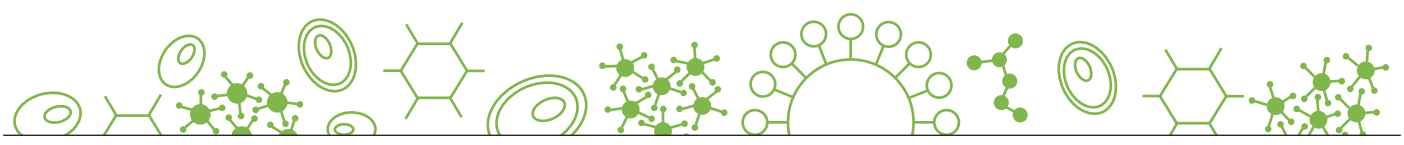
Understanding Stem Cells The Conference

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 task. Small groups work in parallel on the Poster and Pitch tasks. Alternatively, they may complete the *Pitch* task only.

90 minutes

Tasks:
panel, poster, pitch

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?

30-40 minutes

Large group
Panel exercise sheet
Panel material sheets

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.

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

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*.

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.

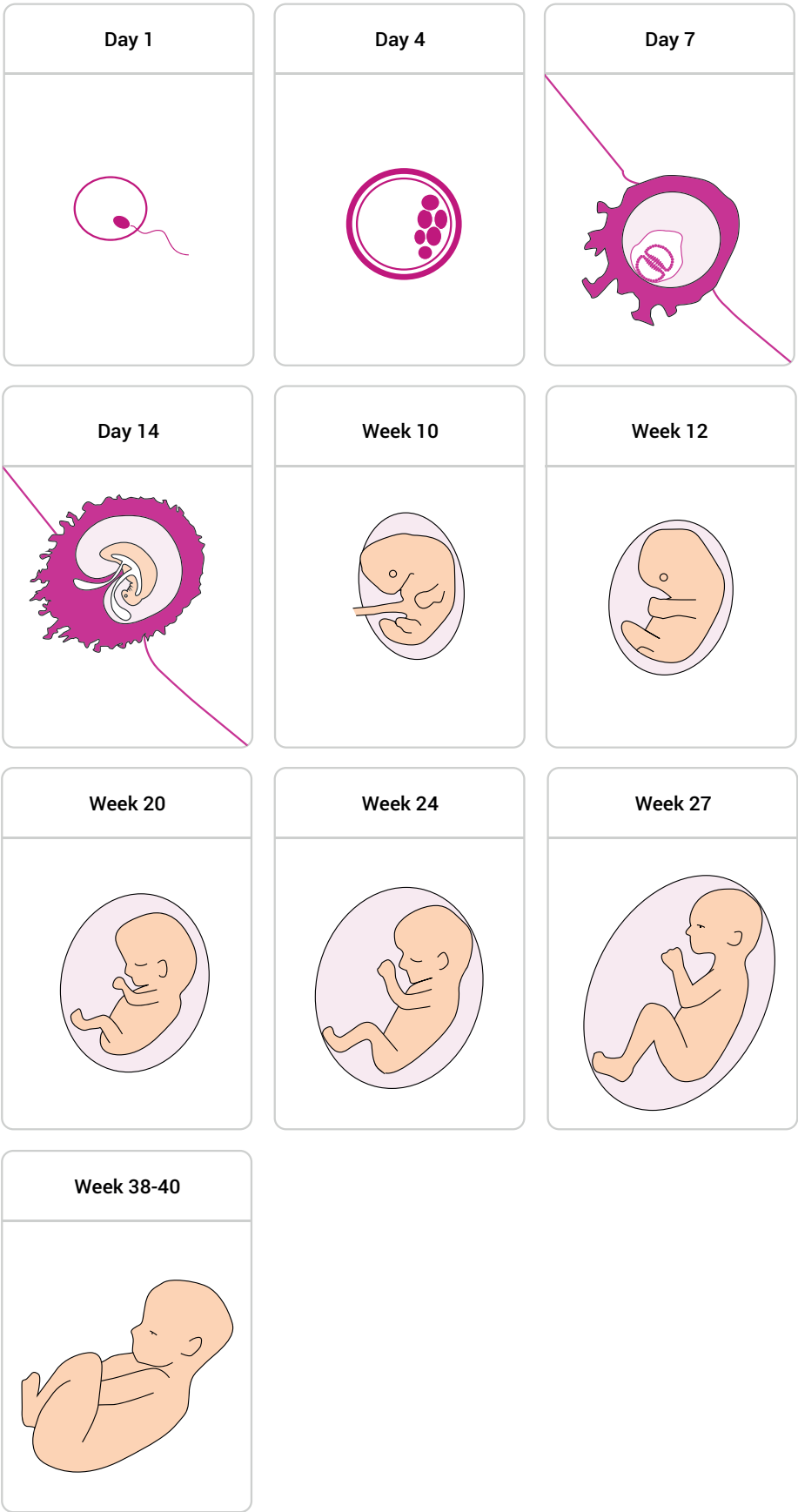
3. The stage of development at which the fetus would be able to survive outside the uterus (approximately 24 weeks) if born prematurely

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 terminati-on 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.

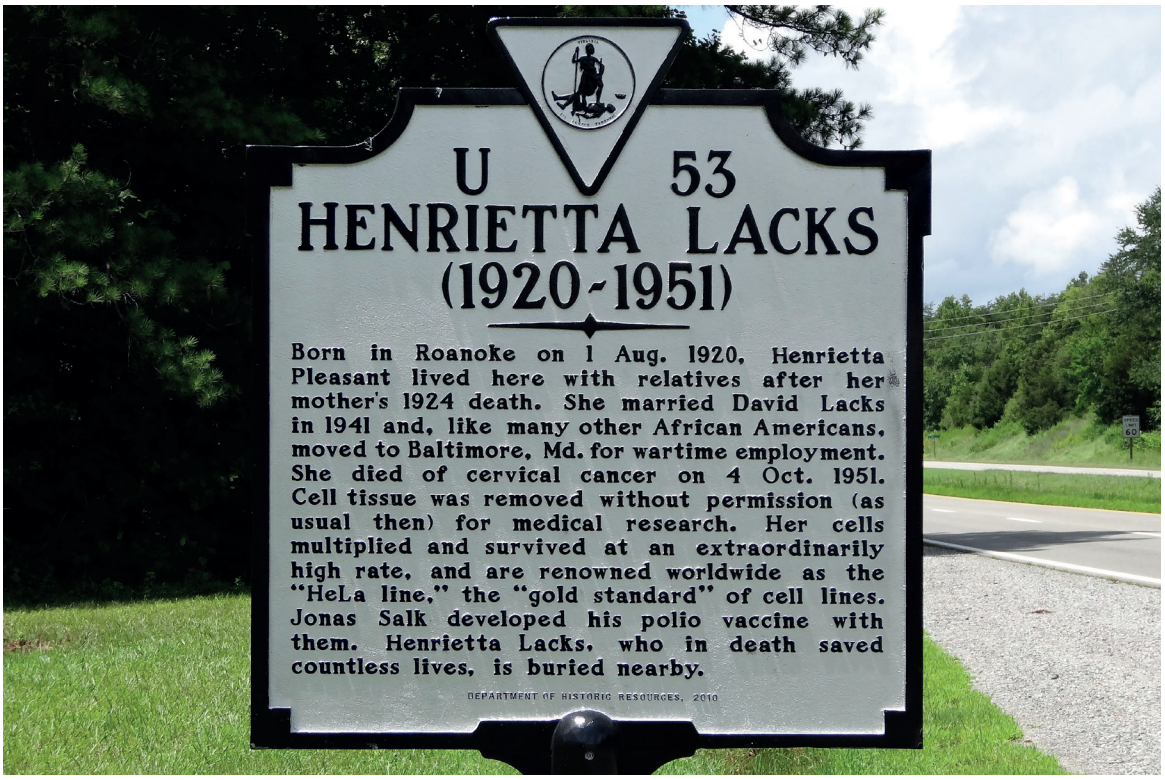
However, the German Stem Cell Act also lays down the conditions under which the import and use of embryonic stem cells for research purposes may be authorized in exceptional cases (§ 1 and § 4).
These conditions include the condition that embryonic stem cells were obtained abroad from surplus embryos 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 individual 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.*

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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