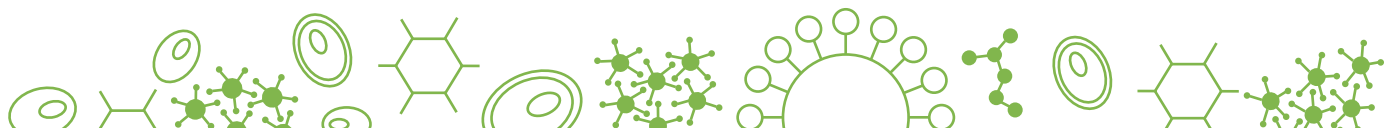


# Understanding Stem Cells The Conference

2 Ethics







## 2 Ethics

In this module, the students work through the legal and ethical basics of stem cell research. As participants in a scientific conference, they prepare a panel, a poster and a pitch.

All students take part in the Panel and Fishbowl task. Small groups work in parallel on the Poster and Pitch tasks. Alternatively, they may complete the *Pitch* task only.

 135 minutes

 **Tasks:**  
*panel, poster, pitch, fishbowl*

 **Material:**  
*Panel*  
*Poster A*  
*Poster B*  
*Pitch*

### Introduction

***“Scientific progress makes moral progress a necessity.”***

Anne Louise Germaine de Stael, French-Swiss Writer, 1766-1817

***“Progress is only possible when you intelligently break the rules.”***

Boleslav Barlog, German director, 1906-1999

### Panel

The students answer the question from a personal standpoint: “At which point on does an embryo represent a life worthy of protection?” A timeline is provided for this purpose. The students should first position themselves on the timeline. Ask individual students about their position. What point in time did you choose? Why?

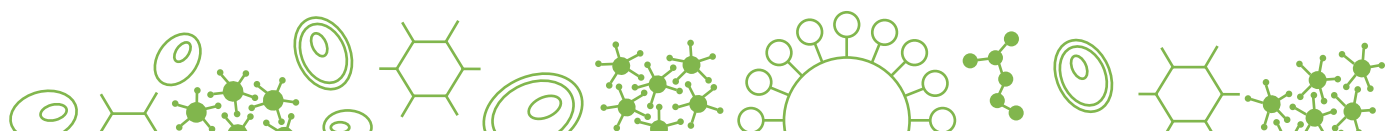
Then distribute the panel material and ask four students to be panel participants and debate with each other. They can each adopt one of the four positions described in the material.

 30-40 minutes

**Large group**  
*Panel exercise sheet*  
*Panel material sheets*

**4 students**


Then distribute either the Poster or the Pitch task





### Poster

Two small groups of students (A and B) each develop a poster. Both groups are given materials on their topic. The students then briefly present their posters. They each have 5 minutes to do this. The audience can ask questions.


 30 minutes preparation  
2 x 5 minutes presentation  
2 x 5 minutes questions

#### 2 groups

Poster exercise sheet  
A poster material sheets  
B poster material sheets  
Flip chart-Paper and pens/  
pencils Stopwatch

### Pitch

The students work in two groups. They all read the research project material. One group prepares a short pitch on the project. The other group prepares test questions on the project. Notes on presentation structure and test levels are given to the students on the exercise sheet.


 30 minutes preparation  
10 minutes presentation  
10 minutes test

#### 2 groups

Pitch exercise sheet  
Pitch materials sheets

### Fishbowl

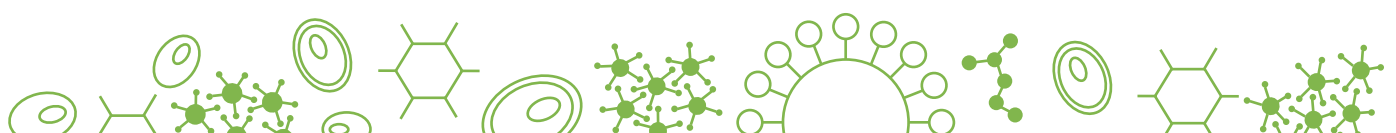
Students work in 3 groups. Everyone reads the 'Fishbowl' handout. Working in their groups, students then prepare arguments for one of the three positions. The worksheet includes information on these positions and a suggested structure for the opening statement. Each group also prepares three critical questions for, or counterarguments, to the other positions.

 20 minutes preparation  
3 x 1 minute opening statement  
20 minutes discussion

#### 3 groups

Fishbowl worksheet  
Fishbowl handout

Place four chairs at the front of the class. Each group sends one speaker into the fishbowl. The speakers each take a seat and outline their positions in an opening statement. The groups then take it in turns to send one person into the fishbowl to introduce one of the prepared questions or counterarguments into the debate. To do so, they take a seat on the unoccupied fourth chair.



**Online fishbowl**

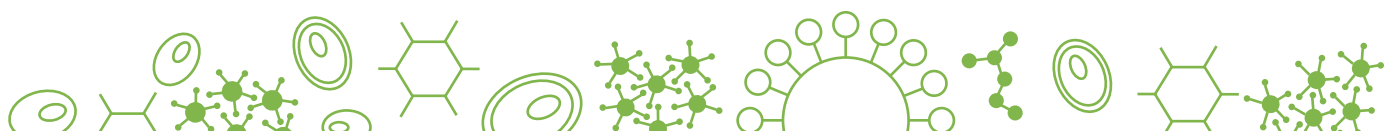
You can also use the fishbowl technique in online lessons.

1. Tell the students to read the 'Fishbowl' handout.
2. Meet up in your virtual classroom.
3. Welcome the class to the 'Fishbowl' online conference.
4. Introduce the 'Fishbowl' worksheet.
5. Divide the students into three groups and use the meeting tool to get the groups working through the exercise (on Zoom, for example, groups can be assigned and activated using "breakout rooms").
6. Come back together in the online classroom for the fishbowl.
7. The three speakers should make their opening statements and begin the debate.
8. The groups then pose their questions and make their counterarguments. To become involved, students can raise their hands or use the appropriate meeting tool feature (on Zoom, for example, listeners can use the reaction button or the messaging feature).

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**Outlook**

"Our conference continues. In the next module we look at therapies based on stem cell research."





# Panel

A podium discussion at scientific conferences is also referred to as a panel. In these discussions, experts exchange their positions on a specific topic.

**TASK** First, imagine a timeline. The timeline begins with fertilization and ends at birth. Stand at the position you represent. Describe your position and why you represent it.

Send four representatives with different positions to a panel. Possible positions may be:

Position 1: **From fertilization**

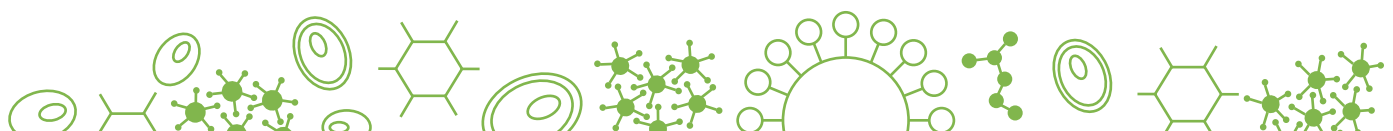
Position 2: **At implantation in the uterus**

Position 3: **The embryo becomes worthier of protection with time**

Position 4: **Only after it is viable outside the womb**

**OBJECTIVE** The four panel participants debate for 10 minutes. The public may then ask questions.

**TIP** In addition to the Panel material sheets, you can also use the Poster A material sheets to give your position a legal basis.





## Poster

Posters are used at conferences to present research projects and results. They are often designed using a template that conference participants use for the presentation.

**TASK** Work in two groups. One group designs a poster on the topic *Legal framework for stem cell research in Germany*. The other group designs a poster on Subject protection: *questions that patients should ask*.

**OBJECTIVE** Your poster offers a brief overview of your topic. The most important regulations should be apparent in the legal framework. Historical developments should be recognizable. Develop a patient checklist for subject protection.

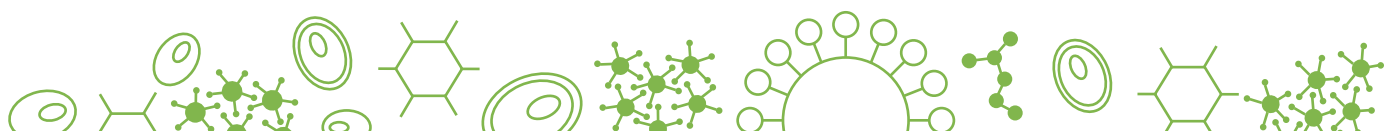
**TIP** Use the Legal Basis and Subject Rights material sheets to prepare, as well as the short film *Patient Cells – an Ethical-Legal View* with Nils Hoppe.

**BONUS** Establish a comparison between international legislation and jurisprudence.

### Poster topics

Poster A: Legal framework for stem cell research in Germany

Poster B: Subject protection: questions that patients should ask





# Pitch

A pitch is a short presentation advertising a project. Scientific pitching of research projects to find support for your research proposal.

**TASK** Work in two groups.

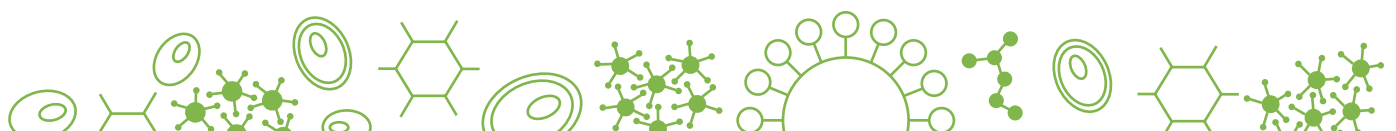
One group prepares a pitch on a research project. The project aims to produce induced pluripotent stem cells for disease models.

The other group are conference participants. They examine the project on three levels:

- 1. Feasibility: Is it legally, organizationally and financially feasible?**
- 2. Benefit: Who profits from the project and who may be harmed?**
- 3. Morality: Are any ethical values violated by the project?**

**OBJECTIVE** Your pitch should convince the conference participants that the project is important and worthy of funding. As a conference participant, you should question this critically

**TIP** In addition to the New Aids for *Disease Research* text, use the material sheet Poster A: *Legal Basis*.





# Fishbowl

A fishbowl is a special type of discussion used at scientific conferences. Conference participants share their perspectives on a specific topic. Participants from the audience are able to join the discussion at any time. An extra chair is laid out, on which anyone can come and sit and explain their point of view.

## TASK

Prepare a fishbowl on the following issue:

Should it be legal to modify the human germline using designer nucleases?

**Work in three groups. Each group should prepare one of the following three positions:**

- 1. No, modifying the germline should not be permitted under any circumstances.**
- 2. Yes, but modifying the germline should only be permitted for the purpose of curing serious diseases.**
- 3. Yes, modifying the germline should be permitted to cure disease and to enhance human characteristics such as intelligence, strength, endurance, and appearance.**

Gather together arguments for your position. Prepare an opening statement.

Prepare three critical questions for or counterarguments to the other two positions.

## TIP

You can use the following structure for your opening statement:

Introduction: Today, we are asking whether it should be permissible to modify the germline.

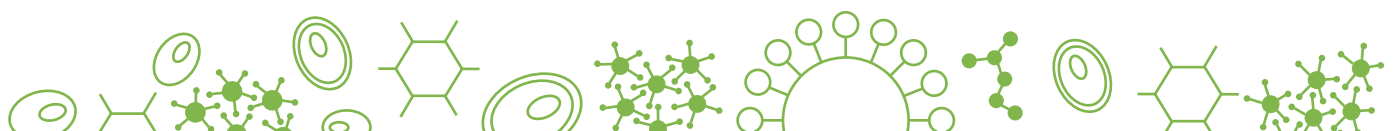
Thesis: We believe: (Position 1, 2, or 3)

Argument 1: One reason for this is ...

Argument 2: A further argument for this position ...

Argument 3: The key reason is that ...

Thesis: It therefore follows that (position 1, 2, or 3)







# From which point on does an embryo represent a life worthy of protection?

## Position 1: From fertilization!

### *Reasoning (example):*

The development of a fertilized egg cell into an infant is a continuous process, and any attempt to determine at what point of development the human individual begins would be an artificial definition. A human embryo is an embryonic human being, comparable to an infant, who is also a human being

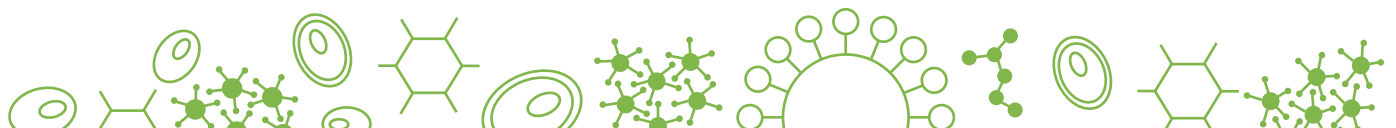
at the infant stage. And although an embryo does not yet have all the characteristics of a full-grown human, it has the potential to develop into one and should therefore be treated with the necessary respect for the dignity of a human being.

## Position 2: At implantation in the uterus!

### *Reasoning (example):*

Successful implantation is the prerequisite for embryonic development. Implantation takes place about six days after fertilization. From implantation on, the embryo must be treated with the necessary respect, namely humanely. In nature, it often

happens that the fertilized egg is not successfully implanted in the uterus but is rejected. We therefore have no knowledge of these embryos. In fertility treatment (in vitro fertilization), this stage is only an accumulation of cells in an artificial environment.





### Position 3: The embryo becomes worthier of protection with time!

#### *Reasoning (example):*

When someone dies, people tend to feel the loss differently, depending on how old the person was. A fertilized egg prior to implantation in the uterus may therefore receive less attention than an embryo or a baby already born. More than half of fertilized eggs are lost for natural reasons prior to implantation. So, if this loss is considered part of the natural process, the use of some embryos in stem cell research should not cause us any moral concerns.

In our legal system, people are granted personality rights only after birth. But there are other protective rights that the embryo already enjoys before birth. There are some stages of embryonic development that could give rise to increasing status worthy of protection:

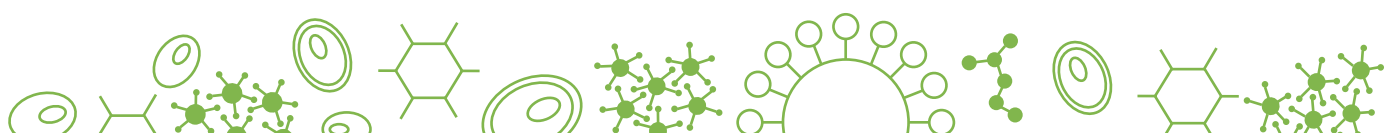
1. Implantation of the embryo into the uterine wall, approximately six days after fertilization
2. The appearance of the primitive streak, which is associated with the first sign of a developing nervous system, approximately at day 14. After the 14th day, it is impossible for the embryo to divide to form twins. Until then, the embryo can still divide to become two or more fetuses, that is, multiple individuals. Likewise, further development can cease completely.
3. The stage of development at which the fetus would be able to survive outside the uterus (approximately 24 weeks) if born prematurely
4. Actual birth (after approximately 40 weeks)

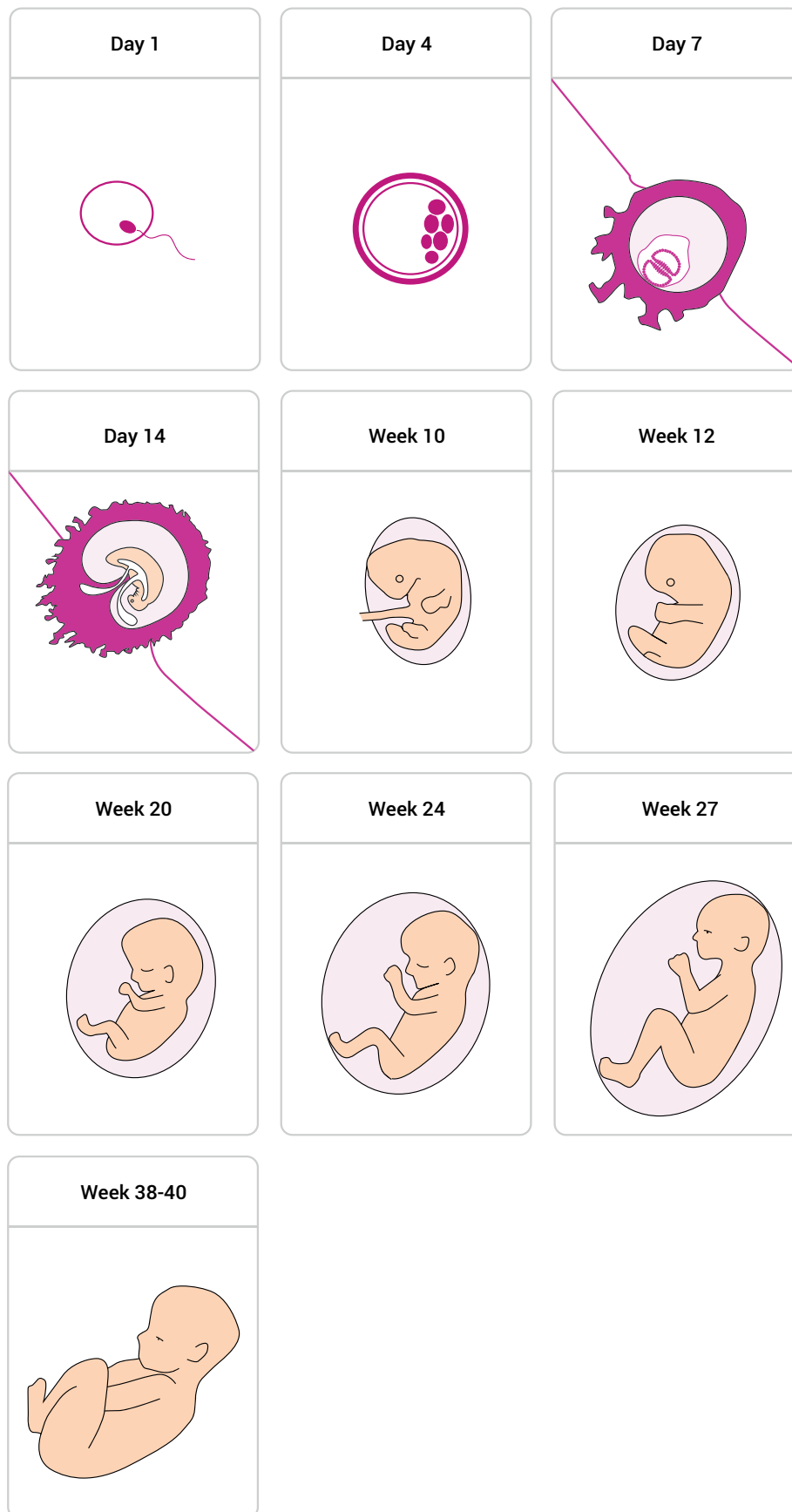
### Position 4: Only after it is viable outside the womb!

#### *Reasoning (example):*

Fertilized human egg cells remain simply parts of the human body until they have developed far enough to survive on their own. We should show the same respect for a blastocyst as we would also show to

the property of others. If we destroy a blastocyst prior to implantation, we do it no harm, as it has no hopes, desires, expectations, goals or intentions that we could harm.



**Day 1**

Conception or fertilization: sperm and oocyte unite.

**Day 4**

The blastocyst forms. The cells separate into placental cells and other cells, the inner cell mass that later forms the fetus. In the laboratory, embryonic stem cells are harvested at about this time from the inner cell mass of the embryo, which is destroyed in the process.

**Day 7**

The embryo is implanted in the womb.

**Day 14**

The first nervous system cells are produced. Many embryos die naturally before reaching this stage. In many countries, for example the United Kingdom, this also represents the limit for embryo research. In Germany, destructive embryo research is prohibited.

**Week 10**

All organs and extremities are already formed. From this stage onward, the embryo is regarded as a fetus. The gender can now be determined.

**Week 12**

The fetus now makes controlled movements and looks human. It has facial features. In Germany, this is the legal limit of impunity for a termination of pregnancy, with the exception of medical grounds.

**Week 18-20**

The mother can feel the movements of the fetus.

**Week 24**

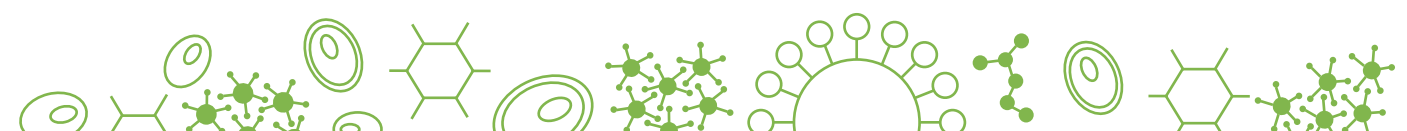
The fetus reacts to light and sounds. Premature births have a chance of survival from this point on.

**Week 27**

The eyes open.

**Week 38-40**

The baby is completely developed.





# Laws and guidelines

## 1. Constitutional law

### Basic Law for the Federal Republic of Germany

The Basic Law is the Constitution of the Federal Republic of Germany. It is the basis for the essential government system and value decisions. It stands above all other German legal norms.

#### Article 1

Human dignity shall be inviolable. To respect and protect it shall be the duty of all state authority. The German people therefore acknowledge inviolable and inalienable human rights as the basis of every community, of peace and of justice in the world. The following basic rights shall bind the legislature, the executive and the judiciary as directly applicable law.

#### Article 2

Every person shall have the right to free development of his personality insofar as he does not violate the rights of others or offend against the constitutional order or the moral law. Every person shall have the right to life and physical integrity. Freedom of the person shall be inviolable. These rights may be interfered with only pursuant to a law.

#### Article 3

All persons shall be equal before the law. Men and women shall have equal rights. The state shall promote the actual implementation of equal rights for women and men and take steps to eliminate disadvantages that now exist. No person shall be favoured or disfavoured because of sex, parentage, race, language, homeland and origin, faith, or religious or political opinions. No person shall be disfavoured because of disability.

#### Article 4

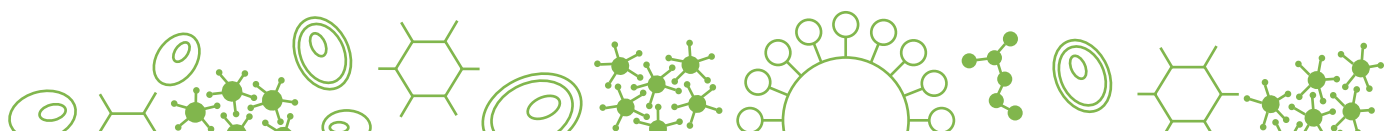
Freedom of faith and of conscience, and freedom to profess a religious or philosophical creed, shall be inviolable.

The undisturbed practice of religion shall be guaranteed. No person shall be compelled against his conscience to render military service involving the use of arms. Details shall be regulated by a federal law.

#### Article 5

Every person shall have the right freely to express and disseminate his opinions in speech, writing and pictures, and to inform himself without hindrance from generally accessible sources. Freedom of the press and freedom of reporting by means of broadcasts and films shall be guaranteed. There shall be no censorship.

These rights shall find their limits in the provisions of general laws, in provisions for the protection of young persons, and in the right to personal honour. Arts and sciences, research and teaching shall be free. The freedom of teaching shall not release any person from allegiance to the constitution.





## 2. Simple Right

### 2.1. Act for the Protection of Embryos (The Embryo Protection Act)

The Embryo Protection Act regulates the artificial insemination and the handling of human embryos. The purpose of the law is to protect human life from the beginning.

§ 8 of the Embryo Protection Act already defines the fertilized, viable oocyte as an embryo. An egg cell can be developed within 24 hours after the merger (§ 8 para. 1). In addition, every cell taken from an embryo is considered an embryo itself if it could develop into a complete individual (totipotency). In § 1 is enumerated which abusive applications of the reproductive techniques are punished. This includes, for example, the artificial insemination of oocytes for a purpose other than to induce a pregnancy (§ 1 Abs. 1 No. 2). Also, no more egg cells may be fertilized than can be transmitted to a woman in a cycle. By doing so, the legislator is preventing high-grade multiple pregnancies that would jeopardize the life of the mother and children. The maximum number of embryos that can be transferred is set at three (§ 1 (1) no. 3). This regulation has the consequence that in Germany with artificial inseminations no so-called „surplus embryos“ arise, since all manufactured embryos (maximum three) are always transferred.

§ 2 deals with the misuse of the human embryo. Here the trade with embryos is forbidden (§ 2 exp. 1). In addition, further treatment of an embryo outside the womb is only permitted if the embryo is subsequently transferred to the mother (§ 2 (2)).

*Source: Federal Law Gazette, Date: November 2011*

### 2.2. Law ensuring the protection of embryos in connection with the import and use of human embryonic stem cells (German Stem Cell Act – StZG)

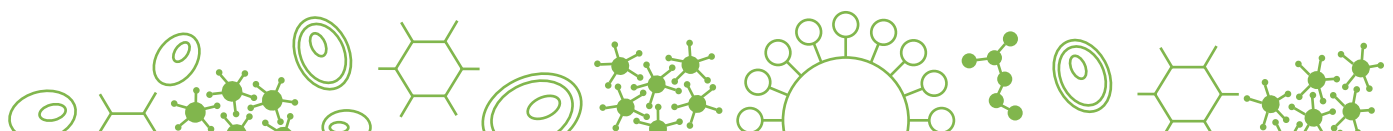
In accordance with the constitutional obligation of the state, the German Stem Cell Act seeks to respect and protect human dignity and the right to life, and to guarantee freedom of research (§ 1 Para. 1).

The German Stem Cell Act is a ban with reservation of permission. It fundamentally prohibits the import and use of embryonic stem cells. It is intended to prevent the commissioning of overseas production of embryos for stem cell research or the production of embryonic stem cells from existing embryos from German soil (§ 1). The production of embryos for stem cell research or the production of stem cells from existing embryos in Germany is already banned by the German Embryo Protection Act.

However, the German Stem Cell Act also lays down the conditions under which the import and use of embryonic stem cells for research purposes may be authorized in exceptional cases (§ 1 and § 4).

These conditions include the condition that embryonic stem cells were obtained abroad from surplus embryos before the deadline of May 1, 2007 and are no longer needed to induce pregnancy. And that no money was paid for the transfer of these embryos (§ 4 Para. 2 No. 1).

The law prescribes strict criteria for research on embryonic stem cells in Germany. For example, the research must serve high-ranking research goals and must not be feasible using other cell types (§ 5).



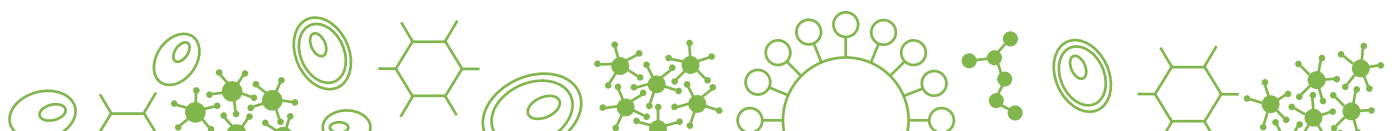


### 3. Institutions

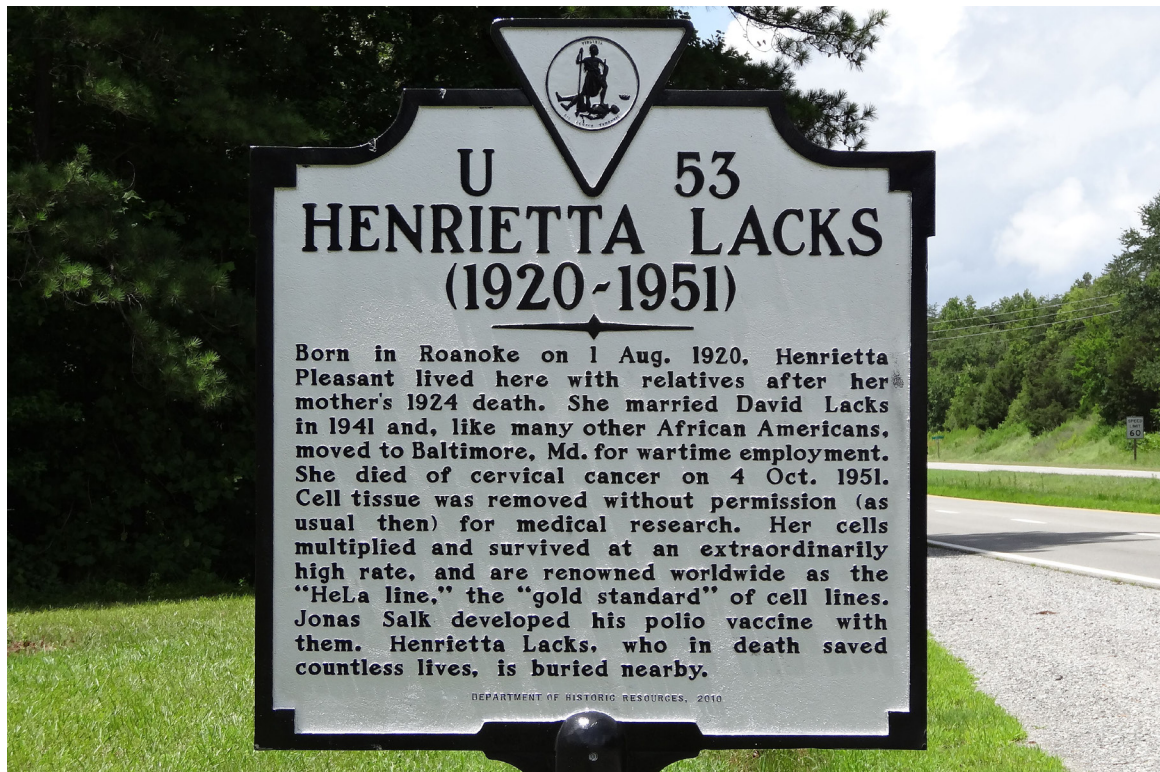
#### **The German Central Ethics Committee for Stem Cell Research**

The German Central Ethics Committee for Stem Cell Research (ZES) is an interdisciplinary commission of experts in the fields of ethics, theology, biology and medicine. It is based at the Robert Koch Institute, the responsible federal institute in the field of biomedical research. The committee examines applications under the German Stem Cell Act and clarifies whether a derogation can be granted. The following questions are clarified: How important is the research objective?

How well has the research project been prepared and clarified? How great is the necessity for the use of human embryonic stem cells (hES cells)? The committee assesses whether the research project is ethically acceptable within the context of the German Stem Cell Act. It submits an opinion to the Robert Koch Institute for each research project in which hES cells are to be used. The German Central Ethics Committee for Stem Cell Research was first appointed on July 1, 2002, when the Stem Cell Act came into force.







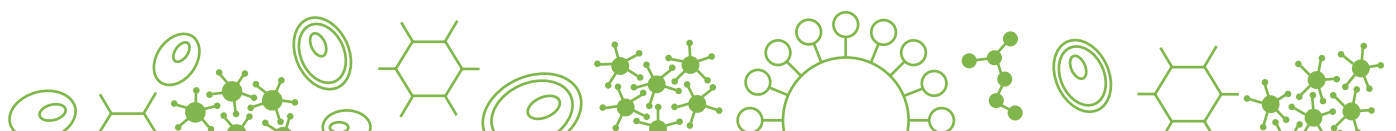
## Subject rights

### HeLa cells

HeLa cells have been used in research since the 1950s. This is an immortal cell line, which is very well suited for testing the polio vaccine, for example. The cell line is now commercially distributed and used for many experiments. Thousands of patents pending worldwide are based on scientific findings from experiments with HeLa cells. There is a special story behind this cell line and its name: Henrietta Lacks was a patient at Johns Hopkins Hospital in Baltimore. In 1951 she was treated there for a cervical tumor. The Johns Hopkins Hospital was one of the few hospitals that also treated African American patients. Often, tacit consent was assumed for participation in studies. Henrietta Lacks' gynecologist, Howard W. Jones, removed a cell sample from the tumor. He handed it over to cell researcher George Otto Gey, who developed the potentially immortal HeLa cell line.

Based on the name of the patient Henrietta Lacks, he called them HeLa cells. Henrietta Lacks was never informed about the use of her cells. Even her family only learned years later of the use of the cells. Excerpts from Henrietta's patient file were published without the family's consent.

In 2013, her genome sequence was decrypted and included in a freely accessible database. This triggered a global debate. Only thereafter was an agreement arrived at with Henrietta Lacks' descendants, which regulates the use of the data. Two family members today have seats in a committee that decides on access to the DNA code.





## Informed consent

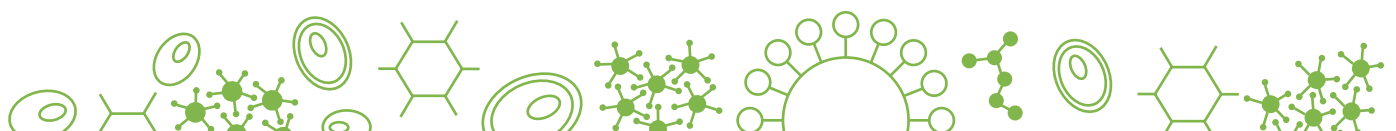
Patients must consent to medical treatments

This includes the use of their cells for research.

By *informed consent* we mean that a patient is in a condition to be able to make the decision for themselves. The legal term for this is the capacity to consent. In exceptional cases, a proxy may also give this consent. The scientist also has a duty to inform. Only when the patient has been informed, can he or she give an informed consent. Informed consent emerged as early as the beginning of the 20th century as an ethical research principle. It has nevertheless been repeatedly violated.

It was not until 1964 that the World Medical Association incorporated informed consent in its ethical principles for medical research on humans at its General Assembly in Helsinki – not least because of the atrocities committed by Nazi doctors on their Jewish prisoners. The document is therefore known as the Helsinki-Declaration.

There is still some disagreement about whether it is possible to fully inform the patient and how the capacity to consent is defined in detail.







## NEW AID IN DISEASE RESEARCH:

# Reprogrammed cells as a model for disease research

*By Christian Unger for EuroStemCell, revised by Tobias Cantz.*

In order to understand and successfully combat diseases, research must be carried out in the laboratory. In order to allow an ideal examination of the disease-specific manifestations in the affected tissues or cells, small tissue samples from diseased patients are an important resource. However, they are not available for all diseases or can only be gained under unreasonable conditions.

*Disease models* can circumvent these problems by enabling scientists to simulate diseases in the laboratory. Because pluripotent stem cells can also be differentiated in a cell culture dish – at least theoretically – to form any of the body's cell types, human embryonic stem cells (hES) and what are known as induced pluripotent stem cells (iPS) are increasingly being used to breed diseased cell types or even tissue types in the laboratory.

## Why do we need disease models?

Whether life threatening or not, a disease can often only be successfully treated if we understand its biological basis. Disease models allow scientists to simulate certain aspects and, for example, to decode them at the molecular level. In this case, a disease model maps the misdirected biology, for example in the computer, in animals or in cells. Such models provide helpful insights into diseases. They make it possible to repeat experiments relatively simply and very robustly in order to obtain reproducible and trustworthy results. Our understanding of complex biological systems in the human organism remains limited. Different manifestations of the same disease are difficult to study and model. A first step in exploring such complex diseases is to analyze only individ-

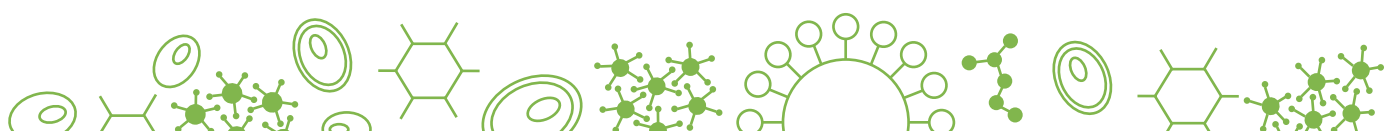
ual cells or groups of cells in the laboratory, rather than looking at complex tissue or the whole body.

## Human cells as a model for disease research

Animal models, such as laboratory mice, are well established in research and can model many aspects of human diseases. However, animals can never reproduce all aspects of human biology or disease. While treatment methods that have been effective in experimental animal models can often provide essential clues and information, they do not always work in humans. In addition, there are a number of diseases, including metabolic diseases or neuronal diseases, for which there are no meaningful animal models. Human cells were first cultured in the laboratory in the 19th century. Since then, our understanding of cells has made great progress. In particular, cancer cells have played an important role, as they are much easier to multiply in vitro than healthy tissue cells.

## What advantage do stem cells have for disease models?

Stem cells can renew themselves and differentiate into different types of specialized cells. Induced





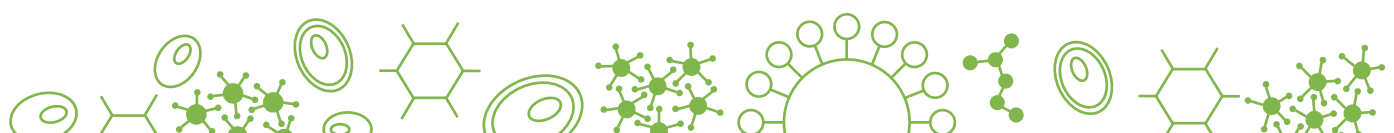
pluripotent stem cells (iPS) offer the new possibility of using pluripotent patient stem cells and of growing the relevant cell types or tissue types from them in the laboratory. The use of iPS is particularly advantageous in those diseases in which genetic components such as defective genes or certain genetic polymorphisms play a role. The reason: they possess the identical genetic make-up and generally reproduce the disease type reliably and authentically. Stem cell models have an additional benefit: many diseases are often only discovered when pronounced symptoms occur, namely, only long after the actual onset of the disease. The original development of the disease is often difficult to reconstruct and understand. Using stem cells, researchers can take a travel for a short period in time and produce every type of cell, whether in an early or a late stage of the disease.

### Current and future developments for stem cell disease models

However, some diseases have a very broad genotype-phenotype correlation: Although the disease is based on the same genetic defect (genotype), the severity of the phenotype is very different in different patients. In these cases, new research approaches attempt to investigate iPS-cells from multiple patients displaying different phenotypes and to repair the underlying genetic defect in each individual patient-specific iPS-cell line using new methods of precise genome editing. Then, for each patient, the healthy and diseased iPS cell line can be examined

in pairs, which allows very reliable observations.

Now, if different phenotypes of the same disease are based on different mutations of the gene in question, the difficulty arises that a specific control cell line would need to be generated for each individual mutation. Given ten mutations, then, two times ten cell lines would need to be investigated. Some scientists therefore prefer to start with an intact control cell line (ES or iPS) and to then generate sub-cell lines into which the respective mutation has been inserted. Given ten mutations, then, only ten plus one cell lines would need to be investigated. In summary, ES-cells and iPS cells offer the possibility of establishing artificial but authentic disease models in vitro. They thus help to better understand a disease. Moreover, the disease models can be used to develop and test medicines and treatment methods directly on the *cell patient*.





## THE ETHICS OF GERMLINE THERAPY

### CRISPR babies

## Is it acceptable to genetically modify embryos?

*By Martin Lindner*

Using sophisticated ‘molecular scissors’, we can, in principle, now make specific changes to an embryo’s genetic material. However, any such changes would not just affect the child that develops from that embryo – they would also affect all of that child’s descendants. In 2018, a Chinese researcher claimed to have carried out the first ever germline therapy intervention in humans – sparking a huge furor. What purpose would modifying the embryonic genome serve? And what about the ethical issues?

### Lulu and Nana

It’s a real-life scientific thriller. In November 2018, Chinese researcher He Jiankui announced the birth of twin sisters who he claimed to have genetically modified as embryos while still in a Petri dish. The two girls are believed to be the first babies in the world to have had their germline genetic material deliberately modified. The girls were nicknamed “Lulu” and “Nana”.

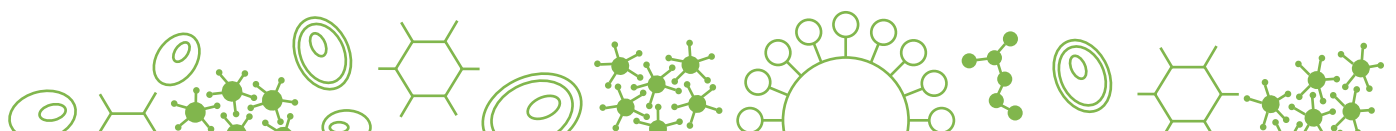
In a talk at an international conference in Hong Kong, He stated that his goal had been to make the children resistant to HIV. During the IVF process, He had used gene-editing techniques on the developing embryos to modify a cell receptor called CCR5. This receptor is used by HIV to get into somatic cells, and people with specific mutations in this receptor gene are immune to most strains of the virus.

The case made headlines worldwide. Instead of publishing it in a peer-reviewed scientific journal – the usual practice among scientists – He announced the birth of Lulu and Nana on YouTube. He emphasized that HIV-positive people suffer discrimination in many countries, and that his experiments represent a major scientific breakthrough. The case unleashed a storm of protest.

### A Brave New World? Gene editing and what happened next

The tool He used is known as CRISPR/Cas9. It has been compared to molecular scissors. CRISPR/Cas9 is an enzyme complex which can be used to easily modify specific genes and remove existing or insert new stretches of DNA. The process is sometimes referred to as gene editing or genome engineering. CRISPR/Cas9 is already used in plant breeding and for genetically modifying animals in the laboratory. There are, however, technical complications to its use. The technique can result in only some of an embryo’s cells being genetically modified. This is known as mosaicism. In addition, unintended mutations away from the target gene (known as off-target effects) can also sometimes occur, giving rise to unforeseen risks.

And the gene editing process in Lulu and Nana was indeed only partially successful. It remains unclear what the consequences of this will be for the two girls. Researchers worldwide accused He and his team – which included his American doctoral supervisor – of being irresponsible in their use of what remains an immature technology.





He's experiments make a mockery of the international consensus that, as things stand today, researchers should not be using gene editing techniques in the context of fertility treatment. Furthermore, He did not properly inform his own university what he was up to and did not properly brief the couple involved. Shortly after his lecture in Hong Kong, the Chinese authorities suspended He's research activities, and in late 2019 sentenced him to three years in prison and a substantial fine. By then, in addition to Lulu and Nana, this unique set of experiments had also resulted in the birth of a third CRISPR baby.

### The ethical debate – is it acceptable to modify someone's genetic inheritance?

Is it acceptable to genetically modify human embryos? Assuming it proved possible at some future date to resolve the scientific uncertainties around the process, could gene editing be ethically acceptable in some circumstances? A key point in the debate is that genetically modifying an early embryo doesn't just affect the child that develops from that embryo. The modifications will also be passed on to all of that child's descendants via the child's germ cells (egg cells or sperm). Changes to germline cells affect a person's genetic inheritance. The issue of the ethics of germline modification is highly controversial. Points of view include the following:

» **As a matter of principle, gene editing in embryos should be prohibited entirely:**

A developing embryo and its potential descendants are possessed of an intrinsic dignity and identity. Its genome should be sacrosanct. This point of view may be motivated by respect for the principles of human life or by religious conviction.

» **Germline therapy is acceptable where the benefits clearly outweigh the risks:**

Future gene editing techniques could be used to help prevent serious genetic disorders such

as cystic fibrosis, hereditary breast cancer, or Huntington's disease (a progressive, degenerative brain condition which causes locomotor problems). As long as the risks are controllable, prohibiting the use of such therapies would be unethical. Doctors in particular often tend towards this view. It is frequently bound up with a conviction that genome editing should only be used for treating or preventing disease, and not for genetic "enhancement", e.g. for enhancing intelligence. It should also be noted that genetic modification of an embryo is always carried out in the context of IVF, which carries its own risks.

» **There are usually alternatives to germline therapy available, rendering it unnecessary:**

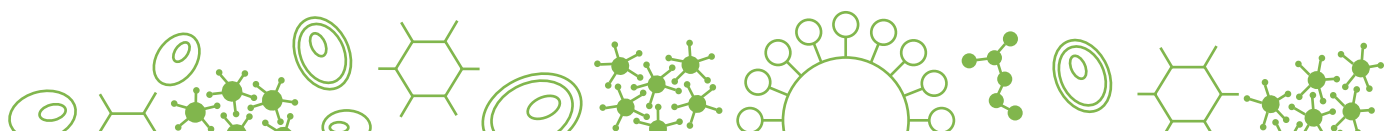
Some genetic defects can also be treated after a child is born – for example, using gene therapy which targets the relevant somatic cells (somatic gene therapy). In addition, using preimplantation genetic diagnosis (PGD), it is possible to identify embryos with serious genetic diseases prior to implantation, and these embryos can then be discarded. But PGD is of no help where both parents suffer from cystic fibrosis, for example, since all of the couple's embryos will also have the disease. In rare cases like this, gene editing would enable such couples to have a healthy child who is biologically theirs.

» **Genetically modified babies harm society, as they create an impression that illness and disability are abnormal and are something to be prevented:**

This argument comes up in the context of various debates in the reproductive medicine field, for example in the debate revolving around PGD. It is raised in particular by organizations representing disabled people, as well as other critical voices. They are concerned that people with genetic defects will suffer discrimination.

» **Parents should be able to decide for themselves:**

On the other hand, parental freedom of choice –





reproductive autonomy – is also of high value. Advocates of this position often cite the rights of the individual in a liberal society.

## Genetically modified embryos in research

Whether germline modification will eventually become established medical practice remains unclear. Researchers nonetheless continue to look for ways to develop these techniques further and to minimize the risks involved. One approach to doing so is to genetically modify laboratory animals, breed several generations of offspring and see if any long-term effects are observable.

In some places research is also being conducted on spare human embryos that are not destined to be implanted to produce a pregnancy. A team from the Francis Crick Institute in London, for example, is editing the genome of embryos left over from IVF and studying them in the lab for a period of one week. Their research is aimed at enhancing our understanding of how genes control early embryonic development. Similarly, researchers from Oregon Health and Science University in the US are exploring the possibility of correcting inherited heart diseases in the embryo.

This kind of research is not without controversy. Although it will not result in the birth of genetically modified babies, such research nonetheless involves the 'consumption' of human embryos for the purpose of research. In Germany, the Embryo Protection Act (Embryonenschutzgesetz) prohibits all such research.

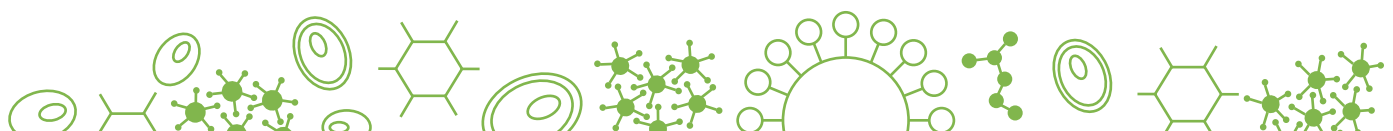
## Changing values – technology, culture, and society

In the 1990s, the boom in genetic research and the development of techniques for cloning animals – and theoretically therefore humans – led to international agreements aimed at protecting human genetic material. The Council of Europe's Bioethics

Convention, for example, permits genetic modification only where it will not modify the genome of subsequent generations in any way – effectively banning germline therapy.

Views on gene editing techniques have altered significantly in recent years, particularly in response to newer, more precise techniques such as CRISPR/Cas9. But if something was wrong yesterday, can it be right today? Or do ethical judgments always depend on the extent to which a technology is viewed as normal by the population? It's certainly true that bioethical questions – and with them our understanding of what it is to be human – are subject to constant debate and renegotiation.

In 2018, for example, an online survey in the Netherlands found that, in principle, many people would be open in principle to the idea of using gene editing to protect their descendants (who can't be asked for their consent) from, for example, an inherited neuromuscular disease. Naturally, the results from surveys like this will vary from country to country, even within Europe. What would such a survey find in Germany? There are also differences between different religions. While the Catholic Church, for example, traditionally objects vigorously to all reproductive technologies, Islam tends to be much more relaxed about these things. That was the finding of a 2020 research project on gene editing by Malaysian scientists. Provided that there are clear rules to prevent abuse and protect human dignity, their research found that CRISPR babies may be entirely compatible with the Islamic world view.





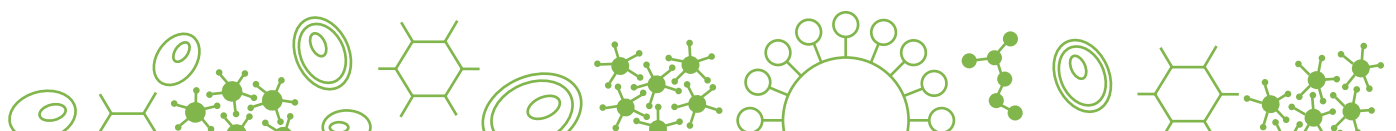
### Three-parent babies – the special case of mitochondrial donors

The availability of fertility treatments has also given rise to a further genetic engineering scenario – the creation of children with three genetic parents. In some rare inherited disorders affecting the brain or muscles, the problem lies, not in the genes found in the cell nucleus, but in a mutation in the mitochondria. Mitochondria – the powerhouses of the cell – have their own DNA. Because mitochondria are passed on to the embryo in the egg cell (and not or only to a very small extent in sperm), mitochondrial defects are inherited exclusively from the mother.

During IVF, genetic material from the mother and father can be transferred into an egg cell from a healthy donor from which the nucleus has been removed. The technique is also known as mitochondrial donation. This produces an embryo with the parents' genetic material in the cell nucleus, and around three dozen mitochondrial genes from the egg donor. These mitochondrial genes are important for energy metabolism.

The first three-parent baby produced using this technique was born in April 2016. The baby was a healthy boy born to a Jordanian couple following mitochondrial transfer performed by US doctors at a clinic in Mexico. Many scientists internationally have reservations about this technique, and it remains illegal in Germany. In the UK, by contrast, following extensive debate around serious illnesses, it has been legalized.

Surprisingly, in the UK mitochondrial donation is not classified as germ line therapy. This is despite the fact that girls born using this technique will pass the donor mitochondrial genes on to their own children. Today, it might even be possible to treat mitochondrial mutations using CRISPR/Cas9 gene editing techniques similar to those used with Lulu and Nana, rather than through egg donation.





## About the lesson series “Understanding Stem Cells - The Conference for Schools”

In this four-part series of lessons, the German Stem Cell Network and the Ernst Schering Foundation provide teachers with fact-checked knowledge about stem cells. The freely usable material allows students from 14 years onwards to actively immerse themselves in current research. The scientific experts at the German Stem Cell Network ensure the technical and professional quality of the material. The Schering Foundation uses its experience in science education to introduce young adults to current research topics using new methods and to encourage their interest in science. This material is available online at: <http://www.understanding-stemcells.info>



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