Cloning

National DNA Day

April 25, 2008

Many thanks to the University of Utah Genetic Science Learning Center. This presentation was adapted from their module on cloning. More activities and information is available at their website: http://learn.genetics.utah.edu

What is cloning?

- In scientific terms, cloning is the creation of an organism that is the EXACT genetic copy of another

- Identical twins are natural clones – the DNA of one twin is exactly the same as the DNA of another twin

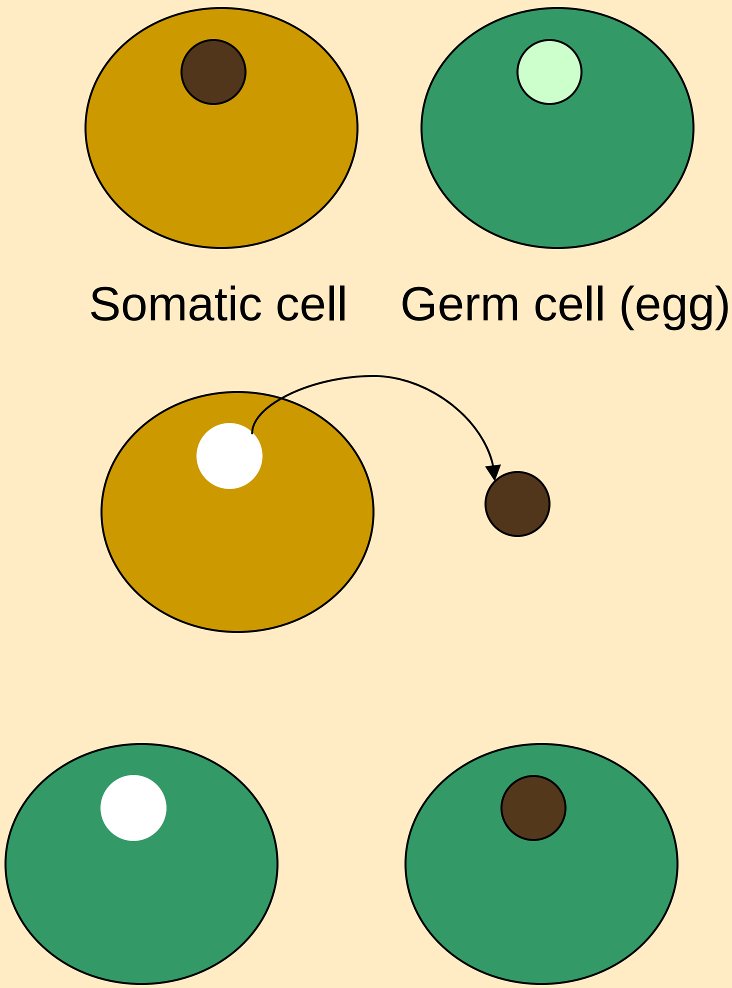
- Cloning can be done artificially in a laboratory by one of two ways:
  - Artificial embryo twinning
  - Somatic cell nuclear transfer (SCNT)

Artificial Embryo Twinning

- Just like twinning in nature, only done in a Petri dish
- Occurs just after fertilization
  - Sperm fertilizes egg, forms the one-cell zygote
  - When zygote goes to divide into two cells, the cells split from one another
  - Each cell divides and matures on its own, becoming individual twin embryos
  - The embryos are genetically identical
- In the laboratory, the egg is usually fertilized by the sperm directly in the Petri dish. The cells of a very early embryo are split from one another manually, so they can continue to divide and mature on their own. The embryos are then placed in a surrogate mother.

Somatic Cell Nuclear Transfer

AKA How Dolly Was Created



- Two types of cells in the body: somatic and germ cells. Germ cells are the egg and the sperm. All other cells are somatic cells.
  - Germ cells have one pair, or 23, chromosomes. Somatic cells have two pairs, or 46, chromosomes.
- SCNT begins with a scientist isolating a somatic cell and removing its nucleus
  - Nucleus contains all of our chromosomes, and therefore all of our genetic information
- Then transfers nucleus to an egg that has had its own nucleus removed.

Somatic Cell Nuclear Transfer

AKA How Dolly Was Created

- The egg now has 46 chromosomes in its nucleus, which is just what happens when a sperm (with 23 chromosomes) fertilizes a normal egg (also with 23 chromosomes)
- Scientists then chemically stimulate the egg to believe it has been “fertilized” and it begins to develop into an embryo
- The embryo is then implanted into a surrogate mother.
- The resulting organism is an exact clone of that which donated the somatic cell nucleus.

Why might we WANT to clone?

- For medical purposes
  - Cloning animal models of disease – study human diseases (especially genetic diseases) in large animal populations
  - Cloning stem cells for research – stem cells may be used to repair damaged or diseased tissues and organs
  - Large populations of genetically engineered cloned animals may be able to produce drugs or proteins for medicine – process called “pharming”
- Revive endangered or extinct species
  - Extinct not likely
  - Endangered possible, but no success yet
- Reproduce deceased pets
  - Now being offered by one biotech company in United States
- Any reason to clone a human?
  - Help infertile couples have children?
  - “Replace” a deceased child?

What are the RISKS of cloning?

- High failure rate – success rate is only about 0.1-3%
  - The egg and nucleus may not be compatible
  - The renucleated egg may be unable to divide or develop properly
  - Embryo implantation or the pregnancy itself may fail
- Problems later in development
  - Many clones are born with large organs which leads to blood flow and breathing problems (a condition known as Large Offspring Syndrome, or LOS)
- Telomeric differences
  - Telomeres protect chromosomes from damage and naturally shorten every time DNA is copied. This shortening is a natural aging process
  - Cloned animals begin life with an older organism's shortened telomeres and therefore may prematurely age
- Abnormal gene expression
  - The transferred nucleus in the cell is NOT a natural embryo and thus cannot entirely behave as one

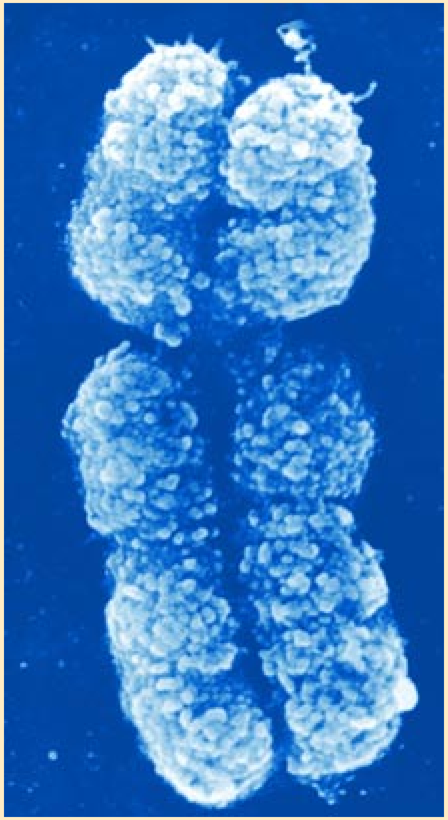
For your consideration . . .

- On December 22, 2001, the first domestic pet ever to be cloned was born: a kitten named CC, pictured here next to her genetic donor, Rainbow.
- Notice anything odd about these pictures?

Why don’t CC and Rainbow look identical? (Apart from one being a kitten and the other a full-grown cat!)

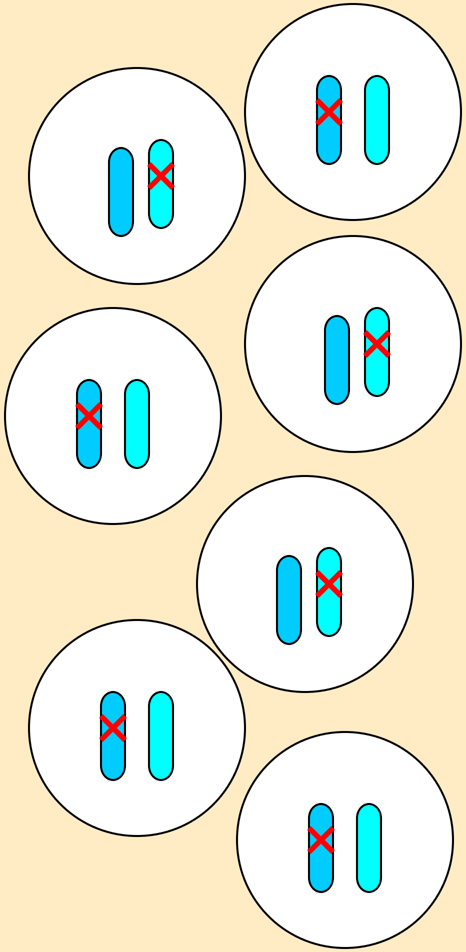
To answer that, we have to do a quickie lesson on the X chromosome

- The X chromosome is one of two "sex chromosomes." The other is the Y. Together, these two determine our gender: females have two X's (XX) and males have one X and one Y (XY).
- However, only one X chromosome is "active" in females, just as the one X is active in males. This prevents females from getting a "double dose" of the effects of the genes on the X.
- In every cell in females, one X chromosome remains active, while the other becomes inactive.



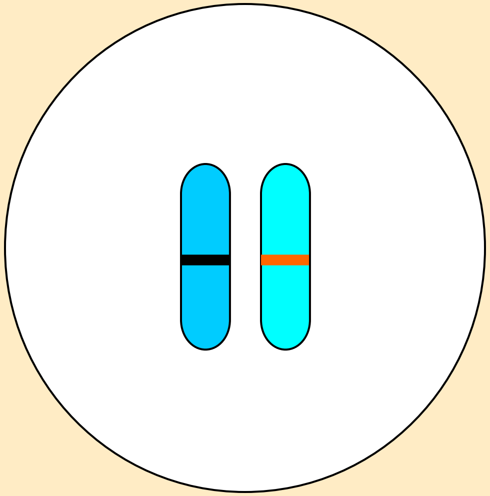
Picture courtesy of Indigo Industries

X-Inactivation



- In every cell, one X chromosome undergoes the process known as X-inactivation VERY early in the embryonic stage.
- X-inactivation is random. This means that one X may be active in some cells and inactive in others. Once inactivated, the effect is permanent.
- The two X chromosomes may have different alleles (i.e. different versions of the same gene) on them. Which means, whichever X is active, the allele on that X will be expressed. The allele on the inactive X will not be expressed.
- One more thing to keep in mind: daughter cells resulting from cell division (e.g. mitosis) will have the same inactivation pattern as their parent cell.

X-Inactivation in Rainbow and CC



- Calico cats have coat color genes on the X chromosome. The gene has two alleles: one for black fur and one for orange fur. Rainbow had one black allele on one X chromosome and one orange allele on the other X chromosome.
- CC, being Rainbow's clone, also had one black allele and one orange allele.
- The color that each cell expresses is dependent on which X is active and which is inactive.

X-Inactivation in Rainbow and CC

- Rainbow's random X-inactivation pattern gave her the coloring she has. Some cells express black fur, others express orange fur.
- The cell nucleus Rainbow donated to CC had already gone through X-inactivation. That cell had the X for black fur active and the cell for orange fur inactive.
- All of CC's cells originally came from that one donated cell and therefore could express the gene for black fur, but not the gene for orange fur, even though she had an allele for both.
- As a result, CC has no orange fur at all!
- To make it *really* complicated, further independent genetic effects result in white fur in some places instead of black or orange. While the appearance of white fur is similar in Rainbow and CC, it is not identical.

What can we learn from this?

- Even if two beings start out as genetically identical, there are many factors which occur after fertilization that lead to differences in appearance. Clones will not necessarily look exactly alike!
- And what about acting alike? It's the old discussion of nature vs. nurture
- Clones are not two versions of the same thing – they are separate individuals

Issues in Cloning: Time for Discussion

- Cloning is a very controversial subject. When discussing cloning, there are three types of issues to consider:
  - Ethical: potential moral outcomes of cloning technology
  - Legal: whether and how cloning should be regulated by the government
  - Social: how cloning will affect society as a whole
- When addressing a certain question about cloning, ask yourself:
  - What are the benefits? What are the risks?
  - Whom will this hurt? Whom will it help?
  - What does this mean for me? My family? Others?
  - Why might others not share my view?

What do you think?

- Is human cloning “playing with nature?” If so, how does it compare with other reproductive technologies such as in vitro fertilization or hormone therapies?

- If a clone originates from an existing person, who is the parent?

- If someone pays to have a clone of themselves created, is that clone “property?” Can they be treated as a slave or bought and sold at whim?

What do you think?

- Does therapeutic cloning (e.g. cloning to create stem cells for use in medical treatments and research) justify destroying a human embryo? Why or why not?

- Do the benefits of cloning outweigh the costs in regards to the uniqueness of human beings?

What do you think?

- What are some of the social challenges a cloned child might face?

- Should cloning research be regulated?