

TERM PAPER BIOLOGY CLASS

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DOLLY

reproductive cloning

1. Preface

Everybody knows Dolly, everybody has heard of her, everybody knows that Dolly has something to do with cloning. But hardly anybody knows what Dolly really was and which biological techniques were applied.

So we decided to take a deeper look at this subject, decide whether Dolly was a good or a bad thing and what Dolly meant for the scientific history of cloning.

An especially interesting feature about Dolly is the ethical discussion. Is it right to interfere in nature's affairs? Should humanity take over the natural process of reproduction? Should the scientists decide over life and death of animals or later even humans?



Fig. 2 | Dolly and her creator Ian Wilmut

- ① Why was Dolly created?
- ② How was Dolly created?
- ③ Was the Dolly experiment successful?
- ④ What has Dolly changed in science?
- ⑤ Did Dolly have a successful life?

2. Introduction

2.1. Context - It's all about cloning!

Cloning is making an exact copy of a plant or animal. This copy is produced out of one cell from the original plant or animal by scientific methods.

Cloning is nothing more than producing an identical copy of an organism. This happens in an asexual way. Cloning is mostly artificial, but happens also in nature (e.g. bacteria, plants and fish).

Dolly was the first mammal that was produced out of an adult soma cell of an adult sheep. But Dolly also was the first "thing to look at" in cloning.

2.2. History of Cloning

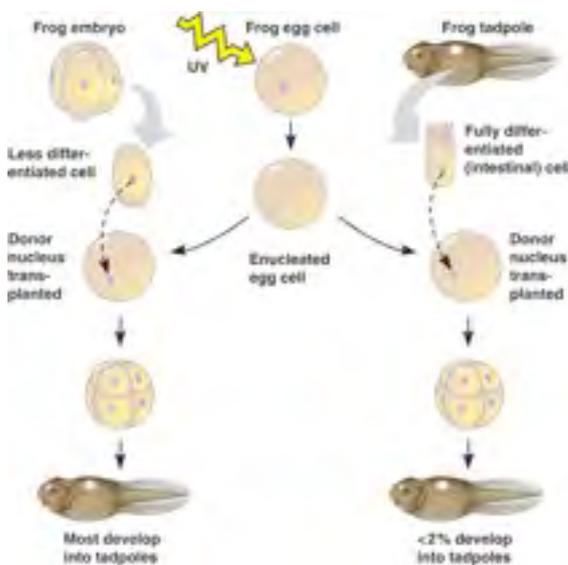


Fig. 3 | The 1950s frog experiment

The early stage of cloning was already developed in 1800 by Hans Dreisch. He wanted to show that genetic material is not lost during cell division.

The next progress was made in the 1950s. Then a frog was cloned. Scientists transferred a nucleus of a frog embryo into a frog egg cell. This was the first time that nuclear transplant was ever used.

In 1986 scientists achieved cloning cow's and sheep's embryos. But still they had problems, for example they could not produce a clone out of a adult soma cell.

The first time scientists cloned a mammal out of soma cells of an adult sheep was in 1996 in the Roslin Institute (→ Chapter 4) in Scotland. Therefore the Dolly experiment is such a famous experiment.

The leader of these experiments was the famous Ian Wilmut.

2.3. Recent Events - Discussion about Eating Cloned Meat

"Die Europaabgeordneten fordern im Gegensatz zu den Ministern, die Vermarktung von Fleisch geklonter Tiere oder deren Nachkommen in der EU zu verbieten.

Die meisten EU-Staaten, darunter Deutschland, hatten im vergangenen Jahr ebenfalls eine eigene EU-Regelung für Klonprodukte gefordert. Allerdings äußerten sie keine grundsätzlichen Bedenken gegen den Verkauf von Klonfleisch. Eine von der EU-Kommission eingesetzte Ethikgruppe war zu der Ansicht gelangt, dass es keine überzeugenden Argumente für die Nahrungsmittelerzeugung mit Hilfe geklonter Tiere oder ihrer Nachkommen gibt. "Fleisch von geklonten Tieren ist nicht in jedem Fall gesundheitsschädlich, aber Risiken können nicht ausgeschlossen werden", so der CDU-Abgeordnete Peter Liese. Bevor entsprechende EU-Vorschriften in Kraft treten können, müssen sich die Staaten mit dem Parlament auf eine gemeinsame Linie

einigen. Sollte der Verkauf von Klonfleisch zugelassen werden, darf dies nur auf der Grundlage einer Vorab-Empfehlung der Europäischen Lebensmittelbehörde erfolgen."

The discussion going on in Europe is about the question whether cloned meat should be eaten or not. The important factors are if it's healthy and ethically correct.

It's still unclear if eating cloned meat is completely harmless. The European 'Lebensmittelbehörde' should work out some guide lines.

2.4. Where And Why Is The Technique Used?

Cloning is used in several industries:

Agriculture needs cloning because they want to avoid variation. Therefore seeds with determined features are cloned asexually.

Therapeutic cloning:

Cloning used to produce native cells for therapeutical uses, say producing healthy cells which can be injected into the patient's body.

Reproductive cloning:

Mainly used in breeding of farm animals or other animals with a special use, for example drug dogs and racehorses.

2.5. Alternative Treatments



Fig. 4 | In-Vitro Fertilisation

Cloning by itself is a unique process. The opposite of cloning is not cloning, there are no alternative treatments. But some different strategies to clone exist (therapeutic and reproductive cloning. One possible "alternative" exists: in-vitro fertilisation.

The mature egg cells of a human female are fertilised with male sperm outside the body and then inserted into the uterus of the same or another human female for normal gestation.

3. Engineering Technique: Reproductive Cloning

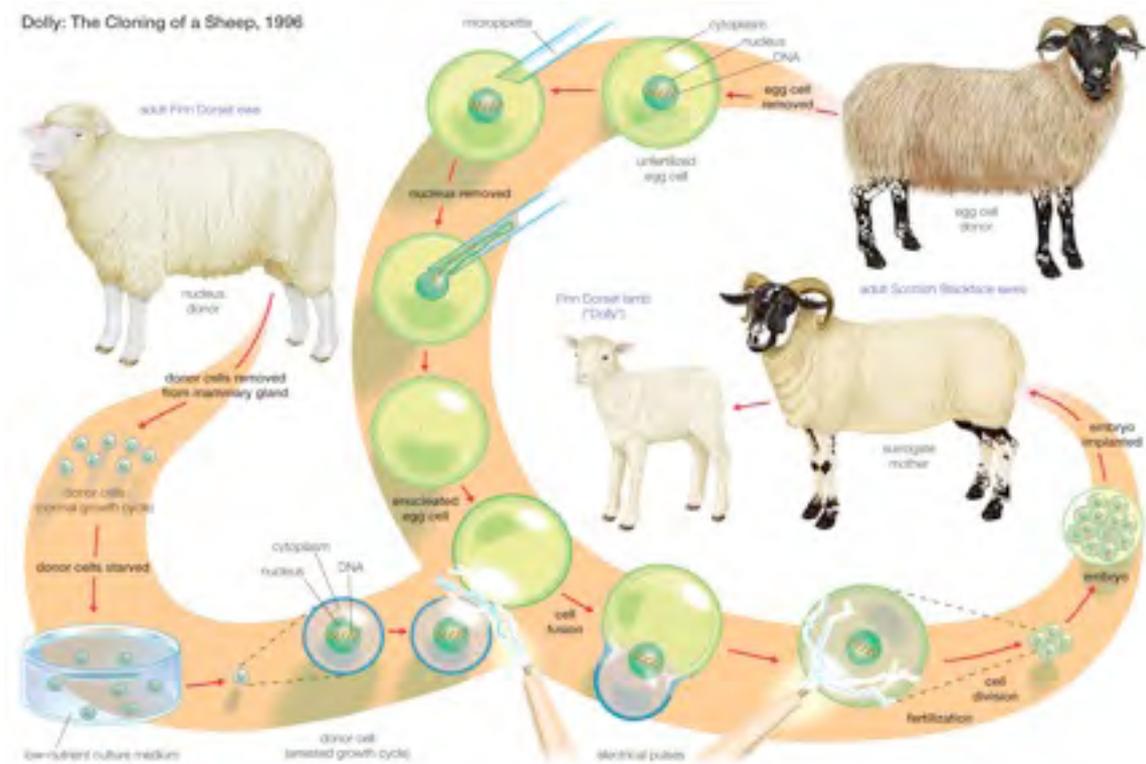


Fig. 5 | Dolly: The Cloning of a Sheep

- ① Donor Cells are removed from the mammary gland (adult Finn dorset sheep, nucleus donor)
- ② Donor cells are starved in nutrient culture medium
- ③ The growth cycle of the donor cells is stopped
- ④ Egg cell is removed from an adult (adult Scottish Blackface Ewes, egg cell donor)
- ⑤ Nucleus of the egg cell is removed
- ⑥ Fusion of the unnuceated egg cell and the mammary gland cell through electrical pulses
- ⑦ Fertilisation
- ⑧ Cell division
- ⑨ Embryo implanted into a surrogate mother, then birth of a Finn dorset sheep

4. Research Institution



Fig. 6 | The Roslin Institute

The Roslin Institute belongs to the University of Edinburgh. Dolly was created there by Ian Wilmut and Keith Campbell. Mostly they deal with Genetics and Genomics, Developmental Biology, Neuropathogenesis, Infection and Immunity and Clinical Sciences.

5. Discussion

5.1. Progress Made

The history of modern cloning began in the 1970s. A lot of techniques which are essential for cloning were invented then. Mice' embryos were developed in-vitro and several experiments tried the embryo transfer of mice and cattle. But very few biologists believed that the cloning of mammals through nuclear transfer would be possible. In the 1980s, nobody could answer these questions. But then an essay by Carl Illmensee about the cloning of mice was published in 1981. It said that three through nuclear transfer formed mice were born in best health. Further experiments of nuclear transfer improved and brought the techniques to perfection. Willadse was the first biologist who cloned a sheep with the help of nuclear transfer. In 1997 Dolly was finally produced.

5.2. Progress Made

Cloning techniques need to be improved so that they can be used in therapeutic cloning. Although therapeutic cloning is not allowed everywhere at this moment, it's a scientific branch with a lot of hope and potential in it, especially for people suffering from genetic diseases. Furthermore the scientists want to avoid any complication possible while applying this technique of cloning. So they want to make sure, that it will be possible to get into contact with cloned animals without any risk for humans (eat cloned meat).

5.3. Discussion

Advantages:

- Big help in medicine
- Important aspect of extensive agriculture
- Food for thought: if one species has got only a few individuals left, cloning could be a way to prevent dying out of this species.

Disadvantages:

- Expensive
- Needs a lot of time because of the time consuming generation shift of mammals
- Low efficiency rate because of imprinting (epigenetic phenomena)

Dangers:

- Disturbing of eco systems
- Disturbing of natural genetic material (which is irreplaceable)
- Loss of value of nature made progress
- Food for Thought: if transgenetic animals are released to natural environment, the whole network of several species getting in contact and eating this animal could be disturbed
- Human's cloning: ethically out of questions

5.4. Questions

- ① Why was Dolly created?
Dolly was the result of about two hundred years of genetical research. The first time a mammal was produced out of adult soma cells. So Dolly was nothing more than the result (or product) of an experiment.
- ② How was Dolly created?
Dolly was produced through reproductive cloning.
- ③ Was the Dolly experiment successful?
Yes, it was. It was all in all successful.
- ④ What has Dolly changed in science?
Dolly was the first thing to look at. She brought up the hot discussion about cloning of humans.
- ⑤ Did Dolly have a successful life?
Yes, more or less. Dolly reached the age of 6.5 years. She died because of Jaagsiekte. Normally sheep reach the age of 20 years, so there were discussions about the early death of Dolly in context to her "production"

6. Summary

Dolly is topic which is or was in everybody's mouth, so we were encouraged to take this topic, especially because nobody really knows which techniques were applied producing Dolly.

Cloning is making an exact copy of a plant or animal. This copy is produced out of one cell from the original plant or animal by scientific methods.

Since 1800, scientist have made a lot of progress. They achieved cloning clone cow's and sheep's embryo. In 1996, finally Dolly was the first mammal produced out of an adult soma cell of an adult sheep.

Cloning of animals is a hot topic. For example, it's still unclear if eating cloned meat is completely harmless.

Cloning is used in agriculture, therapeutic cloning (medicinal reasons), reproductive cloning (drug dogs and racehorses).

There are no alternative techniques to cloning. The in-vitro fertilisation is just another way to force reproduction.

In reproductive cloning, mammary gland cell from one animal is fused with an unnucleated egg cell from another animal of the same species. The cell fusion is forced through electrical or chemical pulses. The embryo is then implanted into a surrogate mother which gives finally birth to the cloned animal.

The Roslin Institute belongs to university of Edinburgh. Dolly was created there by Ian Wilmut and Keith Campbell.

Cloning is an important branch of research, especially in terms of genetic diseases.

7. References

7.1. Books

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Dolly - Der Aufbruch ins biotechnische Zeitalter, Wilmut, Campbell, Tudge (Hanser)
Oxford Student's Dictionary (Oxford)
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7.2. Websites

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History of Cloning: <http://library.thinkquest.org/20830/Frameless/Manipulating/Experimentation/Cloning/longdoc.htm>
Recent Discussions: http://www.aerztezeitung.de/politik_gesellschaft/gesundheitspolitik_international/article/595977/eu-diskussion-fleisch-geklonten-tieren.html

7.3. Images

Figure 1: Google Picture Search
Figure 2: Google Picture Search
Figure 3: <http://www.bio.miami.edu/~cmallery/150/devel/c7.21.6.frog.jpg>
Figure 4: <http://www.babble.com/CS/blogs/strollerderby/2009/02/in-vitro-fertilization-2.jpg>
Figure 5: <http://media-2.web.britannica.com/eb-media/10/70110-050-BBE15F18.jpg>
Figure 6: Roslin Institute-Website

PABLO LABHARDT AND GIULIA OTT, 17.04.2010