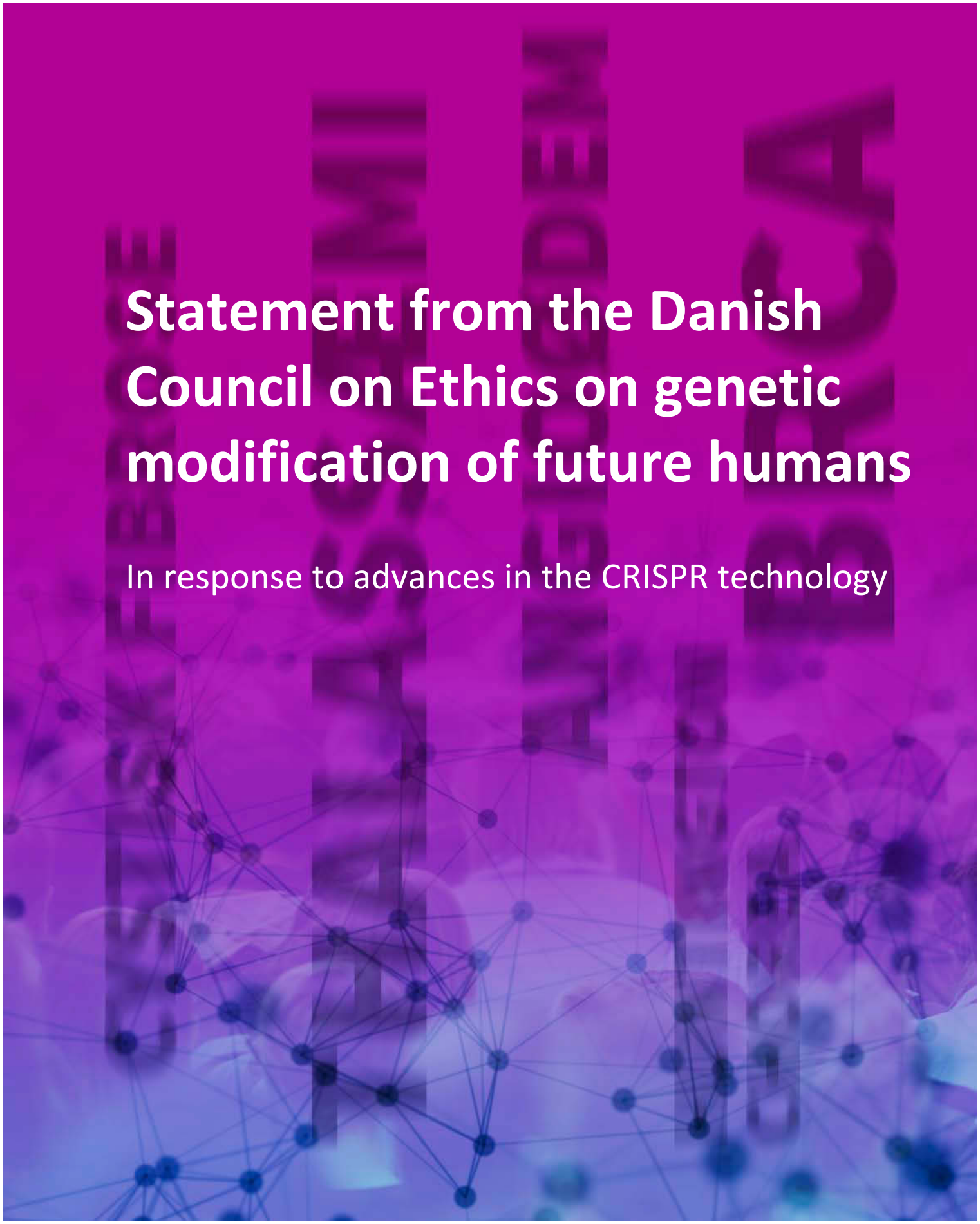
Statement from the Danish Council on Ethics on genetic modification of future humans

In response to advances in the CRISPR technology



THE DANISH COUNCIL ON ETHICS

Contents

Colophon

Statement from the Danish Council on Ethics on genetic modification of future humans

In response to advances in the CRISPR technology

Published by the Danish Council on Ethics 2016

Front page illustration: Danish Council on Ethics, iStock.

Danish Council of Ethics
Holbergsgade 6
1057 Copenhagen K
Denmark

T: +45 72 26 93 70
M: kontakt@etiskraad.dk
W: www.etiskraad.dk

Statement from the Danish Council on Ethics on genetic modification of future humans in response to advances in the CRISPR technology

In the last year, the use of gene technology to modify humans and future humans has spurred on international debate, not least prompted by the emergence in 2012 of a new technology known as CRISPR, which can be used to edit our genetic material (genetic modification).[1]

What makes CRISPR different from earlier known techniques for genetic modification is that it is cheap, easy and quick to work with, which has made it easily accessible. It has meant that thousands of researchers are now working to refine it, and that it might not be that long before the method will be used to genetically modify human beings. It has spurred a renewed ethical debate revolving around the possibility of modifying genes to treat diseases as well as whether the technique in the long term would be used to enhance normal traits.

This statement presents the Danish Council on Ethics' recommendations on whether genetic modification aimed at **removing susceptibility to disease in future children should be allowed in order to give birth to a healthy child,** should this become technically possible.

The Council does acknowledge that there is a large grey area between diseases and the outer limits of normal, and that it will be a challenge to allow the removal of diseases but not enhancements. The Council will also consider this aspect.[2]

If gene modification of future humans was to be allowed, a legislative change is required. The specific techniques would involve the removal of disease genes either from germ cells (eggs and sperm) or from fertilised eggs, so that the foetus and future child would be free of disease. It would thus imply using genetically modified eggs to establish pregnancies, and this is presently prohibited in the Act on Assisted Reproduction.[3]

[1] CRISPR can be used for genetic modification of any organism, humans, animals and plants, and a lot of research is already being done. One example is the modification of mosquitoes to eliminate the spread of infectious disease. However, this statement will focus solely on modification of human beings.

[2] With this delimitation, the Council notes that basic research involving genetic modification of fertilised eggs up until 14 days after fertilisation is already allowed in Denmark under certain conditions provided in the Act on Assisted Reproduction. In addition, research and treatment using gene therapy in humans is already being conducted. Research projects must be approved by an ethics committee, and investigational treatments must satisfy the general rules in the area.

[3] Permitting it would require a legislative change in regard to both research and treatment. Section 27 of the Act on Assisted Reproduction prohibits research with modification of fertilised eggs beyond 14 days, and section 2 establishes that assisted reproduction must not take place "unless the aim is to fuse a genetically unchanged (unmodified) egg cell with a genetically unchanged (unmodified) sperm cell."

Current development – research in modification of fertilised eggs in China and the United Kingdom

In April 2015, media around the world reported that Chinese scientists at the Sun Yat-sen University in Guangzhou had modified human embryos by means of CRISPR/Cas9. Attempts had been made to modify the gene responsible for the serious, genetic blood disorder known as thalassaemia.[4] The long-term goal was to develop foetuses free of this hereditary disease.

The results were not optimal and did not show that CRISPR/Cas9 could be used to achieve safe changes in fertilised eggs. Only a fraction of the modified eggs contained the intended genetic changes, and the scientists also found surprisingly many *off-target* mutations acting on other parts of the targeted genome.

It is not clear if the many errors happened because the embryos were abnormal; They carried an extra set of chromosomes and thus were non-viable. Whatever the reasons, several subsequent studies report to have improved the safety of CRISPR – in some cases reducing the error rate to undetectable levels.[5]

On 1 February 2016, developmental biologist Kathy Niakan from the *Francis Crick Institute* in London was licensed to edit the genes of human embryos to learn more about how genes affect early foetal development. This is a basic research experiment, which will be stopped after seven days, after which the eggs will be destroyed. Similar studies could be conducted in Denmark if approved by an ethics committee.

Problems of genetic modification: lack of knowledge

The advances made by researchers appear after decades of generating more and more knowledge about genes – how they control the organism, and how genetic defects are responsible for a multitude of diseases. Along with the progress it has also become clear how much we still need to learn about genes and not least how they interact with each other and with their surroundings.

One of the challenges is that only very few diseases are caused by a single gene. In the past decades, we have learned that genes interact and impact each other in complex ways. "Multifactorial" and "complex" are some of the terms used to describe common diseases like diabetes and cancer as in most cases they are caused by interactions between many genes (inheritance) and many external influences like food and alcohol, radiation and other environmental factors (toxic substances perhaps). Most of our traits in effect arise from a multi-compound of genes. In fact, a seemingly simple trait like height has turned out to depend on the functions of several hundred genes. And each of these genes may impact several different traits.

[4] Cyranoski et al. 2015. Chinese scientists genetically modify human embryos. *Nature News,* 22 April
[5] Ledford, H. 2016. Enzyme tweak boosts precision of CRISPR genome Edits.
Nature News, 6 January

It has also been a challenge that the techniques used are time and money consuming and unprecise. Unprecise means that there is no complete control of the number of modifications made to the genome, including where they occur. Progress has also been set back by a couple of early investigational treatments where patients developed serious side effects. In the past 5 to 10 years, great advances have, however, been made, and many therapies are being tested.

Genetic modification of germ cells and fertilised eggs

Removal of disease and prevention

So far, all experiments with genetic modification have been conducted in humans after birth. It could, however, be beneficial to correct the defective gene as early as in the fertilised egg when it consists of only one cell or in the egg or sperm before fertilisation. The benefit would be that the healthy gene would be present in all the cells of the future child. But considerable problems must first be overcome to ensure that the technique to modify embryos or germ cells can be done in a safe manner. Experiments with gene editing of fertilised eggs has been considered to hazardous because unanticipated errors would follow the child throughout its life and be passed on to subsequent generations.

The advent of CRISPR has reawakened discussions that perhaps it would be possible to develop safe therapies at these stages – to correct mutations, i.e. disease-causing errors in such a safe way that the risk of unanticipated side effects can be minimised. Potentially, babies could be born without genetic disorders and without genetic defects in their germ cells, which would mean that the disease is not passed on to their children. Research with such interventions is already taking place, at least in the USA, China and the United Kingdom.

But the question to be answered is in what situations genetic modification is necessary to avoid disease genes in future children. Today, Pre-implantation Genetic Diagnosis (PGD) and egg selection in families with hereditary dispositions for serious diseases is used. Here, several of the woman's eggs are fertilised with the man's sperm, healthy embryos are selected, and the pregnancy is established using one of them. This technique can be used in most cases, but in a few cases, e.g. if both parents have the same genetic disease and have mutations in both genes (homozygote), PGD cannot be used.

In theory, one could imagine that genetic modification of embryos could become so effective that it could take advantage over PGD if the couple together had hereditary susceptibility to several serious diseases. In theory, the technique could be refined with such precision that it would be unnecessary to fertilise more eggs than needed for implantation in the woman, thus avoiding the discarding of fertilised eggs. One could also imagine that carriers of a genetic disease would want to have their fertilised eggs or germ cells modified to prevent their children from developing the disease or becoming healthy carriers of the disease gene with the inherent risk of passing the disease on to subsequent generations.

But if it was to become possible to make safe interventions in future humans, some are saying that the next step could be genetic prevention of non-hereditary diseases. It is known that a fraction of people have natural gene variations that make them resistant to certain diseases. A gene variant has been identified that significantly reduces the carrier's risk of heart attack, another that protects against Alzheimer's disease and dementia, and yet another that protects against HIV. In the years ahead, it is likely that we will discover more gene variants that increase the carrier's resilience to various diseases. Some refer to it as a form of vaccine against disease if these genes were added to future children.[6]

Enhancement

The next step after therapeutic treatment could be the enhancement of normal traits, i.e. genetic modification of future humans, not with the aim of bringing people with genetic susceptibility to disease on level with healthy people through the removal of susceptibility, but with the aim of making them better than the "norm". Most people question this type of intervention, but sometimes it is difficult to draw a sharp line between diseases and the outer limits of normal. Consider this: Is it a disease having protruding ears or being very short? While this is debatable, we nonetheless treat both conditions in hospitals. The boundaries of disease are not fixed. They are continuously being drawn and redrawn in different cultures with different opportunities for treatment.

Nor is there a hard-and-fast boundary to normal traits like intelligence, musicality, endurance, appearance, etc. Traits that are often considered to increase the individual's chances of success in a society like ours. We currently know too little about the genetic mechanisms behind these traits to change anything – and the degree to which they are genetically determined is also debated. The way in which the genes determine a trait like intelligence is not known in detail, and many environmental factors impact the development of intelligence. But perhaps in future it will be possible to improve such traits through genetic modification.

Risks

There is a general risk that genetic modification will edit other genes than those originally targeted (off-target effects). Since a multitude of genes control foetal development, the spectrum of undesirable effects in the future child is especially wide. Another cause for concern in connection with genetic modification of fertilised eggs is whether it will be possible to check and control how many embryonic cells are modified considering that the CRISPR process develops while the egg is dividing into several cells to become an embryo. if not all cells in the embryo are modified, this could potentially create a mosaic effect in the foetus. If, for example, the intention is to eliminate a genetic hepatic disorder and exactly those stem cells transforming to liver cells are NOT modified, it means that the genetic disease is not avoided in the future child. And even if the editing takes place at the one-cell stage, there is no guarantee that both genetic copies are

[6] Regalado, A. 2015. Engineering the perfect baby. *MIT technology Review,* 5 March (https://www.technologyreview.com/s/535661/engineering-the-perfect-baby/)

modified. It will take several generations to clarify these matters, or 50-100 years in humans.

That said, we should not forget that 'ordinary assisted reproduction' may also have undesirable effects, which – even after 30 years of use – remain to be clarified fully. We know that there is a risk of damage to the genes' DNA. We also know that thousands of healthy children have been born and that their risks of e.g. malformations are slightly increased at most. The oldest of these children have had children of their own. But we do not know yet if there is an increased risk of disease later on in life. In everyday practice of assisted reproduction, these safety questions do not weigh heavily.

Ethical themes

Below we present some of the most frequent arguments for and against genetic modification of future humans. Since there is no hard-and-fast boundary, we will include arguments about the modification of normal traits even though our statement only considers the removal of disease genes.

Weighing the risks

In genetic modification of future humans, exposure to unintended risks assumes a whole new perspective compared to cell therapy in the developed body. If we make modifications already to eggs and sperm cells (germ cells) or fertilised human eggs, and the procedure goes wrong, the worst-case scenario will be a number of malformations and diseases that will even be hereditary. Any modifications to genes will be passed on even when the interventions turn out to cause unintended side effects.

Given the major risks involved, it is relevant to ask if it can ever be justified to attempt to modify future humans and their offspring? At the very least, it should always be considered whether there are just as good alternatives in the form of less risky and equally effective treatments.

The risks of genetic modification are probably acceptable if it concerns the implementation of thoroughly tested gene-based interventions on germ cells and fertilised eggs to prevent serious diseases and secure the birth of a child that will be healthy. Provided the modification is successful, the child – and its offspring – will be able to live a normal life free of functional impairment, medication and other burdensome therapies. Here, it should carry substantial weight that both the patient and society will benefit highly if such interventions could be implemented.

The weighing is different if the intervention is intended to enhance normal traits. The benefits derived from such modifications would seem more dubious than if it is done for therapeutic reasons. Weighing up the risks and derived benefits suggests that in this case greater emphasis should be placed on the risks of unanticipated hereditary side effects. But if we accept the distinction between disease removal and enhancement, borderline cases will put us to the test as with

the examples of protruding ears or hereditary obesity. Both conditions are treated by the health services, even though it is a matter of opinion if they are performed for therapeutic reasons or to enhance normal traits.

The interests of the future child and of the parents

One of the ground pillars of societies like Denmark is that the individual's ethical status confers a right to treatment for serious illness through the common health services. But when it comes to the ethical status of future humans – fertilised eggs and foetuses – opinions differ. Some might argue that a germ cell or a fertilised egg does not have the same ethical status as humans and thus have no right to have disease genes removed for its own sake. But this view is fully consistent with the notion that if reproduction is the aim; if a pregnancy is being established and the intention is for it to turn into a human being nine months later, then you do have an obligation to the human being that will exist at that time to treat it for disease if possible. Whether that obligation implies that the disease should be treated before rather than after birth would depend on an assessment of risks and alternatives in the individual case.

To this can be argued, that there are alternatives to creating a child of germ cells from humans who are carriers of serious hereditary diseases. In order to genetically modify fertilised eggs, artificial insemination must be performed. Prior to this, there is no future human being whose interests must be considered. In other words, it is the interests of the couple wanting a genetically related child that initiate the process of artificial insemination and the development of a human being. And it could be argued that we should never embark on this uncertain path when the couple has alternatives in the form of donation of germ cells from healthy donors, adoption or not having children at all. When we weigh the interests of the couple against those of the child created through artificial insemination, great emphasis should be put on the major uncertainties that exist in the form of possible unanticipated side effects in the child. There is thus a pessimism in this view with regard to it ever becoming possible to make it safe to remove disease genes from future humans. Rather than running a risk through genetic modification of germ cells or embryos enabling the couple to have a child who is genetically their own, it should be made easier to adopt and to use germ cells from healthy donors. Here a legislative change could be considered, allowing the receipt of both donor egg and donor sperm in cases when this would be necessary.

The right to an open future

German philosopher Jürgen Habermas once argued that in order to be free, you must be created by chance, and that being free should be a basic human condition. If someone has designed a human being, it is not free, because it is born to fulfil expectations of doing well in areas predefined by others. Such expectations will already from the start restrict the individual's freedom to choose its own life. This argument especially applies if gene technology was to be used to enhance the normal traits of future human beings since we generally would not

consider the actions taken by parents to protect their children from disease as a way of controlling their children's lives.

The argument for the right to an open future can be contested: You do not have to be genetically modified to experience high and controlling expectations from parents and the surroundings. Parents seek to influence their children all the time with their expectations by sending them to certain schools, sports activities and musical tuition and restricting what they are allowed to do and so on. Moreover, it is not true that an unmodified genome is a guarantee of freedom, since some genomes may actually restrict the freedom of individuals. For example, people with low intelligence or socially or physically impaired people will often feel less free in the sense of having fewer possibilities compared to other people.

Genetic modification increases and fortifies inequalities

A completely different argument focuses on another aspect of the potential to genetically enhance future human beings. If society cannot make such modifications available to all, the rich might pay to have their children modified to possess many of the traits associated with achieving success in our society. The competitive edge that these children already have will be sharpened further, and the gap between the top and bottom of society will grow wider with the potential risk of increasing existing inequalities within society as well between countries. This argument too is focused on the perspective of enhancing normal traits of future children. When it comes to interventions to remove genes with susceptibility to serious illness, in countries like Denmark, we would (in principle) expect to see it offered equally to everyone through the national health services.

Based on the inequality argument, it could be objected that it is not a necessity to implement the technology unequally. In a democratic society, we can decide that a modification that most people would agree would be beneficial to all should be offered to everyone, which is already the case with conventional healthcare treatments. If everyone e.g. got the opportunity to be modified to having higher intelligence, we could say that equality, not inequality, is increased. The unfairness that can be said to exist when some are born with better conditions than others, genetically and socially, could be reduced if everyone had the opportunity of such enhancements.

The natural order

Another argument attaches importance to the value of a natural order. The genetic variation in a population is there for a reason. To some it means that this order was created by God. Others will argue that nature in itself is controlled by an order or mechanisms whose complexity is beyond our comprehension. In both cases, the proponents of this view argue that human beings should not challenge the natural order, but should accept that there is a limit to their interference with nature, and that certain things are too complex and incomprehensible for human beings to get involved in. Genetic manipulation is one such limit because the interventions involved are far more comprehensive and fundamental than previous therapies. Using them would express a fundamentally fallacious view of

nature and natural things because genetic modification is an expression of a type of arrogance sometimes referred to as the wish to play God. This should be understood as a desire to control the universe instead of finding ones place in it.

The chief argument against this objection is that human beings are interfering with nature all the time. We have done so throughout our history, and this interference has brought us to today's knowledge level. We have primarily made positive progress, and very few would probably want to go back to a low-technology society. To think that mankind with gene technology has reached a point not to be crossed would appear arbitrary; since we have been here before with previous technological advances, which at the time appeared equally drastic. There is no defined limit to how far human beings are allowed to go in their manipulation of nature. Limits should continuously be defined based on our current knowledge level, and we should not proceed with genetic disease interventions before we know more about the risks and consequences of the individual intervention. But when we do, we should progress because eliminating disease is something that would benefit many people.

Biological diversity 1: tolerance and solidarity

Another argument also ascribes value to the existing order of nature. However, it focuses especially on the beneficial consequences that biological diversity can be said to give rise to in that it can be claimed to promote tolerance and solidarity in a society. If the number of deviations was reduced, for example if almost everyone was healthy, physically and mentally, we would lose our understanding of things that are different, and our tolerance for disease and weakness would diminish. Perhaps it would become a requirement to accept an offer to have your future child genetically modified in order to benefit from public services.

Some might argue that we already have many therapeutic treatments, and that it has neither lowered our tolerance for differences nor prompted requirements for ill people to accept treatment in order to receive social services. It therefore seems rather unfounded that the consequences of treatment at the genetic level would be to make it mandatory to accept them in order to benefit from social services. In addition, it could be argued that it seems plausible that most people, given the choice, would choose to be healthy rather than ill. If being ill is something that you yourself, and almost everyone else, would not want, it could be argued that illness in itself is a bad thing to the person being ill. We should therefore not sacrifice the individual's possibility of living the best possible life, i.e. without disease, to achieve an overall good such as tolerance for differences. If people at in order to achieve social tolerance are not offered solutions that would improve their lives, they are reduced to means to achieve another end, namely that of (perhaps) promoting societal tolerance. Finally, it could be asserted that even if we eliminate all diseases, there would still be lots of divergence between human beings that could be conducive of tolerance for differences. Diseases are not necessary to maintain a tolerant and solidarity-based society.

Biological diversity 2: standardisation and totalitarianism

There is another version of the argument that biological diversity is good because it leads to positive consequences. This argument attaches more importance to the problems that may arise if technology is used to enhance the traits of individuals that are associated with achieving success in current our society. If a society was to use gene technology systematically to enhance certain traits in citizens and remove those that did not fit in, we would risk a degree of standardisation ultimately bordering on totalitarianism. In a totalitarian society, the regime would be able to exploit technology to promote certain human types, the ultimate horror scenario being the Nazi pursuit of the "Aryans". Again, this is not primarily an argument against using genetic modification to remove disease genes from future human beings, but against using it to change normal traits.

We could also argue that most technologies, even really low-technological ones like knives, can be abused in the wrong hands. Today, we are surrounded by technology that records and monitors our every move. In a totalitarian society, this information could be used for truly suppressive purposes. The fact that technology can be abused in the wrong hands is not a valid argument not to develop it when it can also be used for something beneficial. It is rather an argument against letting a society develop towards totalitarianism and to consider in each individual case whether and how to implement techniques that have the potential of being used in ethically problematic ways.

Recommendations

Should genetic modification of germ cells and fertilised eggs be allowed with the intention of removing susceptibility to disease in future children and their offspring?

Gene-based therapy should not be offered until the technologies are far more developed and safety tested than the case is today, and there are major technical problems to overcome before this will be the case. Some of the Council members are sceptical that is will ever be possible to gain the knowledge required to ensure the development of adequately safe treatments, and they therefore also question the value of researching and developing such initiatives. However, if safe removal of susceptibility to disease from germ cells or fertilised eggs should become possible, it will be necessary to consider if such interventions should be allowed in Denmark. Research has developed beyond our imagination before, giving us results that no one would have believed possible – recall Dolly the sheep cloned from a cell from its mother's udder. It is therefore relevant to consider these future scenarios regardless of the fact that we may point to many and considerable obstacles standing in the way of realisation.

A majority of the Council members (Lillian Bondo, Anne-Marie Gerdes, Mickey Gjerris, Gorm Greisen, Kirsten Halsnæs, Bolette Marie Kjær Jørgensen, Anders Raahauge, Lise von Seelen, Christian Borrisholt Steen, Signe Wenneberg and Christina Wilson) find that ethically it will be irresponsible to offer genetic modification of future human beings due to the major risks this would imposed on

future children. These members, however, do not find that risks are the only relevant cause for concern, as there are several other fundamental problems associated with genetic manipulation of future human beings. They attach importance to one or more of the following arguments:

- This is not a therapeutically urgent matter affecting an ill, perhaps suffering or life-threatened fellow human being.

- Special risks are associated with genetic modification at this early stage, where unanticipated side effects may not emerge until many years later and will be hereditary in all subsequent generations. The members consider that the research phase alone, which at some stage would have to go from animal trials to trials with births of children with modified genomes, is far too risky and costly to ever go down that path. Delayed side effects could appear after several generations .

- To design future humans would amount to crossing a limit that should not be crossed by human beings. Doing so would be interfering with human nature at a more detailed and more precise level than we have been capable of so far. It expresses a view of nature and natural things that is fundamentally wrong. Human beings obviously keep pushing the definition of normal, and it is therefore difficult to set clear limits and to define precisely when a treatment crosses the limit of what humans should interfere with. However, changing genomes of future generations crosses that limit, because it not only changes a born individual who has consented to the treatment, it changes unborn human beings and every subsequent offspring.

- There are alternatives for human beings with susceptibility to serious diseases to have children – alternatives that are not as risky for the future child. The members point to the possibilities of egg selection (PGD), donation of eggs or sperm from donors without genetic susceptibility to disease or adoption. It may well be recognised that the health services should try to help all citizens with strong wishes of having children when this is possible and justifiable. But it does not follow that such help should consist of performing risky interventions in the genomes of future children. Instead, couples should if possible be offered egg selection if they do not want to use donor germ cells or adopt.

- It is important not to narrow the perception of normality and tolerance towards people who are different. There are people who learn to live good lives with a serious disease with the support of their surroundings. Therefore major risks should not be taken to prevent diseases, but efforts should rather be made to improve the conditions for those who are born with a disease and to develop treatments that only affect the individual person.

- The difficulty of drawing a line between disease and normality is yet another reason to refuse the use of genetic modification of future human beings. The members fear a slippery slope effect that will keep pushing the limits of what

modifications will be allowed in the direction of ever more questionable changes. Therefore, we should generally not go down this road by attempting to eliminate susceptibility to disease in future human beings.

Other Council members (Jørgen Carlsen, Poul Jaszczak, Thomas Ploug, Karen Stæhr, Steen Vallentin and Signild Vallgårda) find that the weighing of risks and benefits, like with disease treatment in bodily cells, should move in favour of allowing genetic modification of germ cells and fertilised eggs provided it is only used to eliminate serious diseases. It is, however, important that gene-based therapy is not offered before the technologies are far more developed and safety tested than the case is today, and the members are aware that there are major technical problems to overcome before this is the case.

The members have therefore chosen to apply a principled approach to the situation that safe and effective measures to eliminate susceptibility to serious diseases before birth would be developed. If so, they recommend that such treatments should be offered since there is no principleddifference in offering treatment before rather than after birth. It is true that there may be a risk of effects in the long term that can never be fully eliminated, but the same can be said for other methods of assisted reproduction and other therapeutic treatments, e.g. involving radiation or extensive medical or surgical treatment. Complete security can never be guaranteed, and therefore it is sometimes necessary to act on the best available knowledge, balancing the risks, potential benefits and alternatives.

An alternative could in many cases be egg selection by screening out fertilised eggs with genetic susceptibility to disease (PGD), but even in these cases genetic modification of the fertilised egg or the preceding germ cells could be preferable. This could for example be the case if it was possible to make the modification in such a simple and precise manner that it would be unnecessary to fertilise and destroy more fertilised eggs. It could also be the case if there was a wish to remove susceptibility to a disease entirely from a germ cell, so that the future child would neither become ill nor carry the disease. Finally, it could be the case that genetic modification could be used to remove several different predispositions to disease from a germ cell or a fertilised egg, which would be difficult in PGD. Alternatives should always be weighed before proceeding with the techniques in the individual situation.

The members moreover attach importance to one or more of the following arguments:

- It is important to many people to have their own children, which is why this possibility should, if possible, also be offered to those so unfortunate as to have been born with a serious genetic susceptibility. Ill people are already placed in a more difficult situation than healthy people, and society should therefore attempt to help them to have their own children just like healthy

people. In the interest of the future child, it should be attempted to remove the genetic susceptibility, since in most cases it is better for individuals to live a life without serious disease, and since an unmodified genome causing a serious disease would restrict, not increase, the freedom of the future child. All in all, they find that the regard for each and every human being to live a life free of disease should weigh the most.

- It is valuable to remove genes that predispose to disease so that the future children will not become carriers with the risk of passing the disease on to their children. This way, the burden of genetic disease in the affected families and society is limited.

- The members find that the problems associated with genetic manipulation of human beings primarily revolves around attempts to enhance normal traits. Such measures would indeed also be ethically problematic both for individuals who would experience that others are trying to control their lives and for society because the predictable changes might foster inequality while reducing diversity and promoting standardisation. It is therefore paramount that genetic modification of future humans is used only for purposes of disease elimination.

- The members recommend that CRISPR should only be used for treatment of disease, but recognises that there is a grey zone, and that it may prove a challenge to draw a sharp line between disease elimination and enhancement of normal traits. However, the health services will always have to draw these lines. This has always been the case, and the drawing of these lines is manageable. Although the members admit that the grey area may widen if it becomes possible to modify even more traits, they still find that the appropriate control measures will make it possible to draw lines in each individual case, also in the area of genetic modifications.