Genetic Engineering

In Humans

The Prospect Of Perfecting Humanity

By Tracy Koduah, Terence Tutumlu and Tristan Handschin

“You can stop splitting atoms, you can stop traveling to the moon. But you cannot reverse a new life form”

-Erwin Chargaff

Content

Preface

Human Genetic engineering, essentially the modification of an organism's genes to one's specific wishes, is a very broad and complicated topic, though highly fascinating and most relevant to society, especially in the future. Already now in industrialized countries, heavy debates are taking place about gene therapy, the process of altering human's genetic material in order to repair or compensate for the effects of mutations or abnormalities, and to which degree it should be legal. This, however, is only a taste of what is to come in the future. As technology improves and becomes more secure and exact it will become increasingly difficult to forbid genetic therapy and ultimately genetic engineering.
What could possibly speak against preventing genetic diseases in humans? It could help millions and millions of patients by "simply" modifying a human's genome. But where does it end, when does it become unethical and when exactly do we start playing god?
We chose this topic exactly because of its controversy and its prospects; we'll certainly hear a lot more about this topic in the course of our lives. We find the line between the reasonable fight against genetic diseases and playing god in potentially manipulating genes to one's wishes to be extremely interesting. How should one reasonably limit genetic engineering in the future, to which extent is it necessary and how could this affect society as a whole? As such, we want to answer the following questions in order for us to understand this topic and thus have a voice in the future:

- What exactly is human genetic engineering?
- How does human genetic engineering work?
- What kinds of techniques exist?
- How do these techniques work?
- What are the ethical aspects, what speaks for and against human genetic engineering?
- How does a geneticist feel about human genetic engineering?

We believe it is only possible to discuss the very important topic in the future if you understand what it's about. Consequently, we want to come to a conclusion about whether or not we would support human genetic engineering and to which extent we would want it to be allowed. So ultimately, it is in our best interest to learn as much as possible about this topic.

Introduction

This contemporary topic has been and will be newsworthy for a very long time. Currently, laws in many countries are being passed on gene therapy, newspapers and magazines are full with articles about this topic, both in positive and negative tones, society is having to deal with the prospects and fears of human genetic engineering and many parents would wish to employ these techniques to either eliminate severe diseases for their child or to create “designer” babies with chosen traits like blue eyes. These procedures won’t be cheap, so only the rich could afford these techniques in the future, could society handle that?

Basically, the two biggest considerations surrounding human genetic engineering in the future are ethical and safety considerations. The few successful techniques used in gene therapy, which exist already today, are rather new and thus an element of risk is present. The fear of new man made genetic problems, genetic discrimination, etc. is great.

At present, reproductive genetic engineering is rather inexistent as a medical procedure and to which extent gene therapy is allowed (gene therapy is applied to non-reproductive cells) varies greatly from country to country. In general, Switzerland is relative restrictive concerning any form of reproductive genetic manipulation, but there are ambitions to widen the spectrum of allowed techniques. However, it will take years and years for reasonable solutions to be found.

In conclusion, countries will have to decide on how far one can take human genetic engineering and which techniques should be legal. There are no alternative treatments as genetic engineering will always be, genetic engineering.

Techniques of Human Genetic Engineering

Using DNA for health benefits is called gene therapy and can be separated into two types.
Germ line therapy: Sex cells are modified, the genes are hence inherited by the next generation. This type of therapy is prohibited in humans due to ethical, as well as technical reasons.
Somatic gene therapy: Somatic cells in the human body are modified but the changes are not inherited by the next generation.

In General

In order to equip an organism with a specific trait the required genes must be inserted into the cells. The first step is finding out which segment of the DNA is responsible for the desired trait, then it is isolated. Afterwards the isolated gene has to be carried into the cell where it should “feel” comfortable to be able to produce its corresponding protein. Jesse Gelsinger's death in 1999 indicates that the transport of the genetic information is a challenge. He suffered from a rare genetic defect which caused the ammonia concentration in his blood to increase constantly, poisoning him. The doctors who treated Gelsinger used adenoviruses as transport vehicles, so called viral vectors, due to the fact that viruses inject DNA into their victims which makes them useful. However, they cause strong reactions of the immune system. Unfortunately the dose of 38 trillion virus particles in Gelsinger's blood was too high damaging his body tissue and therefore killing him.

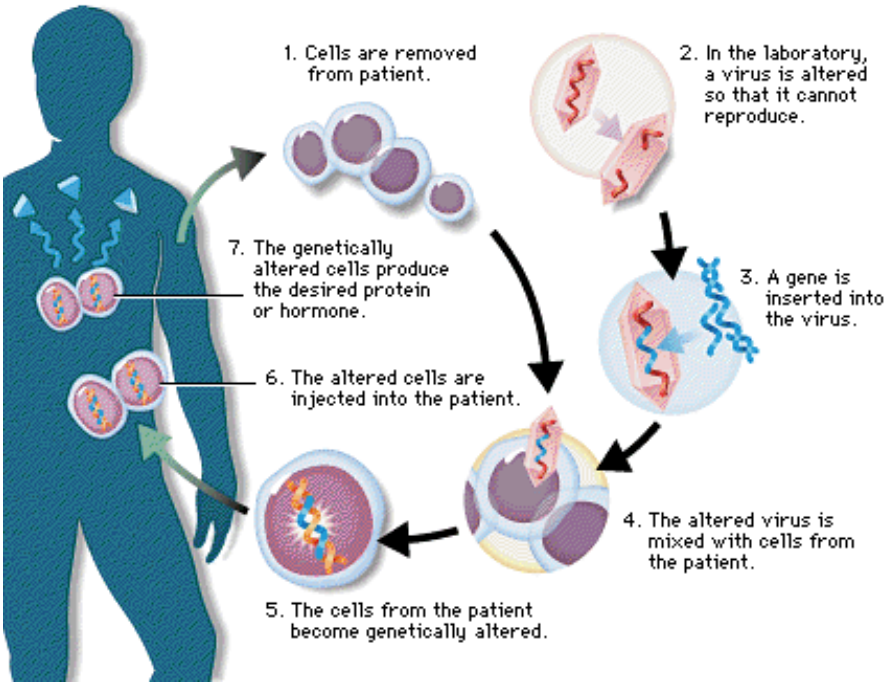

Image 1: General procedure

This setback shows that gene therapy is still in an experimental stage.
Researchers try to avoid the dangerous viruses and utilize liposomes (fat pellets), polyribosomes or even “naked” DNA without envelope instead. A relatively new invention are the nanoparticles that are supposed to attract genes and carry them into cells. Nanotechnology is the scientists' new hope. A few other non-viral methods are:

Electroporation: High voltage pulses form pores in the cell membrane allowing the DNA to pass through.

Sonoporation: Ultrasound disrupts the cell membrane enabling the DNA to pass through.

Gene gun: Gold particles are coated with DNA and then bombarded into the cell. The gold is left behind on a stopping disc.

Dendrimers: Are large branched molecules. It is possible to positively charge their surface hence attracting the negatively charged DNA. The whole complex is then absorbed through endocytosis (see vocabulary).

Hybrid methods: Different methods may be combined to be more efficient. For example liposomal with viral methods.

Technical example.

Regarding diseases, genetic engineering is of immense importance as it can save lives. September the 14th 1990 the first experiment to cure a human employing genes was performed. Ashanti DeSilva's four-year-old body was not capable of producing an enzyme vital for the immune system called ADA (adenosine deaminase). If it does not work properly dangerous toxins aren't split and those destroy cells of the immune system, particularly T lymphocytes. Affected people could thus die just because of a harmless influenza. The cause is a genetic defect that became famous through David Vetter (Image 2), known as “Bubble Boy”. In order to stay healthy he lived in a bubble and even received a suit from the NASA. He died at the age of twelve.

Image 2: Bubble Boy wearing NASA suit

To get down on the root of the disorder the doctors removed a few of Ashanti's leukocytes. In the laboratory (ex vivo) they inserted the missing gene with retroviruses as vectors into the cells and then put the ADA producing leukocytes back into her body through infusion. Today Ashanti is a young woman and leads a normal life.
If this process were in vivo, than you would genetically modify the cells directly in the body without removing them (see vocabulary).

Interview with Professor Dr. Peter Miny

What exactly is human genetic engineering?

The laboratory of the "Felix Platter Spital" where Dr. Miny works

This is a rather difficult question. We are medical geneticists, our task is genetic diagnosis, not genetic engineering. Techniques which could be called human genetic engineering, in my understanding, include techniques which would change something, like genetic therapy. But it's not a routine procedure in current genetic medicine. It's a rather difficult field and many people are disappointed. But the lack of progress in this specific field has been discussed for the last decades. When the molecular genetic revolution started, people were very optimistic that it would be a matter of years before many of the severe genetic conditions could be treated by the so called method of genetic engineering. And this has proven to be very difficult and it doesn't work for most of the conditions we are dealing with. There are only very few rare genetic and inherited immunological conditions where such a treatment has been conducted successfully. So this is not a story we're very proud of. It's a difficult business.

In your opinion, what would be the most important pro and con of human genetic engineering?

I think the pros would be treatment of severe genetic conditions. These are rare conditions but the number is very high. There are several thousands conditions due to mutations in single genes and some of them have very severe consequences. Most people would

agree one should try to change the genes. I couldn't imagine that people have ethical objections against it. But it is completely different, when it comes to changing the germ line genes or engineering genes in the gametes which is another point most people wouldn't agree with. There is quite a bit of discussion among the geneticists about the ethical concerns surrounding the germ line therapy.

If you could use this technique, would you?
Not here. German speaking countries are very conservative when it comes to genetic engineering or reproductive techniques in general. Things like pre-implantation diagnosis have been forbidden in Switzerland as well as in Germany and Austria. So many other countries in Europe are completely different from each other and don't have many objections against these technique as the country we're living in.

How would you protect the privacy of patients if hospitals used gene therapy to treat them in the future?
I don't believe that things would change drastically. If you visit a doctor or hospital with a very private condition you're already exposing yourself today. Secrecy or privacy is at a good state in at least developed countries and in western style democracies. There are laws set for protecting your privacy.
So people are very aware and concerned about privacy. In the medical field this can be easily observed. For us, it is very difficult to write a publication with a description of a patient nowadays. Its going to be a challenge, because we have to get all sorts of informed and written informed consents even if you don’t reveal a picture but just tell the story. Doctors aren't allowed to retreat a patient when they name certain details of the patient’s disease. This whole privacy issue is a little overemphasized.

Are there ethical grounds to manipulate certain genes in humans in order to change aspects of their lives, like preventing inherited diseases or insuring your child will have “blue eyes”? Where do you think the borders lie in using these techniques?
This is a very important question. But since it is not possible at the moment, it's a question we have to answer in the future. As I mentioned before, most people would agree to actively engineer genes if it would be used to treat severe conditions. When it comes to changing eye colour, opposition is probably rather high, for a good reason though. I see a risk that there will be people, who will try to sell these techniques. It is like choosing the

gender at the moment and this is a popular examination in certain parts of the world. People are experiencing consequences already. China, India but also in Europe, for example Yugoslavia, where the rate of the sexes has already changed drastically

There are many arguments against human genetic engineering, one of them is the possible creation of so called "designer-babies." Wouldn't this be inevitable if genetic engineering was legalized?

No, maybe in 2000 years but not in the near future. Our understanding of the action of genes is so limited. We have some experience with single genes now and we are very proud of being able to treat a few gene conditions. We have absolutely no idea of the individual collaboration of a large number of genes in creating a blue eye colour. I think eye colour isn't a primary interest. One would rather be looking good or being good at school and being successful at the office etc. It isn't clear which genes are involved and what the effect of the environment exactly is. I would consider this unlikely to happen in the foreseeable future. There is a more realistic fear that people might start to look at genes which are just associated with bad performance, whatever performance that is. We know a number of genes and polymorphisms which might be related to difficulties at school. This "designer-baby business" isn't that realistic. Today it is done by just looking at the chromosomes of babies. There are chromosomal abnormalities which are very severe were the babies have no chance. But there are others were the consequences might be infertility or minus fifteen points of the IQ scale. There are parents who consider this a good reason for termination of pregnancy. This is a more realistic fear I would share, not the "designer-babies."

It is heavily assumed that certain genes are responsible for binge eating and alcoholism, could one maybe manipulate them thus curing these conditions? Would you support this kind of treatment?

A very important condition would be that we know exactly what we do. Changing or engineering genes without knowing what their role is in the very complex biological conditions is extremely dangerous. If your are severely ill, like having cancer, you get pills which have a certain effect on these cancer cells. Before you start manipulating genes you should be aware of what you are doing. In the case of cancer it's a matter of surviving, but in the case of changing a gene for liking a drink or binge-eating it's a different story.

How long do you think it will take for society to be ready to legalize genetic engineering for treatment of patients? Which prerequisites would be necessary?
It is a good idea to just go ahead with care. In many European countries, the law is quite liberal compared to Switzerland. In Switzerland, there is no such thing as pre-implantation diagnosis or egg donation. A lot of Swiss people just go to England or east Europe nowadays to get some eggs donated. I don't see a possibility for a major step forward in the next few years. This would be a task of the next 50 years that we would really start to change our genetic constitution. I wouldn't be too concerned about the legal limitations at the moment. We are fighting for pre-implantation diagnosis here in Switzerland just for very obvious reasons, because we have patients who ask for it.

Could you imagine that one-day gene therapy could be normality in hospitals? Even in our lifetime?
It would be possible, but not in our lifetime. There might be single aspects or first steps but I don't think that it would be a major genetic therapeutic business in the next decades. If you look at the importance of genetic testing then the largest effect on practical medicine has been in oncology. The results of genetic testing which are not constitutional but testing with tumours in (mutantology) has changed the actual treatment a lot. In constitutional conditions, the progress is rather slow.

Could one say that the character of a person could be changed by genetic engineering?
It is a realistic concern. If you change genes you changes pathways and you might change the development. It's a very complex collaboration of genes and other factors and my concern would also be if we really know what we are doing when we start certain manipulating genes. Taking a pill is a different story. If you realize that it hurts you, you can just simply stop taking it. But once you manipulated your gene it's rather difficult to reset it.

Organs are trying to be grown in petri dishes. How exactly does this work and could all organs be grown by gene manipulation and inserting own cells into the tissue?
I'm quite convinced that this is a realistic aspect, but it wont happen neither tomorrow nor the day after tomorrow. Because the prerequisites of growing organs in a chamber would be to be able to manipulate the very complex developmental processes. You have to switch on and off a number of genes and cells and none of all at the same time. This is not

an easy task to do. I'm quite sure that it will be possible one day. The short term growing of organs wouldn't be realistic. We use insulin which is made from bacteria which were genetically manipulated. But an organ is a rather complicated business.

Let's assume you insert genes into a person. What would be the worst thing that could happen if you did something wrong?

If the person dies. That would be one major catastrophe or if the person will suffer for the rest of his life because of this fatal mistake.

So if only a simple gene would be manipulated, like the gene which determines the hair colour, would that cause a domino effect? Is this far fetched?

No, it isn't. Because we always learn of effects of genes we wouldn't have expected. In genetics, we're put in a situation where we gain new knowledge weakly. It's frequently, that effects occurs nobody really has considered. Because the regulation of genes during development is apparently a immensely complex process.

Another challenge is, bringing the DNA into the cells. There are several techniques like viral or non-viral. And which technique would you consider as the best?

I'm not active in that field, but it is a very important question. Several people have died due to complications from such viruses used to get DNA into a cell.

What exactly do you work on?

I'm a medical geneticist or clinical geneticist. I treat patients at the children's hospital with genetic conditions or malformations. We also look at babies with metabolic disorders and do prenatal testing.

Dr. Miny presenting us the computer which reads chips carrying DNA pieces

Do you support genetic engineering for the future and why?

I do support it. One reason is to fight against severe disorders. This is one therapeutic approach and I think it can be very successful once we have the knowledge which is required. But we don't have this knowledge yet. But I'm very optimistic that this would change. And the change will come a lot slower than most people expect. But this promises

made about the genetic revolution and to find a cure to cancer or the Parkinson disease will shouldn't be taken to literally. This is only told the public to generate funding for genetic research. But I still stick to my belief that in future, it will be a real therapy, for genetic conditions. So if there is a faulty gene, and if you are able to "repair" it, this could be considered as therapy and not only just taking a pill to cure some side effects. It is a long way to go and even longer than most people expect.

Our impressions

It was very interesting to meet a real geneticist and talk about his views of the future. Dr. Miny answered all our questions in great depth and obviously was extremely knowledgeable. Interestingly, he mostly spoke of "we", referring to the scientific community, and not only of himself. After the interview, Dr. Miny also showed us around the laboratory where he explained the many functions of all kinds of machines and the work his employes were completing. The most fascinating device was the incubator where the cells of the patients are cultivated for diagnosis. Though we all found it interesting to work on this topic, the interview was definitely its highlight! We learned a lot from the interview and got a glimpse of what it means to be a scientist, believing in one's work and its purpose.

Incubator

Discussion

Progress and Future Steps of Human Genetic Engineering

Reprogrammed stem cells:

Stem cells aren't that easy to get and in addition are a very controversial issue. One now seeks for a way to put every arbitrary cell (for example skin cells) in the mode of stem cells. This is done in order to let the cells appear as another one.

Scientists of the University of Kyoto and Wisconsin reported in 2007 that they were able to transform body cells of an adult into induced pluripotent stem cells. In this process, resting development-genes in cells were activated to put them back in an embryonic state. Through the artificial reprogrammed stem cells, scientists were able to cultivate matured cells, like nerve and heart muscle cells in a petri dish.

In 2008, Craig Venter presented the first programmable cell. Every form of DNA can be inserted. He was also able to completely synthesise a bacterium with his team by putting the genome together by hand.

Decryption of the genome:

The decryption of the human genome is progressing. In 2000, it was announced that the decryption succeeded, but it took almost 6 years until the whole order of base pairs were sequenced, nearly. Even today, at every 10'000th base pair a mistake occurs.
At present, the order of the DNA-base pairs is known, but how our approximately 25'000 genes work, how they interfere with each other and if or how variations of gene sequences cause diseases is still not completely known. Scientists can whether tell the looks of a human by its genome nor can they determine the persons traits, but they are still working on it and trying to get to that point.
Scientists need data to associate genomes with diseases and traits. During the first tries of decryption, thousands of scientists needed to apply a lot of time, money and energy. Now, this process works even faster. The last few years were successfully used to decrypt a fistful of complete genomes of humans which were later published. New technology enabled sequencing in a very short period of time. The shortest sequencing process didn't take longer than a month and the monetary loss was greatly decreased.

Pros and Cons of Human Genetic Engineering

The human body could be seen as a construction site of science. Science has the ability to change certain traits in humans, such as inherited faults, which could be passed on to further generations. This is genetic engineering and sounds reasonable. But there is always a downside to the advancement of technology, especially when it comes to the human body.

Pros of Human Genetic Engineering

To prolong natural life span:
Everyone longs for a fulfilled and long life. Human genetic engineering has the potential to greatly increase the human life span. 100 to 150 years of life could become common. Once the genetics of ageing are completely understood, it would be possible to reverse or slow down some of the cellular mechanisms that lead to human ageing. The so called telomere, a DNA-segment on the end of a chromosome, could be prevented from shortening, as the shortening is known to contribute to cell “dulling”.

To heal diseases:
Many people die due to inherited diseases and have to experience their friends and family members do so as well. The genome isn't as strong as we would like it to be and genetic mutations either directly cause harm such as cystic fibrosis or are responsible for it for the most part. If the benefits of gene therapy are realised, the “bad” genes could be replaced by correctly functioning copies.

Additional advantages of human genetic engineering:

- The knowledge gained by this advantages of human genetic engineering could help with the design of more efficient medical products which are able to reach specific genetic mutations in each individual person.
- Through human genetic engineering, humans could potentially have improved strength, speed, intelligence, healing etc.
- A greater understanding of the natural evolution process could be achieved.
- The ability to form new organs could be made possible.

Cons of Human Genetic Engineering

The lack of safety:
The main argument against the manipulation of genes is that it could lead to unexpected outcomes and side effects. The methods used in genetic engineering are artificial and the natural reproductive barriers of humans are breached. Thus, the main worries of scientists are unpredictable alterations in the genetic make up of individuals. Also, it's simply not known, how big the ramifications could be.

The disruption of the natural DNA:
It is heavily debated, whether the insertion of genes is done precisely in living cells. However, often, it isn't clear where to insert genes into the DNA. There is a risk of damaging genetic information present and disrupting gene expression in the DNA.

The fear of creating “designer” babies:
It would be unfortunate if parents could assemble their kids genetically, to be more athletic and smarter or to have a particular eye colour. The individuality of children will be lost and there would be no need of encouraging unique traits in children any more. So children would be created to the parents own preferences, who want their children to be a specific way and have the best of life by manipulation of genes. But these parents would als harm their children in two ways: they decrease their ability to form an own character as well as they deny the child’s right to its own life!

“Playing god”:
Last but not least the aspect of religion is taken into account. Religion does not agree with genetic engineering at all, since religious people are rarely content with science as they have to review their material and beliefs. First of all, god is meant to be omniscient and unbeatable. He, according to the bible, created our planet and gave life to all organisms. The different species living on earth today were designed by him. Since every organism exists for a certain reason, certain boundaries are set for them, genetic engineering causes disruption and chaos in humanity and all other organisms. Nature wouldn't be as it is today. Additionally, Christianity states that genetically modified living being and trying to create new life is challenging the “power” of god and doing such would be a sin. Genetic engineering is therefore blasphemy.

Further arguments against genetic engineering:

- Where is the limit and who is in control? Who will stop scientists and doctors with bad intentions to abuse genetic engineering for example, creating a new life form ?
- As the world is complicated enough as it is, it would get even more complicated trough genetic engineering.
- Humans will no longer be on top of the food chain. “Novel humans” will take their place.

Summary:

Although the scientists' knowledge of genetics is immense already today, there is still much to explore as this topic is extremely complicated. Genetic engineering in humans is not save and not successful enough by a long stretch. Many complications can occur even just because of the vectors utilized to transport the DNA.
It is only a question of time until the techniques are sufficiently improved and patients will be heeled by manipulating genes. Gene therapy is of enormous importance for people with specific genetic diseases. But there are ethical and religious reasons that speak against genetic engineering in humans. When do humans cross the line of playing god and perfecting themselves? Clearly, when it comes to changing gametes and interfering prenatally in a life that is not able to express its opinion yet...
Mistakes would have severe, irreversible consequences for the descendants.
So gene therapy should only be applied in somatic cells for health benefits and not for aesthetic reasons.

Acknowledgments: We would like to thank Dr. Miny for the informative interview.

Vocabulary:

ex vivo: describes processes in which cells are removed from the body and cultivated outside the living organism
in: vivo: the cells are modified directly inside the living body
vector: vehicle that transports the DNA into the cell
endocytosis: intake of the cell through the membrane
leukocytes: white blood cells, responsible for immune response
T lymphocytes / T cells: type of leukocytes
puripotent: capable of giving rise to several different cell types
telomere: a DNA-segment on the end of a chromosome
blasphemy: the act of speaking sacrilegiously about god
pre-implantation diagnosis: refers to genetic profiling embryos prior to implantation

Sources:

picture_front page:
http://www.nature.com/polopoly_fs/7.5895.1345140906!/image/C0139971%20SPL%20reduced.jpg_gen/derivatives/landscape_300/C0139971%20SPL%20reduced.jpg
picture_bubble boy: http://www.savemefromboredom.com/images/smithsonian/bubble-suit.jpg 4.11.13, 22:11pm
picture_general procedure: http://sgugenetics.pbworks.com/f/1301871442/how%20it%20works-gene%20therapy.gif 4.13.13, 00:13pm
All the pictures in the laboratory are self-made.
http://en.wikipedia.org/wiki/Gene_therapy 4.11.13, 21:51pm
http://en.wikipedia.org/wiki/In_vivo 4.11.13, 21:59pm
http://en.wikipedia.org/wiki/Vectors_in_Gene_Therapy#Non-viral_methods 4.13.13, 00:52pm
Claudia Eberhard-Metzger: Das Molekül des Lebens; aktualisierte Neuausgabe 2003
http://www.livescience.com/27206-genetic-engineering-babies-debate.html
http://www.dnapolicy.org/pub.reports.php?action=detail&report_id=3
http://www.nature.com/scitable/topicpage/genetic-inequality-human-genetic-engineering-768
http://www.oregonlive.com/health/index.ssf/2012/10/human_genetic_modification_exp.html
http://getnloose.com/wp-content/uploads/2010/07/8-3.jpg
http://www.123recht.net/Reproduktive-Gentechnologie-__a720__p4.html
http://www.johanna-dohnal.at/fortpflanzungsmedizin-und-gentechnologie
http://www.zeit.de/1988/13/kommen-bald-die-wunschkinder-a-la-carte
tp://www.buzzle.com/articles/genetically-modified-organisms-pros-and-cons.html
http://www.livescience.com/27206-genetic-engineering-babies-debate.html
http://www.allaboutpopularissues.org/human-genetic-engineering.htm
http://www.sein.de/archiv/2009/september-2009/gentechnik-roboter-und-kuenstliche-intelligenz-wohin-geht-die-reise.html