells. Could he tie off the two cells with a length of thread, dental floss, or even a

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 "twinning" to form multiple organisms – but only up to a certain stage in development.

Technique



IT'S TRUE: THE NUCLEUS IS IN CHARGE

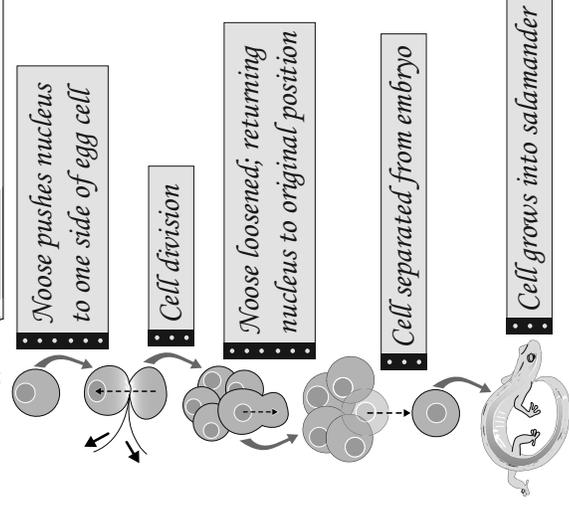
HANS SPEMANN

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

Technique



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.

FROGS CALORE! 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.

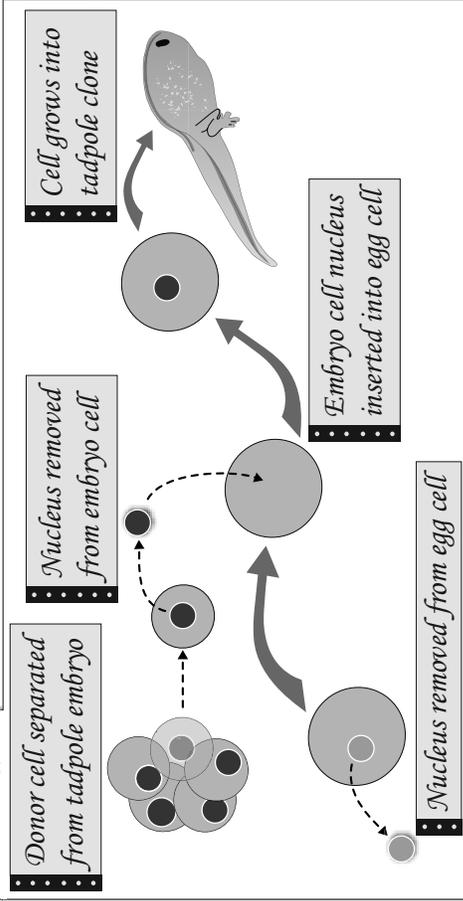
Their first challenge was to isolate the nucleus from a donor cell: in this case, a cell from an early tadpole embryo. Next, they had to prepare a recipient frog egg cell by removing its nucleus – a process called enucleation. Last, the donor nucleus and the recipient egg cell were united. Even if all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



FOR CLONING. ANY NUCLEUS WILL DO

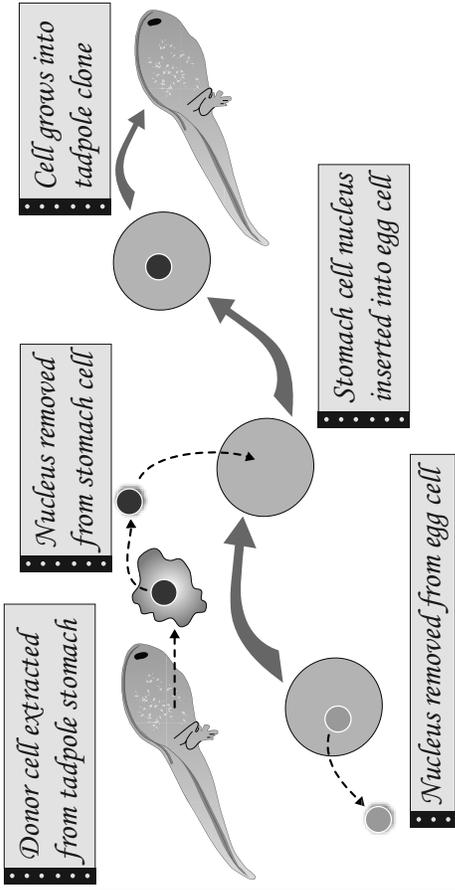
JOHN GURDON

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.

Technique



CLONING WITH A WEE WITTLE WABBIT EGG

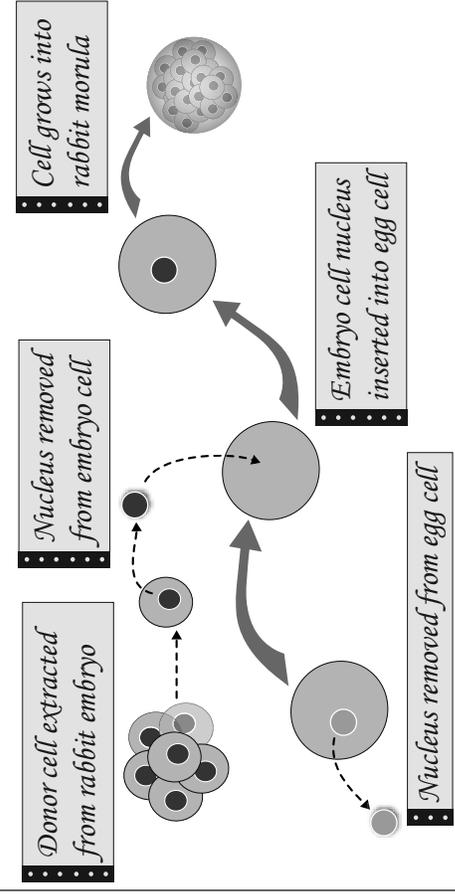
J. DEREK BROMHALL

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,

Technique



developed after a couple of days.

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

BAA-BAA FROM AN EARLY KIND OF CELL

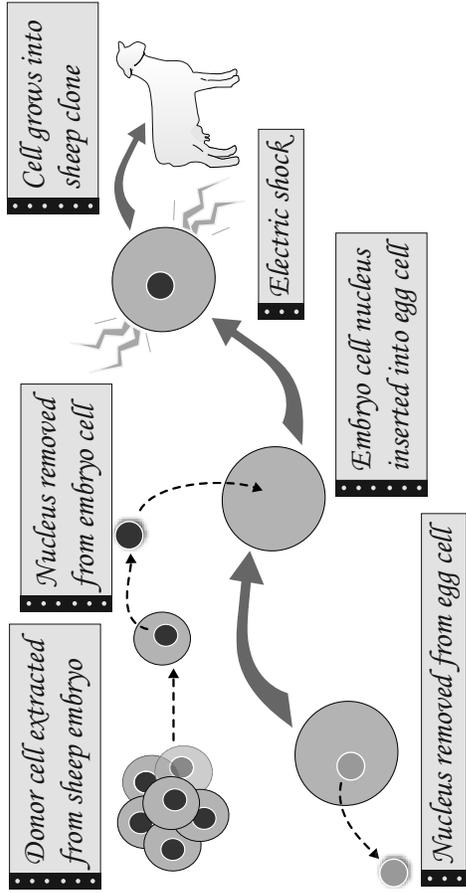
STEEN WILLADSEN

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

Technique



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.

MOOOVE OVER FOR HAVING A COW!

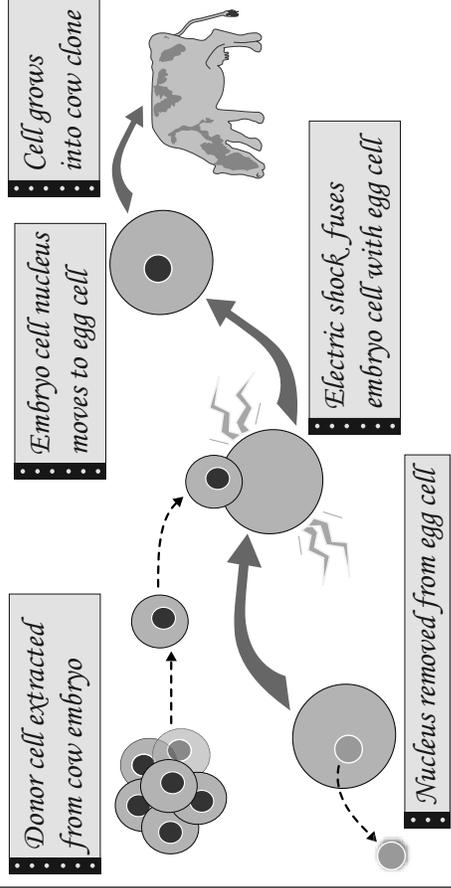
NEAL FIRST, RANDAL PRATHER, AND WILLARD EYESTONE

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

Technique



by nuclear transfer. Still, mammalian cloning was limited to using embryonic cells as nuclei donors. Cloning adult somatic cells wasn't thought possible.

CLONING LAWS APPEAR ON THE HORIZON

WILLIAM JEFFERSON CLINTON

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



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.

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.

BAA-BAA TIMES TWO FROM A PETRI DISH CELL ZOO

IAN WILMUT AND KEITH CAMPBELL

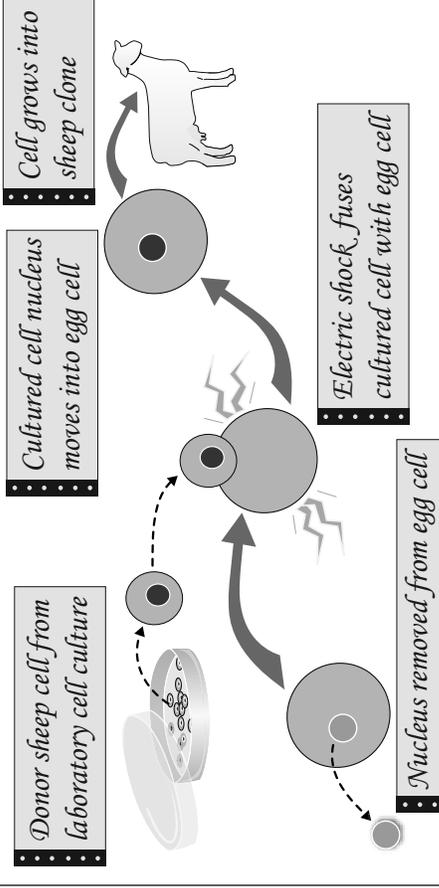
Sheep cloned by nuclear transfer from cells grown in the laboratory.

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

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

Technique



HELLO, DOLLY!

IAN WILMUT AND KEITH CAMPBELL

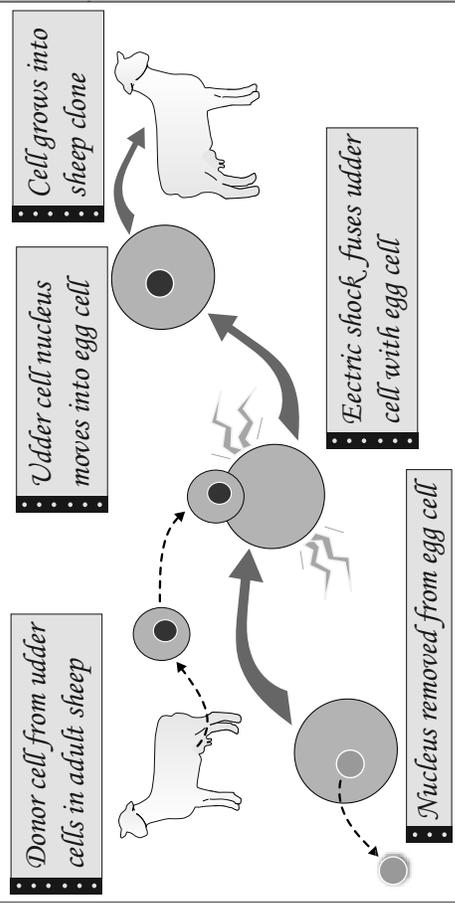
Sheep cloned by somatic cell nuclear transfer.

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,

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.

PROMISES AND PITFALLS OF HUMAN CLONING

WILLIAM JEFFERSON CLINTON

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



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.

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

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.

MONKEY SEE, MONKEY DO. MONKEY MONKEY CLONED AS TWO LI MENG, JOHN ELY, RICHARD STOUFFER, AND DON WOLF

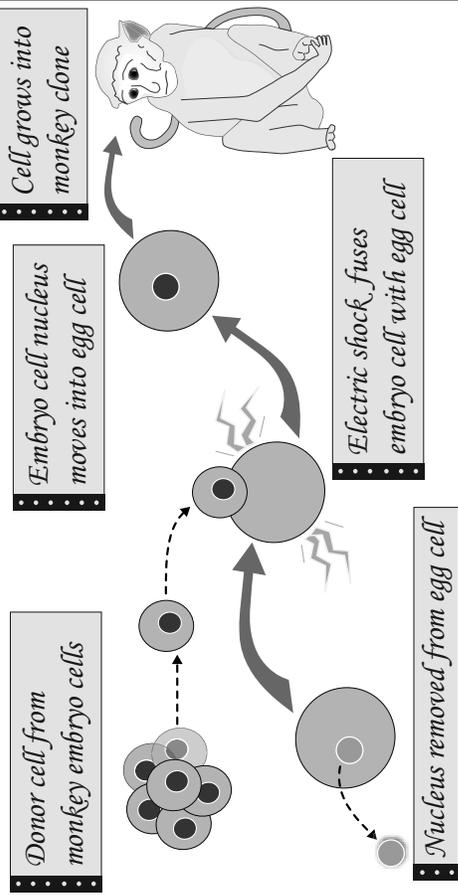
Monkeys cloned by embryonic cell nuclear transfer.

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

Technique



FOLLOWING DOLLY, PHARMING POLLY ANGELIKA SCHNIEKE, KEITH CAMPBELL, IAN WILMUT

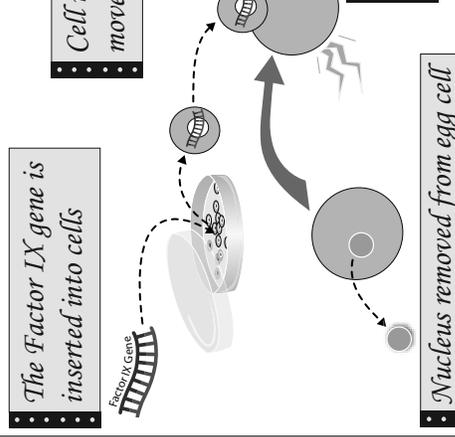
Transgenic sheep clones can produce treatments for human medical disease.

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.

Technique



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.

Wilmut, Campbell

TO CLONE OR NOT TO CLONE?

RICHARD SEED, LEE BO-YEON

Perspectives on cloning humans and human cloning research.



Richard Seed



Lee Bo-yeon

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 Boyeon'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.

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.

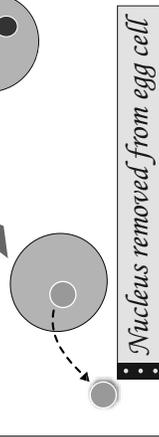
The new cell was chemically stimulated to

Technique

Cumulus cell extracted from adult female mouse



Cumulus cell nucleus injected into egg cell



Nucleus removed from egg cell

Cell grows into female mouse clone



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.

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.

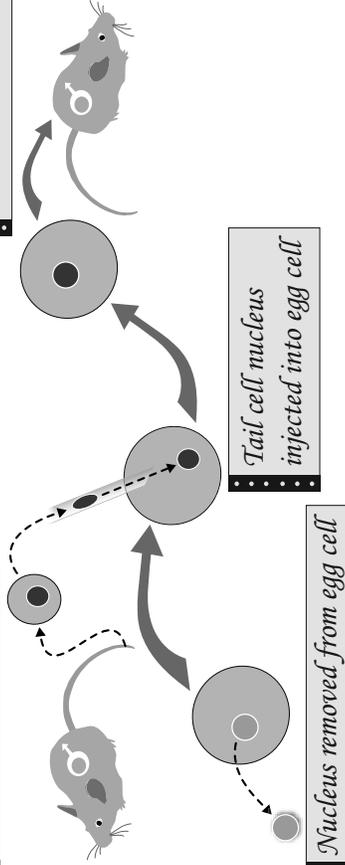
Can a male-derived adult cell be used to generate a male mouse? Wakayama and Yanagimachi isolated donor nuclei from cells collected from the tail tips of adult male mice. After injecting these nuclei into enucleated egg cells, the scientists transferred the resulting embryos into surrogate mother mice. 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

Tail tip cell extracted from adult male mouse



Nucleus removed from egg cell

Tail cell nucleus injected into egg cell

Cell grows into male mouse clone

INFERTILITY DRIVES CLONING RESEARCH

SEVERINO ANTINORI AND PANAYIOTIS ZAVOS

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



Panayiotis Zavos



Severino Antinori

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.

HUMAN CLONING TO BOLSTER STEM CELL THERAPIES?

ADVANCED CELL TECHNOLOGY

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

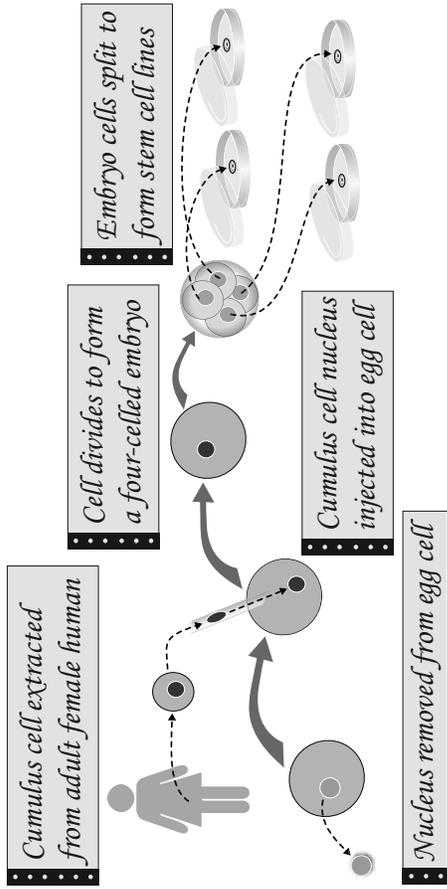
How might cloning a human benefit medical research?

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



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.



Rael with model of alien spaceship

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.

