Gene Therapy

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1. Preface

Our motivations to work on the topic of gene therapy were that we wanted to learn more about it, because it is pretty interesting when you dive deeper into it. What is especially interesting are all the pretty recent discoveries that have been made in the field of gene therapy regarding the new strategies of cancer treatment. Of course the whole history of gene therapy is pretty captivating, with what this field of medicine has already accomplished and what it will accomplish in the future. Also the many ethical discussions that are around our topic made us go bit further into to many sources to discover the pros and cons of our topic, we found ourselves asking each other about our personal thoughts on the topic because we were really thinking about what can and should be done with gene therapy.

The questions we wanted to be answered after our assignment were the following:

- What is gene therapy?
- What can be done in gene therapy?
- What exactly are the processes in gene therapy?
- What are some past and future milestones in this field?
- What ethical controversy is around it?
- What can go wrong?

2. Introduction

2.1. Context

Gene therapy is a therapeutic method in medicine which is still experimental but has gained a lot of importance in the last few years, where a person's genes are somehow modified so that a genetic mutation causing troubles of the organism can be reversed. This makes it possible heal numerous diseases more efficiently, more easily and faster or even to heal diseases which had no available treatment so far.

2.2. Scientific history

The first time that gene therapy as we know it today was proposed was in 1970, by Stanfield Roger, which had the idea that inserting some stretches of „good DNA" into cells of patient's with genetic damages could possibly heal those. Two years later, two researcher published a paper called „Gene Therapy for human genetic diseases?", keeping Roger's idea up. Scientists carried on the research around this topic, and in 1985, two colleagues started working together to show the scientific world how the DNA of cells from humans with adenosine deaminase (ADA) deficiency (a metabolic disorder caused by a gene defect causing severe immunodeficiency, similar to SCID ⇾ see chapter 2.3.) could be changed and thus „healed" in a cell culture. In the following years, they tested their procedure on animals, first by transplanting the corrected genes into bone marrow, then into white blood cells, this method being way more efficient since these cells were much more receptive for the modified genes.
Although other attempts at changing the human genome had been performed since 1980, the first time a person was successfully treated with gene therapy was in 1990. The white blood cells of the four year old girl affected by ADA deficiency were taken from her, corrected and then reinjected into

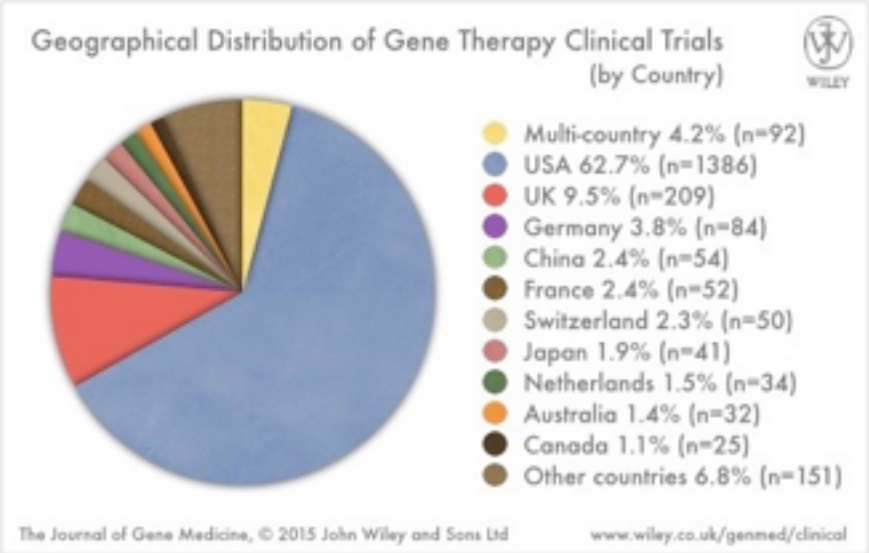

Fig. 1

her blood over two years. In 1993, the gene therapy was executed for the first time on newborns.

One year before this, in 1989, the scientists had tested how effective and safe their method would be on patients with cancer by culturing tumors, but the first attempts to actually carry it out on real patients were done much later.

Between the first attempt in 1990 and the year 2015, 2'210 trials have been conducted, more than 60% of it in the US.

2.3. Latest progress and events

Of course, progress in gene therapy is made every day around the world. Some of the most important advances of the past few months are listed below.

- **Plan to perform gene therapy directly in the womb for babies**
  Trials should begin next year to treat a condition called fetal growth restriction. This disease is mainly caused by some disfunction of the placenta, slowing down or even stopping completely the growth of the fetus. There is no known treatment yet, and even the babies that survive are mostly disabled in some way. In Europe, 10% of pregnancies are concerned by some form of fetal growth restriction. For the worst cases, scientists want to try to give gene injection to the mother, hoping to increase the blood flow to the placenta so the unborn child can finally be provided with all it needs to survive again. The altered cells would express a protein called VEGF, know for its blood flow boosting characteristics. It's unlikely that this intervention only will make it possible to finish the pregnancy, but event a prolongation of four weeks would totally change its outcome.
  It's the first time that gene therapy will be tried directly in the womb, and that is why the genes are given to the mother: Any genetic intervention at a fetal state could make the situation far worse than it already is, and would also be more difficult form an ethical point of view. But, as long as the treatment is injected to the mother, there are neither legal nor ethical reasons that would make a trial questionable.

- **Severe combined immunodeficiency**
  SCID is caused by a genetic mutation, leading to the lack of functioning T and B cells and therefore no antibody response, making this disease the most severe form of primary immunodeficiencies. Because they are extremely vulnerable to any infectious disease, they have to live in sterilized bubbles so they do not get in contact with any pathogen, this is why SCID is also known as bubbly boy disease. Affected people usually die within the first two years of their life, unless they managed to restore their immune system in any way.
  In Europe, there is no approved medicinal treatment for this illness, although bone marrow transplantation, or rather the transplantation of blood-generating stem cells, has already been tried many times to try to treat it, since the bone marrow produces our blood cells and thus also the ones of our immune system. The problem was that, especially when the donor was not closely related, the rate of surviving patient was quite small, because the donated cells happened to attack the ones of the recipient.

But newly, gene therapy has been used as an alternative to the transplantation: „healthy“ bone marrow cells, with corrected gene mutation, were injected to the bone marrow of the patient. Normally, this should make their body able to produce a functioning immune system able to fight off infections for a lifetime. The procedure has several advantages: the patients do not have to look for a matched donor, it prevents that donated cells attack their own, and reduces drastically the amount of chemotherapy they need to survive. The first trial ended with half of the participant having leukemia, but a rectification in the altered cells made it possible to increase the success rate and to make the therapy a quite secure method, although with some side-effects, especially fever and anemia.

Fig. 2

At the beginning of April 2016, the EU regulatory panel, together with other european medicine committees, communicated their positive opinion on the use of gene therapy for SCID, recommending the approval of the technique.

- **British scientists get permission to modify the genes of human embryos**
  <u>Note:</u> *This article contradicts the information given by Mr. Banfi, the person we have had the interview with, that the only country where genome editing of human embryos is allowed is China. But since this report was posted only few months ago, at the beginning of February, maybe he was not informed about it yet. We found several articles about that, so it probably won't be a faulty information.*
  The Human Fertilisation and Embryology Authority allowed British researchers genetically modify human embryos. It permits them to make experiments within the first seven days of the embryo, without, of course, allowing them to implant them into woman, since this could have unpredictable consequences.
  The goal of the research is to get a better understanding of the early development of a healthy human embryo, also to understand how the different cell types are specified at this early stage and to then develop better treatment for infertility and prevent mothers from loosing their baby in an early stage more efficiently. With a gene editing tool (CRISPR-Cas9), the group will switch on and off different genes to observe the consequences for the developing baby. Consequently, this would also reveal the accuracy of this quite new editing technique.
  All around the world, people reacted to this decision, in very different ways. Proponents of this idea see it as the first step to GM babies, whilst other found it to be unacceptable. Altogether, the possible benefits of this research probably outweighs the risks: as long as it stays to only research: the real ethical problematic will come when the first genetically manipulated babies will be implanted into women and finally born.

2.4. Use of the technique

You could, in theory, treat an incredibly high number of diseases with gene therapy: since the injected cells contain modified DNA, if these gene somehow express a protein making you resistant to an illness, killing the pathogen or anything similar, you could heal the patient with gene therapy.
But of course, science focusses on severe diseases, mostly with no alternative treatments or treatments which are everything but optimal. Thus, the most studied uses are treatments for genetic disorders, especially immunodeficiencies (in theory, healing AIDS is possible with that method), metabolic disorders and similar illnesses. But in the past few years, the research also focussed on possibilities to cure cancer with gene therapy (this will be explained in the following chapter).
As said, there are mostly no alternative treatments to gene therapy, making it an incredibly valuable method. An example of a disease with alternative treatment would hemophilia: but the

treatment consists of infusions which have to be taken regularly. So treating it with gene therapy has the big advantage that it has to be done only once. Sometimes, gene therapy is also used to enhance some other sort of treatments, making it some kind of complementary treatment.

3. Description of the technique

3.1. Gene Therapy - Overview

Gene Therapy is a treatment which consists of inserting DNA into a human body over a vector to prevent or cure a disease. This vector is mostly viral, but can be non-viral as well. The virus is of course altered to make it inactive, but a risk remains. But not all procedures which change the patients genetic information are considered as gene therapy: organ transplants, for example, have been found to alter a human's DNA, but since this effect is not volitional and not aiming for therapeutic effects, these procedures do not count as gene therapy.
Researchers are trying to find possibilities to cure a number of diseases with gene therapy, among others hereditary diseases caused by a gene defect like hemophilia, but also many others like cancer, Parkinson's and even HIV. Although this technique is still experimental, quite a few therapies have already been successful.

3.2. Types of Gene Therapy and Process

You can classify gene therapy in three different ways:

What they aim to:
- Replacement of a mutated gene
- Inactivation of a faulty gene
- Insertion of a new gene supposed to fight a disease

What cell type it is executed on:
- Somatic cells
- Sex cells (egg or sperm): In this therapy, the therapeutic effect is passed on onto later generations, so it is of great potential but also a risk since quite a few things can go wrong.

Where the therapy is done:
- *In vivo* therapy, where the gene of interest is directly put into the human body over a vector and produces the therapeutic protein inside the human body.
- *Ex vivo* therapy, where the vector with the therapeutic gene is transferred into a culture of the patient's cell, which is then brought to express the therapeutic genes and then introduced in the patient's body again.

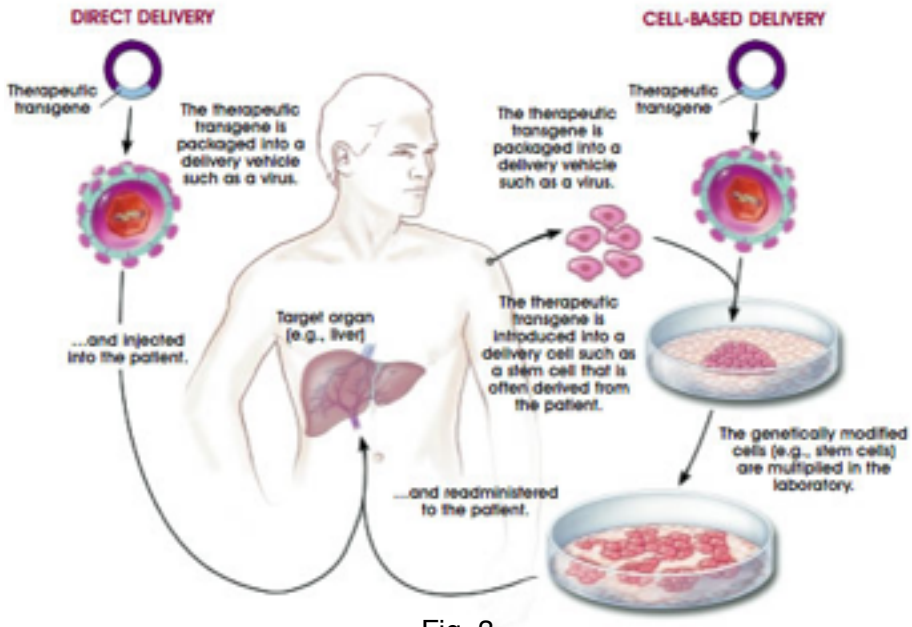

Fig. 3

3.3 Process

- First we have to choose the therapeutic gene. For monogenic diseases (caused by the malfunctioning of only one gene, e.g. hemophilia or cystic fibrosis), the choice is rather easy: a correct copy of the defect gene is introduced into the cell. But for multifactorial diseases (caused by more than one gene or influenced by environmental factors, e.g. cancer or diabetes), many other facts have to be taken into account, thus a higher knowledge of the disease has to be achieved. When gene therapy is not used to treat genetic diseases, but just to make the body produce a protein which then actively attacks the pathogen, you also have to know a lot about the disease itself and the possible therapeutic proteins. Additionally, we have to determine where and when the therapeutic protein has to be expressed, so the choice of the right promoter is vital for the process.
- Then follows the choice of the vector. The optimal vector enters the target cell and delivers the genetic material at a rate as high as possible without activating any immune response. Vectors are classified in viral and non-viral vectors. Each vector has its own set of characteristics. The choice of the vector depends on the tissue where the therapeutic protein has to be expressed, if it is a short-term or chronic treatment, therefore if the vector can express its DNA over a short-term or long-term period and if it has to be able to enter non-dividing cells.
- After the choice of both the therapeutic gene and the vector, the gene is inserted into the vector during a recombination process. Special enzymes permit to include it into the vector's DNA.
- Afterwards, the vector is injected either directly into the patient or into a cell culture, depending on if it is in vivo or ex vivo therapy.
- If it was in vivo therapy, the process which has to be done by humans is completed.The vector will invade the target cells, modify their DNA and help the patient in some way — if everything goes well, of course. If it was ex vivo therapy, the cultivated cells are injected into the patient and then take over their function, as in vivo therapy.

3.4. Cancer gene therapy

Cancer gene therapy got more and more important in the last few years, and will probably become even more important in future. There is still no optimal treatment for cancer, and millions of people die of it every year (around 15% of the deaths of 2012 were caused by cancer), millions of others are affected by it.
There are more than a dozen different treatments for cancer, each one with its advantages and disadvantages, the most common or famous ones being chemotherapy and radiotherapy, and if you look for cancer drugs, there are lists of several hundreds of different possibilities, but still: no cure. We should not expect gene therapy to be the miracle treatment which can cure cancer, but it could be a serious progress in numerous aspects. According to Mr. Banfi, gene therapy as a method to fight cancer could be approved within the next five to ten years: a lot of clinical trials have already been going on in the last decade, though. In the last year, two-third of gene therapy clinical trails were for cancer gene therapy.

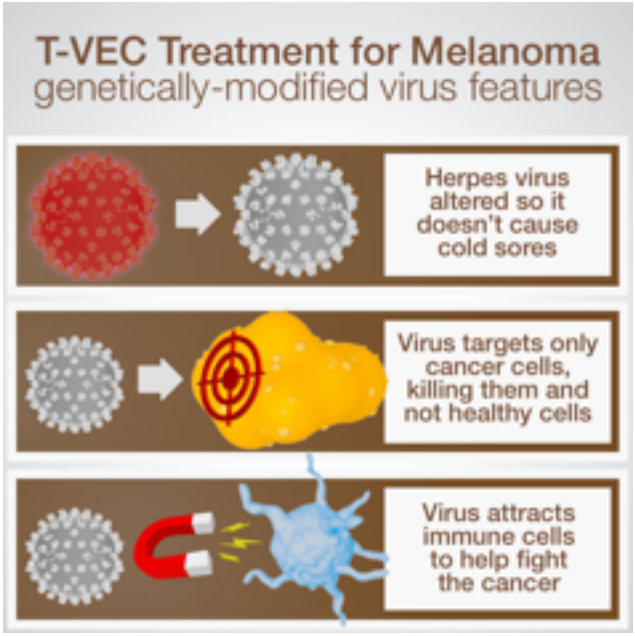

Fig. 4

But how do you treat cancer with gene therapy? Cancer is caused by a DNA change in a cell due to several mutations, most of the time through lifestyle influences, so that the cell replicates unbridledly. In some, more rare cases, cancer generating genes are even inherited to offspring, considerably rising their cancer risk. These inherited genes can, once

detected, be exchanged with gene therapy to lower the risk again.
When the cancer has already started, it is too late to change the DNA of the cells since the cancer has already developed. But there are multiple other possibilities: most aim to enhance a certain treatment. The three most important ones are listed below:

- Improving immune response: The genes of the patient are changed in a way to boost the natural way of the body to defend itself against illnesses.
- Improving treatment: For that type of gene therapy, the cancer cells are targeted directly, making the more sensitive to chemotherapy, radiotherapy or the like.
- Killing tumor cells: This one does not improve some kind of treatment: it just insert genes into the cancer cells which then kill the damaged cell.

4. Discussion

4.1. Pro and contra

Pro	Contra
Almost unlimited potential, it can be used for a huge amount of diseases	The method is still quite risky, and a damage of the gene pool could has always to be taken into consideration
The method can be adapted quite quickly in the case of a new disease emerging	Since the vector is mostly a virus, a wrongly altered virus could result in a new disease
Gives the power to eradicate diseases which have affected the human race for centuries and to get rid of disorders like Alzheimer's, Parkinson's, etc for good.	If it gets to the point of changing human embryos, gene therapy could easily be misused to decide what your offspring will look like and to try to make a „better" race: this would not be acceptable from an ethical point of view

4.2. Successes

Huge progress has been made in gene therapy during the last few years. The rate of successes in clinical trials is rising and the point when gene therapy will be accepted as a general technique is getting nearer and nearer. Here are some of the most important successes of gene therapy so far.

- Immunodeficiencies: Success has been reached for a couple of immunodeficiencies, mostly by correcting a flawed gene in the blood stem cells of the patient. One example has been shown in the introduction of this paper, the SCID.
- Hemophilia: Some clinical trials have also been going on for treating hemophilia. Afterwards, most of the patients produced small amounts of the factor permitting their blood to clot and reducing the number of their bleeding incidents. It is not a full success yet, but it is a progress.
- Blood diseases (sickle cell disease and beta-Thalassemia): These disorders, inhibiting proper oxygen transport due to damaged genes coding for the red blood cells, have been successfully treated by modifying those genes, similar to the approach for immunodeficiencies.
- Cancer: Cancer has been already mentioned several times in this paper, so it is needless to say that this is surely one of the biggest successes in recent gene therapy.

It's important to understand that, when we talk of success in gene therapy, that does not mean that 100% of the participants were cured. Since most of the therapies are still in experimental stage, such a result hardly ever occurs, if ever. But it shows that some patients have managed to recover from a disease thanks to gene therapy: and that therefore the scientists are on the right path.

4.3. Ethic

There are almost none ethical discussions when the goal of gene therapy is only to treat e person's disease. It is a treatment like any other one, and the patient decided to be treated in this way.
The more difficult point is the modification of a human embryo, or even to change the sex cell of a human so that his modified genes will be inherited to all of his descendants. If this damages the genome, these damages may be irreparable, giving the following generations disabilities or even turning them kind of inhuman. The other problem is that, if gene therapy gets more and more common, this could provoke the mergence of consumer eugenics, meaning that parents will be able to choose what genes their baby should have, if the modifying of a human embryo gets legal. But then, who decides what is „good" or „bad" use of gene therapy, who says if something is really a disease and can therefore be treated with gene therapy, and what is only a trait that shouldn't be changed. People could start to make their babies look prettier, be more intelligent and so on beginning with the rich, probably, since gene therapy is relatively expensive — what represents another problem: the fact that gene therapy will probably not be available for everyone. This could lower the acceptance of people that are somehow different even more, and all these facts make gene therapy a really difficult topic concerning ethics.

4.4. Future

What will research be focussing on in future? It seems that, next to cancer, which is really near future, though, there will be a lot of research around cardiovascular gene therapy. There have already been attempts on this in the past ten or fifteen years, which failed because there was still a lack of understanding of the technique. But now, the scientists plan to carry on these researches, since cardiovascular diseases like strokes, peripheral artery disease, arteriosclerosis and such are the most frequent diseases in the world. The human population gets older every years, and these diseases make millions of people unable to work or even to fulfill their everyday tasks and represent a high economic burden for society.

5. Summary

As a summary of the paper, we will answer the question we asked ourselves at the beginning of our work.
Gene therapy is an experimental treatment which has made a huge progress in the last couple of years. It is performed by carrying a foreign piece of DNA into the patients cell respectively a culture of his cells over a vector.
The potential of this method is nearly endless, since you can treat almost every disease just by changing the gene carried by the vector — if a good understanding of the disease is present, of course. Gene therapy has known success in treating many different diseases, especially immunodeficiency diseases like SCID or blood diseases like hemophilia. In near future, research will focus on fighting cancer and cardiovascular diseases with gene therapy, while the research for cancer gene therapy is already quite advanced. However, all these processes can go wrong at many levels, and a mistake could have incredibly severe consequences, since messing with human genetics could lead to things we would not even expect.
There is ethical controversy around it, but at the time it does not really slow down research. The problems will come later, when the human race could be changed forever — and quite rightly.

Attachment

Interview

We had our Interview with Mr. Banfi, working at the Biomedicine department of the University of Basel and making research about Gene therapy, on April 15th:

- *We first wanted to ask you what you studied to get this job at the university.*

I studied medicine in Italy and then I got a residency in clinic oncology so I became a specialist in this field. But I was interested in basic research since the beginning of medical school. So I started being a student in the research laboratory of the cancer institute in Geneva from the second year of medical school and stayed there until I got my residency. Then I started doing more and more of my own projects there and by the time I finished the residency I still found the research department to be way more interesting than clinical medicine it was agreed with my supervisor that I should 100 percent of my time to it, so I moved to the United States where I worked at the Stanford university. After four years I was looking for an opportunity to return to Europe and I found it here in Basel in the department of biomedicine to start a research group and of course by then clinical medicin was out of the question.

- *What are you working on right now?*

I´m working on many things but to make it very simple and broadly we are working on understanding the mechanisms by which blood vessels grow. But not during development or spontaneous growth but specifically as a consequence of therapeutic delivery of growth vectors which is the situation in which you would like to grow blood vessels in a clinical situation: so the idea is that we need to grow blood vessels in a variety of clinical situations where not enough blood flow arrives in tissues. In order to be able to do this we need to understand how they grow. Not necessarily what happens during the organized and spontaneous growth of blood vessels during embryonic development for example has exactly the same mechanisms as if you put a drug inside of the tissue to grow new blood vessels, so the conditions are different. In fact we are figuring out that there are specific mechanisms that take place in this situation that are different from what happens in development and in order to devise strategies to grow blood vessels therapeutically, we think it is important to understand these mechanisms rather than developmental ones. Then we try to transform this knowledge into approaches maybe the principal is that using certain techniques that are ok for studying the principal but you cannot use them directly to treat the patient. We try to hold on to the principal to develop other approaches that can keep the principal but make it applicable in a clinical situation. This is then eventually linked to gene therapy because it is one way that we can use to grow blood vessels we use the viral vector to put the gene for an androgenic factor, so for a factor that can grow blood vessels, inside of the body and therefor express the gene and use the factor inside the body to grow blood vessels where we want them to grow. That's the final step.

- *When you talk about your job and what you do with gene therapy are there sometimes ethical discussions coming up?*

Ethical discussions on gene therapy at the level that we do, do not really exist. Because we are not aiming at using gene therapy to permanently change the genome of a patient. We are aiming to use it as a tool express a therapeutic factor for a certain amount of time in order to achieve a response. Ethical considerations arise when people want to permanently change the genome of a patient because of an inherited disease. They really aren't there until you start thinking about changing the genome of the gametes. But this is not the case of the vast majority of applications and in fact it is forbidden!

- *What are, from your point of view, the most important discoveries that were made recently in gene therapy?*

There are significant successes. The first really big discovery of gene therapy was the treatment of the bubble boy disease. It is a very rear immune deficiency in which the children are born with a deficit in one enzyme and they basically don't have any immune cells. So they cannot live in a normal way, they have to live in a bubble in which they are completely protected by any kind of bacteria or other things. So the first thing that was possible to treat these children is to take their hematolytic stem cells, so the stem cells that make all the blood cells, and give them back the missing gene. So that through bone marrow transplantation they could regenerate all their immune system and the children were completely cured. The problem is that the vectors used were in an early stage and people did not realize that these vectors could integrate close to other genes there were onco genes and could therefore activate tumors. About half of the children developed leukemia´s in the years passing by, some died and some could be cured. In step two, this shows that you can achieve something and when there is another problem you can go back. That led to the discovery that the vectors inside the genome can do that and to the discovery of modified vectors that lost this property and could be integrated into safe harbors, or in places in the genome where no problems could be generated and now this can be achieved again but with safer vectors without for example leukemia.

- *What are the greatest achievements that could be reached in the future?*

So cancer would be probably almost now the second biggest achievement of gene therapy, because it's not so much in the future, it´s almost present now. From the discovery of two things: one is the fact that you can give viruses to the patient that selectively infect tumor cells and kill them, the so called oncolytic viruses. And the other thing is actually immune therapy of cancer. Very recently there has been a newly discovered special immune molecule that can be given as gene therapy. This molecule finally really activates the immune response very potently against a large number of tumors. We hope that a lot of patience can be treated that way. For the future cancer is definitely important but we hope that also cardio vascular gene therapy, which has been attempted 10-15 years ago, when we knew very little about the biology of growth vectors, and therefore didn't really work, with what we know now it could soon be used again because of course ischemias, heart attacks and peripheral artery disease and the consequences of ortho sclerosis are the most prevalent diseases in the world. So by sheer numbers it is actually many more people that are affected by these than by cancer. Besides the high mortality rate there is also a high economic burden that is caused because it leaves many people unable to work.

- *What is your point of view when it comes to changing a patience's sex cells so that further generations won't have his hereditary diseases?*

This is the extremely complex ethical discussion that current technologies enable but we need to absolutely choose what should be done and not necessarily all that can be done. Because at some point technology becomes more powerful than our ethics so we need to make our choice. I personally think that it´s, although there are certainly situations in which you can see how this can do good, it´s a very, very dangerous avenue! I think it is regulated and it is prohibited almost everywhere in the world and I think it should be, because of at least two considerations: one which is obviously just purely ethical. Which is ok you can do it to let's say knock out a specific gene that will cause the inheritance of a predisposition of tumors for example and you can allow this person to then have children that then will be healthy, but of course the first examples are always very black and white. How do you decide what is something that is good and what is something that instead is now let's change the gene for the color of the eyes or I only want sons and I don't want daughters or anything else, or I just want a better race I mean pretty soon it becomes very scary from an ethical point of view. That's in consideration of if everything actually works exactly as you want. As we saw before with the treatment of the bubble boy disease. Scientists have performed

years and years of very careful animal experiments and worked out very correctly how the whole steps could be done and yet, when finally going into the human disease unexpected consequences happened in the form of tumors. This fault could not be seen in the animals because, they don't live long enough, because there is not enough time for such cells to transform and so on. So how do we actually know that what we intend to do has a change on the genome of an inheritable trait will actually do only that and not something else? Human embryos are not, let's say experimental dishes. Once you have done something that person will be born and is a person. The risk, even if low, of creating a monster, who did not decide to become a monster is of course ethically not acceptable.

- *So if there could be some dangers, do we already know what they are?*

Well the most recent report is that, like last week, for the second time a Chinese group reported having actually modified the genome of human embryos for three days in culture and then destroyed the embryos. This is already well beyond what is approved and legal in any other country in the world. In China here is no regulation for that and so scientists can legally perform these experiments on human embryos. Of course for the moment there has been two groups, both in China with experiments that carried on the cells for three days after the change of the genomic consequences, so it's really working out some technical flaws. So no, we don't know. But we can expect from experience form other situations that the genome is extremely complex and it's not just like a library that you can think that if I know where a book is, I can go and take out that book and I put in another book with a different color and that's it. I don't have any influence on anything else in the library. No, the genome is like a library in which every book has a lot of threads connecting to other books and it´s completely not really known in what way you influence which other books. It's not just a theory, it does happen, it's just that we don't know how and we cannot exactly predict it. If you start doing it to human beings, to embryos or to the sex cells, then the consequences are not exactly good.

- *Are there hopes to cure, for example Aids?*

It can be done, of course it is also one of the possible applications. I mean gene therapy simply means, the capacity to interfere with the genetic sequence of a cell. One or more cells. So when the bubble boy disease is a disease of the immune cells, because you don't have immune cells, because you miss an enzyme, if you can put that enzyme back into the stem cell, so the original one cell that can create all the cells of the blood, then the daughters will be normal and so you can have immune blood cells that are actually working immune cells. What happens with Aids is that you have a normal immune system and the virus gets into your lymphocytes and it kills them. If you find, let´s say, the protein that allows the virus to get in, or if you find genes that can kill the virus once it is inside the cell. This comes from the studies of those very few patients that naturally are resistant. It´s well known that by now there have been, without any kind of treatment a very small percentage of patience simply never get the virus despite having the disease. By studying those patience it has been discovered that they have very small mutations or changes in certain genes so the virus can get in but has no effect on its host. If you can take that mutation/ protein/ gene that makes these patience resistant and the other people don't have and you put it inside of their stem cells and you give them a bone marrow transplantation you can regenerate their immune cells with a new breed of immune cells which are now resistant against the virus. Therefore you can cure it.

References

Books (Text):

Kleinert, Reiner / Ruppert, Wolfgang / Stratil, Franz X.: Abitur-Training *plus*; Biologie; Genetik. Langenscheidt, München, 2013. (S. 148-150)

Internet (Text):

Author unknown, (2014). Cancer Research UK - Gene Therapy. http://www.cancerresearchuk.org/about-cancer/cancers-in-general/treatment/biological/types/gene-therapy [26.04.2016]

Author unknown, (2013). Cancer Research UK - Worldwide cancer statistics. http://www.cancerresearchuk.org/health-professional/cancer-statistics/worldwide-cancer [26.04.2016]

Author unknown, (various dates, 2016). Gene Therapy Net - Gene Therapy News. http://www.genetherapynet.com/gene-therapy-news.html [26.04.2016]

Author unknown, (2015). Gene Therapy Net - What is Gene Therapy. http://www.genetherapynet.com/what-is-gene-therapy.html [26.04.2016]

Author unknown, (2016). Genetics Home Reference - What are the ethical issues surroundind gene therapy?. https://ghr.nlm.nih.gov/primer/therapy/ethics [26.04.2016]

Author unknown, (2014). Learn.Genetics - Gene Therapy Successes. http://learn.genetics.utah.edu/content/genetherapy/gtsuccess/ [26.04.2016]

Author unknown, (2015). OccupyTheory. - List of Pros and Cons of Gene Therapy. http://occupytheory.org/list-of-pros-and-cons-of-gene-therapy/ [26.04.2016]

Author unknown, (2016). Wikipedia - Gene Therapy. https://en.wikipedia.org/wiki/Gene_therapy [26.04.2016]

Author unknown, (2016). Wikipedia - Severe combined immunodeficiency. https://en.wikipedia.org/wiki/Severe_combined_immunodeficiency [26.04.2016]

Bosch, Fatima / Roca, Carles / Anguela, Xavier / Ruzo, Albert, (2011). CliniGen Noe - Gene Therapy, a New Tool to Cure Human Diseases. http://www.clinigene.eu/video-intro-gene-therapy.html [26.04.2016]

Edelstein, Michael, (2015). The Journal of Gene Medicine - Gene Therapy Clinical Trials Worldwide. http://www.abedia.com/wiley/continents.php [26.04.2016]

Mandal, Ananya, (2014). News Medical - Gene Therapy History. http://www.news-medical.net/health/Gene-Therapy-History.aspx [26.04.2016]

Internet (Images):

[Front page] http://www.studentpulse.com/articles/914/gene-therapy-current-treatment-options-and-likely-near-term-developments
[Fig. 1] http://www.abedia.com/wiley/continents.php

[Fig. 2] https://media.npr.org/assets/img/2013/12/06/scisource_bn9565_wide-76ab203b8ae3f97dfb01b405cb42c7f5351b524b.jpg?s=4

[Fig. 3] http://stemcells.nih.gov/StaticResources/info/scireport/images/figure111.jpg

[Fig. 4] http://learn.genetics.utah.edu/content/genetherapy/gtsuccess/