# The DNA Dialogue

**By Gerard Feller**

The DNA dialogue consists of a series of discussions and debates that take place between the middle of 2019 and the end of 2020 throughout the whole country. The goal is to find out what the Dutch society thinks about the modification of the DNA in embryos. The outcome of the dialogues are gathered and presented to politicians, scientists and the Dutch society (1).

The 20th century was the ‘golden age’ of the development of computers, the 21st century is the ‘golden age’ of the genetics. Worldwide there is much discussion about the question whether we are allowed to modify the DNA of embryos. If you modify this DNA, you actually also change the DNA of the next generations. The modification of DNA at such an early stage in life is called Germline genetic modification.

**What is the DNA dialogue about? (2)**

1. The modification of DNA in embryos.

2. The selection of embryos to prevent the child from carrying a hereditary disease.

3. The cultivation of human organs in animals.

4. The production of 'artificial embryos.

**Definition** (3)

Genetic technology or gene technology is a modern form of bio technology whereby the DNA of an organism is directly modified. This is in contradiction to the classic biotechnology whereby the DNA of an organism is indirectly modified, for example by cross breeding (4).

Genetic manipulation is the insertion of a particle of DNA of one organism into the other. This technique is called a recombinant DNA technology.

This is a much more radical and far-reaching than genetic modification on body cells.

The basic principle of all techniques passes a fixed number of steps.

1. The isolation of the gene to be modified (extraction of DNA from the cells).

2. The possible modification of the isolated gene.

3. The transfer of the gene into a suitable vector (for example a virus, a particle of bacterial DNA, liposome\* or a DNA coated golden bullet).

4. Transformation of the cell or organism to be edited. For example the ‘shooting’ of the DNA or via bacteria.

5. Selection of the modified cells or organisms.

(\*a liposome is an artificially synthesized particle composed of a substance which is enclosed by a membrane)

The DNA must be integrated into the so-called genome. The genome is the total of the hereditary information of a cell. The techniques of the transfer of the genes are still far from successful. Scientists have to know which cells have really received the DNA. For that purpose they attach a so-called 'gene marker' to the new gene before it is transferred. Such a gene marker for example identifies resistance to an antibiotic or a pesticide. Then the genetic cells are cultivated in a breeding ground with the antibiotic or the pesticide. Then, only the organisms that have integrated the new DNA with the new gene including the attached marker, will survive. The cells are further cultivated and continue to develop. It is often impossible to properly regulate the insertion of the new gene. This randomness can disturb the highly regulated network of the DNA in an organism.

**CRISPR-Cas9 a method for Germline genetic modification**

In November 2018 the world was shocked when the Chinese researcher He Jiankui announced that he had changed the DNA of two babies. With the help of the CRISPR-Cas9 technique he changed the DNA in the embryos in such a way that the children would later have a smaller chance of contracting the AIDS virus. **This germline genetic modification is the essence of the DNA dialogue.** The mutations in the germline cells of an embryo are permanent, and as a result, the changed DNA is passed on to the offspring. The Chinese researcher was way ahead of what is considered scientifically, clinically and ethically acceptable.

He did this experiment in secret, without consulting a scientific or ethical council. The scientific world criticized him. They claimed that he had taken too many risks and acted irresponsibly. Later, the Chinese researcher acknowledged that the experiment was unsuccessful. At the moment it is not clear where the girls, called Lulu and Nana, are. The birth of Lulu and Nana shows why scientists need to handle the CRISPR-Cas technique with caution.

The picture below give a schematic view of the recombinant – DNA technique

To edit a wrong particle of DNA (mutation), there are three things needed:

1) A guide RNA which recognizes the wrong particle of DNA.

2) Cas that cuts the DNA (shooting or via bacteria).

3) A particle of DNA without error.

Cas and the guide RNA search for the wrong particle until the guide RNA recognizes the wrong particle of DNA. Then Cas cuts out this wrong particle. The space of the wrong DNA will be filled with the good DNA without error. So, wrong DNA can be repaired. This technique offers possibilities for treatment to people with a hereditary disease. With CRISPR-Cas it is also possible to edit the DNA of embryos, so that people can be prevented from transmitting hereditary diseases to their children.

**The future of genetic manipulation**

In the Netherlands, the experiment of He Jiankui would not happen because it is not permitted to ‘create’ embryos for scientific purposes. An artificial insemination is only permitted with pregnancy as a goal, not for science.

The Dutch scientists are also not yet permitted to edit the DNA of an embryo, so cutting out diseases in DNA is not possible in the Netherlands. In the United States, the United Kingdom, Sweden and Belgium it is permitted.

In the Netherlands, however, there is mention of a possible amendment of the Embryo Law, amongst others in 2016 by former minister of Health, Edith Schippers.

She proposed to extend the law for embryo research in favor of fertility problems, cancer and serious hereditary diseases. In March 2017, the Health Council advised the minister to allow it. The council argued that this is not in conflict with human dignity when the breeding embryos (under strict conditions) are used for research that is focused on the prevention of serious diseases. According to the NPV (the Dutch Patients Union) an embryo is life at an early stage and is intrinsically valuable. Therefore embryos deserve protection. The NPV claims that embryos are not to be used, but to be fully fledged in the safe environment of a uterus (5).

**Possibilities with Crispr-Cas**

With the entry of Crispr-Cas, the cut and paste technique with which DNA in the body of a patient can be accurately repaired, the gene therapy seems to enter a new century. Repairing and correcting DNA, pasting and adapting genes: now the complete genome of man has been mapped, it seems possible to erase, or at least blur the misprints from the book of life. The restoration of those errors can make the malfunctioning factory in the cell to function again. So a patient with a hereditary disease can actually make his own medicine.

“What we're doing so far, is quite remarkable”, acknowledges the stem cell biologist Staal from the LUMC (University Medical Centre from Leiden). “In the classical gene therapy, we add a healthy gene in the cell, just like when you have a broken headlight in a car and the garage owner says: we’ll put an extra light on the roof, so you have some light”. With Crispr-Cas the headlight itself can be repaired, but Staal is reluctant about that. “The possibilities are exaggerated. In order to repair a gene you must be able to reach it, but DNA is pretty much wrapped up in a cell core. And what works in a breeding bowl or in a mouse, doesn’t necessarily have to be effective with a human being. For a baby alone, you’ve got to get 50 million stem cells to be repaired (6)”.

After decades of promises, also in the Netherlands the first genetic treatments have now come on the market, amongst others for leukemia and for the serious muscle disease SMA. Two gene therapy medicines, for patients with a hereditary retinal disease and a blood disorder beta-thalassemia, have been assessed.

Recently, the first registration request for gene therapy for Hemophilia A, has been submitted to the European Medicine Agency (EMA). All over the world, there are hundreds of ongoing assessments on the use of genetic therapies, of which about ninety are in the final stage, according to a statement of the VIG, the dome of pharmaceutical companies, in a recent report (6).

The approach routes at all those treatments vary, depending on the disease that the scientists want to deal with. They put a healthy part of DNA in deactivated viral parts, which then find their way, just as a letter with special contents is delivered at the right destination. Or they make a sort of mask that masquerades a genetic material in cell cores, so that they do not function anymore. Or they extract immune cells from the body and edit them in such a way that they can recognize a tumor after they have been re-inserted. Or, the last addition in the field is, that they send out small synthetic cut and paste machines into the body that can correct a DNA error.

**The cure of the disease of Batten?** (6)

The eight year old Mila Makovec came in the international media in last autumn, because American physicians had designed a genetic medicine just for her. Mila has the fatal disease of Batten; due to a DNA error, toxins were accumulating in the cells of her body, with the result that she deteriorated rapidly. Owing to a tailor-made genetic plaster, paid with three million dollars fundraised by her parents, they were able to mask the error, which caused her deterioration to stop. The story of Mila created worldwide expectations that also approached the office of the professor of Translational genetics from Leiden, Annemieke Aartsma-Rus.

Every month she receives new questions, she says, from patients, parents and scientists that only want to know one thing: what was successful in Mila's case, is that also possible for another genetic disease? Mila was helped with a so-called antisense-oligonucleotide (ASO), a sort of band aid that prevents the wrong code in her DNA to be transmitted to the factory in the cell. The developments regarding those ASO's are rapid, according to Aartsma-Rus: worldwide there are ten medicines on the market, out of which six are from the last few years. The coming period there will also be a research in the Netherlands on the use of ASO for the deadly Huntington disease. “But now the misconception”, Aartsma-Rus says, “what was possible for Mila, is really not the case for all diseases. Tim Yu, the American geneticist that produced the Mila medicine, recently warned for false expectations at a congress” (6).

**Cultivating embryos for research goals are needed to further develop the Crispr-Cas method.**

With embryo selection, the birth of a child with a serious genetic disorder can be prevented. Embryo selection is carried out with couples that run a strongly increased risk of having a child with a genetic disease, such as cystic fibrosis, the Huntington disease or a serious muscle disease. Another word for this method is PGD, Preimplantation genetic diagnosis. By an in-vitro-fertilization treatment, embryos are created. These embryos are analyzed for the presence of the disease in question. Then on the fourth or fifth day after the fertilization, it is determined which embryo is considered for replacement in the womb.

The remaining embryos are disposed. The chance for pregnancy after replacement is approximately 25 percent.

In the Netherlands, the parents as well as the embryos are protected by many laws, as established on the basis of scientific ethics. In 2002, the Embryo law was introduced. In this law it is stated what is permitted and what is not permitted in an embryo research and IVF treatments (in vitro fertilization, also called test tube fertilization). Parents who want to have children by IVF, give multiple eggs and sperm to the hospital, from which they make embryos. The remaining embryos may be used for research on the improvement of IVF. Currently, only ‘residual embryos that are four days old are permitted to be used, not before.

After 14 days these 'residual embryos' are to be disposed. The tissue of the aborted children are also permitted to be used with the consent of the parents.

Defenders of the cultivation of embryos, indicate that also with a 'natural reproduction' many mistakes occur. Only one out of five natural generated embryos, makes it to the final stage of the pregnancy, because the major part dies already after the fertilization, due to serious defects. That often happens even before the woman even knows that she is pregnant. Besides, five percent of the babies which are born alive, has a genetic disorder (7).

**When does life begin?**

Strikingly enough, a lot of Christians have no difficulty with IVF, while with this method 'residual embryos' are killed or used for genetic research. Fortunately, there is also a majority among Christians that in general terms reject the 'cultivation' of embryos for research purposes. A very important fundamental question in the entire DNA dialogue is: When is it a case of life?

Steve Jacobs, a well-known researcher, asked 5,577 biologists the question about when human life begins. Almost all of them (96%) affirmed that a new human life begins after the fertilization (8). Abortion was legalized in the USA after a crucial lawsuit (Roe vs. Wade 1973) because at that time there was no consensus on when human life begins. Remarkably it was then decided to legalize abortion for they did not know if with abortion a human life is killed.

Today the legislation is different in many states in the USA.

Some states ban abortion, but other states, on the contrary, legalize it at any point of the whole pregnancy. The final product of a mammalian fertilization is a fertilized egg (zygote). It is a new mammalian organism in the first stage of the life cycle within the genome of its kind.

In a previous Promise article we have elaborated on when life begins.

In this article Francis J. Backwith claims the following: “In the course of history, many criteria have been mentioned in the abortion debate, in order to determine when a human organism in its development has reached the point that it can be called a complete human being. Some criteria are based on so-called 'decisive' moments in the development of the fetus. Other criteria are based on certain conditions that a creature, whether born or unborn, must meet to be considered a human creature.

And yet others claim that there is no 'decisive' moment, but that as the unborn grows, there is an increasing potential possible for being human. I think that all these views are poor. In this article I defend the view of pro-life, which implies that the being of a complete human begins with the conception. This is the most coherent and is in agreement with our fundamental values. To defend this view adequately, I will criticize some criteria that are used against the pro-life vision”, according to Barkwith (10). Also in this Promise Magazine we defend the protection quality of the embryo in the article 'Is pro-life hermeneutics possible?”.

Many Pro-Choice activists also admit that “The Pro-Life groups are right about their statement that the place where the baby finds itself, whether in or outside the uterus, is not relevant”. Therefore it is illogical that we think it's alright if a baby is killed one week before birth, while as soon as it is born, everything must be done to keep the baby alive.

**Artificial fertilization**

In the magazine 'Leef (Live)' of October 2019 (9), Shanti Bolt states that the LUMC researchers have tried to use donated female embryos and fetuses for the research into more far-reaching artificial reproduction. The female embryos themselves actually also have a reproduction organ. It contains future eggs for the next generation. They were researching which environmental factors are necessary for the development of these eggs. This was the key to the formation of eggs out of stem cells. In this way they ultimately succeeded to produce reproduction cells (eggs and sperm cells) from stem cells out of the skin of adults!

This implies, according to Bolt, that ultimately we wouldn't even need a uterus, because they're already working on a 'cultivation bag' in which the child can grow in a right environment for nine months (9). That could mean in the future that 'residual embryos' will not be needed anymore 'to make' life. At the one hand it could mean that no 'residual embryos' will be used, but on the other hand, having a child will be more and more a manufacturability 'project' of the parents. Beside the DNA, in the Biblical view of man, the relationship of the soul and spirit of a human being is decisive for his development.

Dr. Henk Jochemsen, the former director of the Lindeboom Institution, also admits that an embryo is a man in formation and therefore enjoys full protection.

He welcomes in principle that hereditary diseases are combatted by the germline genetic modification, provided that the technique is safe and there are no embryos needed for research. At the same time he asks the question in the Linde Magazine whether the application of technique will remain limited to this. “There is no hard line to be drawn between the cure of diseases and 'human (gene) editing'. Do we get a 'human to order' in future, where we stick the desired characteristics in the DNA?

That is, according to Jochemsen, in conflict with receiving life as a gift and the awareness that fullness will only be in God's future (11). A designer baby to order is likely to be on its way. Scientists seem to make less and less distinction between what they can and what they must do. David Hirsch says that postmodernists must be well aware that it is impossible to fragment a human being into parts without making the individual worthless in the real world (10).

The legal distinction between life and machine, between life and product, is beginning to disappear. We are witnessing a depersonalization of human life, if all parts of humans and genetic materials are sold and patented, processed and developed.

**PGD**

PGD is an abbreviation of Preimplantation Genetic Diagnostics. This is a method with which the birth of children with a serious genetic disorder can be prevented. PGD is carried out with couples that have a strongly increased risk of having a child with a genetic disorder, for example a chromosome disorder, cystic fibrosis, Hemophilia, Huntington disease or a serious muscle disease.

For PGD, an IVF treatment is necessary. Here – after the fermentation of eggs with sperm cells outside the body – one cell is extracted from embryos. This cell is tested in the laboratory for the presence or absence of the disease in question.

On this basis it is determined on the fourth or fifth day after the fertilization, which embryos are qualified for the placement in the uterus. Only embryos without the genetic disorder on which the test was focused, will be placed in the uterus. The chance of pregnancy after replacement is approximately 25 percent (PGD The Netherlands; Handyside 2018). (12) As mentioned earlier, the killing of residual embryos is a bridge too far for many Christians.

**Next Generation Sequencing**

In the Linde Magazine of November 2014 (it is not mentioned in the list of literature, but something from 2019 is mentioned) the risks of an increasing genetic screening are also discussed. Further fragmentation of the human DNA profile has become possible by the so-called Next Generation Sequencing (NGS). The possibilities regarding the prediction of contracting diseases have increased tremendously compared to the 'old DNA screening method'.

Many more base pairs (hereditary material) can be read at the same time than in earlier days. Additionally, by the means of NGS, it is now possible to determine a diagnosis and a prognosis faster than in earlier days. By this new method of screening, legal and ethical objections against gene screening is highlighted.

**A practical example (7)**

Diagnostics for the prevention to be a carrier of diseases. The question is whether IVF-PGD can be permitted to meet the desire of the future parents.

This desire is: “My partner and I **do not** want girls, for girls will be carriers of hemophilia (7). We want to prevent the possibility of this disease to be transmitted and that our grandchildren could get it and we also want to prevent our children (in case they are girls) from facing the same challenging question when they consider to have children themselves”.

In order to permit this request, which is moreover understandable, they, for the time being, must permit through the IVF procedure, the killing of residual embryos.

**Are there alternatives? (7)**

The alternatives are: (a) refraining from having genetic 'own' children, (b) using sperm or eggs from donors or choosing for surrogate motherhood, (c) using prenatal diagnostics (NIPT – noninvasive prenatal testing) and possible termination of the pregnancy, (d) sperm selection, (e) germline genetic modification, (f) going to another country where the treatment is possible, (g) or accepting the risk of having a child to be a carrier of a disease.

All these alternatives are questionable. Sperm selection and germline genetic modification still have a long way to go and it is not clear whether it will reach ethical acceptable applications at all. It seems to me that the most mentioned options are not desirable for Christians, because of the objections mentioned earlier in this article.

The acceptance of the risk of having a child that is a carrier would be an option for Christians who in prayer can trust that in case of a hereditary disorder, God will grant them the strength and vision to raise their children in challenging circumstances. Alternatives that may be an option for some people are: refraining from having genetic own children and moving on with adoption or foster parenthood so they can still raise and take care of children.

**The cultivation of organs in animals?**

This is actually about two types of human-animal combinations, namely cybrids and iPS cells (induced pluripotent stem cells).

The first - cybrids - momentarily do not play a significant role (anymore). These cybrids are the result of inserting a nucleus of a human cell into a de-activated animal egg cell. This is how an embryo comes to being with 99.9 percent human DNA in the cell core and 0.1 percent animal DNA in the mitochondria. Cybrids were intended as an alternative for research with human embryos, but that promise has not been fulfilled.

In the second type it is about iPS cells, 'ordinary' cells that are reprogrammed into stem cells with embryonic features. When human iPS cells or 'ordinary' embryonic stem cells are inserted in an animal embryo, we have to do with a ‘chimaera’. The idea is, that through this way, eventually, inherent organs of the human body will be cultivable in animals. Fundamental research has shown in the meantime that this is possible in principle (14).

In the meantime they have succeeded to cultivate a pancreas in pigs with stem cells of other pigs. In the same way they can possibly grow stem cells of humans in an animal to produce the desired organ. This organ is expected to be very suitable for transplantation, especially also because 'custom made' organs can be made by using stem cells (cells of the patient himself). Or actually: the desire of man to create human-animals, called chimeras ('mixtures'), in order to grow in this way human kidneys, hearts and other organs. This sort of research is under discussion in the Netherlands, and prohibited under the current Embryo Law. In 2017, the Ministry of VWS had a report written for the public debate on prohibiting or not prohibiting the cultivation of human organs in animals and the ethical questions involved.

**Christian view on chimaeras** (15)

A fundamental objection in this respect is the 'respect for human dignity'.

Imagine that the formation of chimaeras leads to a partially human brain, or to the formation of human reproductive cells? In case the research with human-animal mixture is going to be permitted in the future, then the NPV would recommend that it must be required that no human embryos would be 'spent'.

In a Christian view there is a fundamental difference between man and the human society at the one hand and animals at the other hand.

Which, by the way, doesn't imply that we can do whatever we want with animals. The production of a human-animal mixture, whereby human brain cells are developing in the brains of an animal, doesn't necessarily produce a humanlike creature of that particular animal, but it can cause the animal to suffer. Is the creation of a human-animal not an approach in which the reality – the nature – is set according to our mind? Whereby natural borders or regulations are violated, which can cause new problems? Is it not better to focus on other forms of organ donation, than focusing on creating mixtures?

**Does genetics open the door for fascism and other energetics?**

Materialistic naturalism is advancing among secular science. These are the words from Robert Museum Haynes, chairman of the 16th international congress of genetics. “Three thousand years ago, the majority of humanity was convinced that man was something magical. That is a Jewish-Christian conception. The possibilities of manipulating genes of man, make much clearer that we are crucially biological machines. The traditional thinking, based on the idea that man is something special, something unique or even something sacred, is outdated” (17). In the Second World War there was the 'item' of race purity.

It only became really dangerous when the Darwinist philosophers tried to formulate the scientific application as a basis for the Nazi eugenic program”.

Ernst Haecel (18) already stated much earlier: “Hundreds of thousands of incurable lunatics, people with cancer, are kept alive artificially without the slightest profit for themselves or for the benefit of others in general!” Those who did not fit in the Aryan image, were considered genetically inferior. When economic and social pressure are combined with different biases, the postmodern constructivism offers an attractive basis to exterminate “undesirable features” from the gene database.

**A challenge for Christians** (4)

We are entering a new era in the battle for human rights. The ever more developing secular world view, which is rooted in a genetic determinism and postmodern constructivism, leaves little room for the dignity of human life.

If man will ultimately be cloned anyway, will it be a person with constitutional rights? We are witnessing the depersonalization of human life, in case all parts of men and genetic materials are sold and patented, edified and developed. We will also have an unprecedented change of traditional, social and legal definitions. Traditional conceptions of life, birth, disease, death, mother, father and person begin to waver and will disappear in the end (16). With the depersonalization, important moral differences are obscured by scientific and legal jargon. The result is that genetic research and technology are ethically and humanly less and less anchored.

I think that faith in God and man as His image carrier, is the only basis with which we can limit the present developments. Christians should take a well-informed position on genetic manipulation and cloning. This applies to both the use of genetic technology and the possible risks. Professor dr. A. Houtepen, a roman catholic theologian, stated: “genetics must also be considered from the perspective of the finiteness of man and the vulnerability of the universe.

Neither an anthropocentric exploitation drive nor a cosmic equation of man with animal and plant is fitting in stewardship (4). It is not desirable to suffice with technical solutions under the continuation of today's lifestyle.” Or as Frits Lange states in a protestant view on the cloning of man and animal: “Not only the question 'how did God create the world?' is important, but above all, *what* did God create the world *for?*!” Gene technology should be as every therapeutic means, a means that can be blessed by God, and therefore an extensive test by the Spirit is imperative in every form or application (4).

Gerard Feller, February 2020

Translated by Ursula Moestapa

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Kader (4)

**Bezwaren gentechnologie (Objections to Gene technology)**

Geen gentechnologie op de kiembaan (No gene technology on the germline)

Geen gentechnologie zonder bescherming van het embryo (no gene technology without protection of the embryo)

Geen gentechnologie voor niet-geneeskundige doelen (No gene technology for non-medical goals)

Geen gentechnologie voor superras (No gene technology for master race)

Geen gen screening met statistisch dubieuze voorspellingswaarde (No gene screening with doubtful predictive value)

Geen gentechnologie alleen voor elite. (No gene technology for elites only)

Geen gentechnologie die de biodiversiteit verminderd (No gene technology that reduces the bio diversity)

Geen klonen van mensen (No human cloning)

Geen gentechnologie die de generatiekloof verder vergroot (No gene technology that further enlarges the generation gap)

Geen gentechnologie die discriminatie van ras of gehandicapten bevordert.(No gene technology that increases the discrimination of race or the handicapped)

Geen gentechnologie die het begrip ziekte oprekt.(No gene technology that extends the conception of disease)

Geen commerciële exploratie en oneerlijk gewin bij octrooien. (No commercial exploration and dishonest profit with patents)

Geen overmatige rol gentechnologie in behandeling van de gehele mens naar geest-ziel en lichaam.(No excessive role of gene technology in the treatment of the whole human to spirit, soul and body)

Gentechnologie moet net als ieder therapeutisch middel een middel zijn dat door God gezegend kan worden, en daarvoor is een uitgebreide toetsing door de Heilige Geest en Gods Woord onmisbaar.**(Gene technology must, as every therapeutic means, be a means that can be blessed by God and therefore it needs to be extensively tested by the Holy Spirit and God's Word)**

**Voordelen gentechnologie**

Erfelijke afwijkingen eerder ontdekt en mogelijk voorkomen.(Benefits of gene technology: Hereditary disorders can be found earlier and possibly prevented)

Erfelijke afwijkingen genezen door middel van gentherapie (Hereditary disoders can be healed by the means of gene therapy.)

Efficiëntere antibiotica, enzymproductie door fermentatie.(More efficient antibiotics, enzyme production by fermentation)

Resistentie en profylaxe tegen sommige ziekten.(Resistance and profilaxis against some diseases)

Geneesmiddelen via recombinant DNA-technieken.(Medicines via recombinant DNA techniques)