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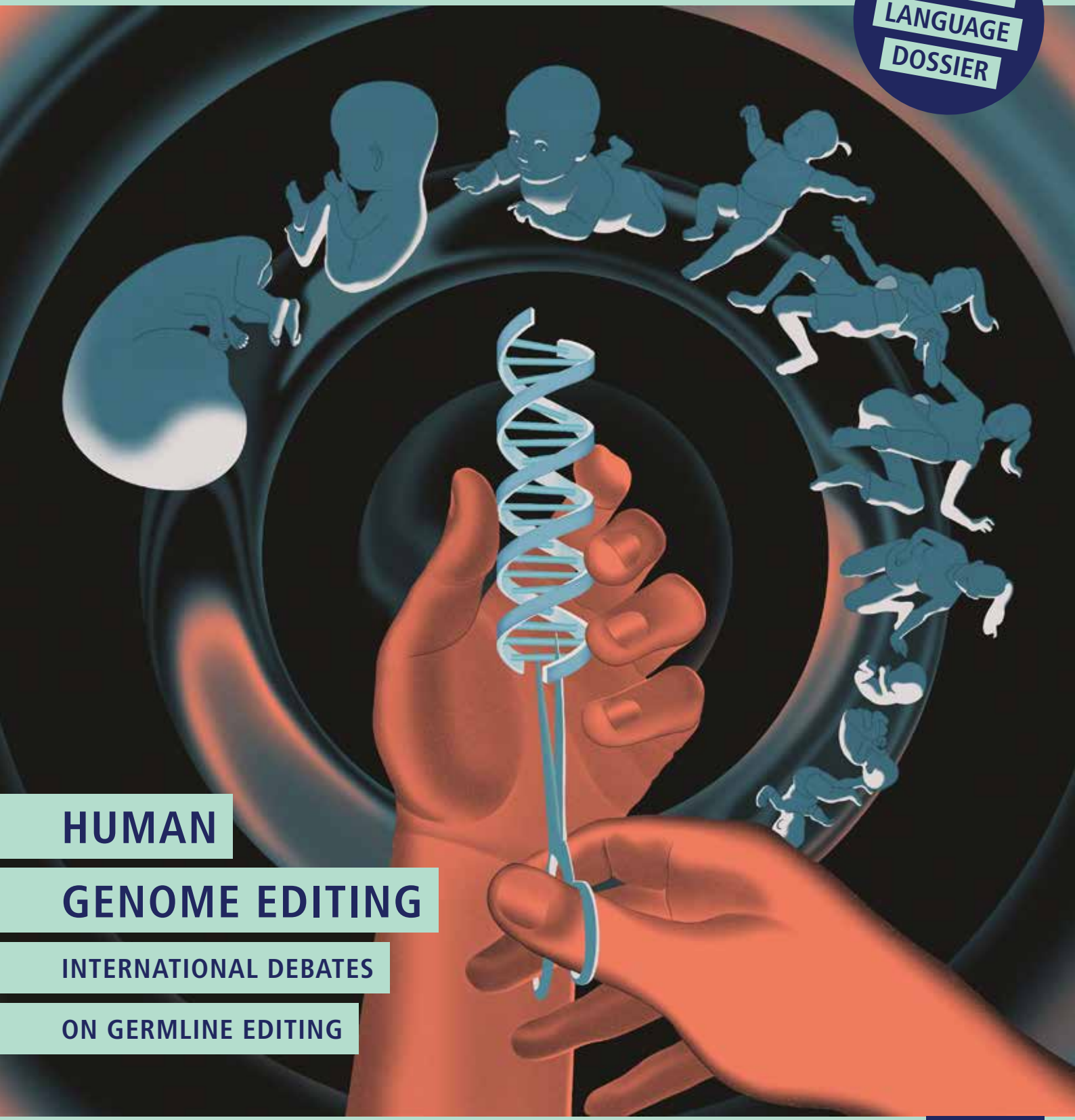

HUMAN GENOME EDITING

INTERNATIONAL DEBATES ON GERMLINE EDITING

The CRISPR-Cas „genetic scissors" enables genetic changes to be made faster than ever before. While the first patients are being treated with CRISPR therapies, germline interventions are still the subject of international debate. Their application carries a high technological and social risk.

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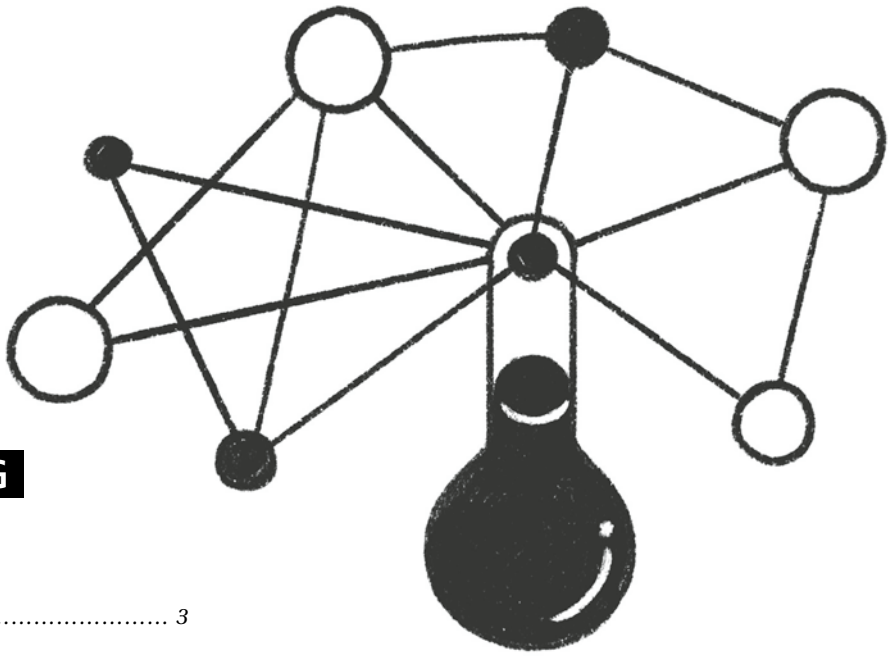

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HUMAN GENOME EDITING

INTERNATIONAL DEBATES ON GERMLINE EDITING

The CRISPR-Cas „genetic scissors" enables genetic changes to be made faster than ever before. While the first patients are being treated with CRISPR therapies, germline interventions are still the subject of international debate. Their application carries a high technological and social risk.

DOSSIER ONLINE

As heritable human genome editing is an international issue, we have compiled all the articles of the issue 268 of our German language journal GID as an English-language dossier – which you are reading now. Please feel free to pass it on to potentially interested parties.

www.gen-ethisches-netzwerk.de/HHGE

By Lilly Presser,
biology student and student assistant at GeN and
Dr. Isabelle Bartram,
molecular biologist and Program director at GeN.

Genome editing describes new molecular biology technologies that can be used to precisely modify DNA. In particular, the discovery of the so-called „gene scissors" CRISPR-Cas9 has brought the topic to the attention of the media. This article is intended to provide an overview of the current state of development as a basis for this issue of GID, which focuses specifically on the debate on germline modification through genome editing.

CRISPR generates hope for the development of new therapies due to its more precise and efficient application compared to previous genetic engineering methods. In basic biomedical research, for example, the development of model organisms like knock-out mice, where certain genes are inactivated, has been significantly accelerated. However, the genome editing method gained publicity not only due to its simpler application. In 2018, the Chinese scientist He Jianku announced that he had created the first genetically modified babies using CRISPR technology - a scandal that added pressure on the international debate on genetic modifications in humans.

Scientists promise to be able to alter the human genome in a targeted and precise manner in order to treat and cure diseases. Such interventions can take place somatically or at the level of the germline. In somatic gene therapy, people with diseases caused by small gene variants can be treated. Either cells are removed, modified in the laboratory and reintroduced into the patient (ex vivo), or the genome editing complex is injected directly into the patient (in vivo) where it modifies the genome of cells. Another option is germline interventions - as put into practice by He Jiankui - in which germ cells or embryos are genetically modified. Unlike somatic approaches, these changes are passed on to the next generation and are hereditary. While germline interventions are illegal in most countries with corresponding legislation (1), the first CRISPR-based gene therapies are currently reaching clinics around ten years after their development began.

The first CRISPR therapy

Two genetic blood disorders - sickle cell anemia and beta-thalassemia - are now to be treated for the first time using CRISPR-Cas. These two diseases are caused by an aberrant variant in the gene for the blood pigment hemoglobin. In the case of sickle cell anemia, this means that red blood cells do not have their typical concave shape, but are partially sickle-shaped or curved, resulting in clumping. Oxygen transport in the blood is impaired, which can lead to severe physical pain, organ damage, and a greatly reduced life expectancy - on average around 40 years - for those affected. The first CRISPR therapy for sickle cell was approved in the UK in November 2023, followed by approval in the USA in December. It is called exa-cel (exagamglogenic autotemcel or Casgevy) and was developed by Vertex Pharmaceuticals and CRISPR developer Jennifer Doudna's company, CRISPR Therapeutics. The European Medicines Agency (EMA) also recommends approval for exa-cel. The therapy consists of removing blood-forming stem cells from patients and modifying them using CRISPR-Cas. Instead of treating the defective hemoglobin gene itself, so-called fetal hemoglobin is reactivated. This form of hemoglobin is active at a specific embryonic stage and is silenced after birth. Using CRISPR-Cas, it is reactivated in blood stem cells from patients in the laboratory and transplanted back into their bodies. There, the cells will produce red blood cells and the fetal hemoglobin will compensate for the symptoms of the blood disorder.

As small as the intended genetic intervention by exa-cel may be, the treatment represents a massive intervention in the patient's body. The therapy only works if the body's own blood stem cells have been destroyed beforehand. The chemotherapy required for this is very physically demanding. One advantage of gene therapy over conventional stem cell transplantation is that the risk of the patient's immune cells rejecting the modified stem cells is significantly lower than with donated cells.

The results from clinical studies with a total of around 100 patients have been promising so far, with almost one hundred percent of those treated reporting the disappearance of pain. However, the duration of the effect and potential long-term side effects are not yet known. Some scientists, including those within the FDA - the US Food and Drug Administration - are concerned about possible unwanted genetic changes caused by the Cas enzyme that remains active.(2) There is also the question of who can afford such a therapy, as it costs around two million euros per person.

Problems and hopes

Even though CRISPR-Cas is more efficient and precise than previous genetic engineering methods, new studies repeatedly show that the technology is far from being as flawless as presented by some media reports. One example of unwanted effects is He Jankui's attempt to make „CRISPR twins" resistant to HIV by means of genetic modification at the embryonic stage. The CCR5 gene contains the information on building blocks for a protein that is a target for HIV on the surface of immune cells. He tried to induce a naturally occurring change in the gene that is known to cause HIV resistance. Affected individuals are missing 32 base pairs in both copies of the gene, the variant is therefore called CCR5-Δ32. Even if the germline intervention has worked as planned, it is difficult to predict how a change in the protein will manifest itself. Genes often have a pleiotropic effect, i.e. they are not only responsible for one function, but for several. CCR5, for example, also plays a role in brain function.(3) Thus, enormous health consequences are at stake.

In addition to the problem that the consequences for the protein cascade are not directly apparent, the actual precision of the gene scissors is also called into question.(4) This is because the term „scissors" is actually also very misleading. The nuclease that causes a double-strand break in the DNA is not nearly as precise as a pair of scissors. It is not a simple "cut" but chemical bonds that are broken. A double-strand break can therefore also occur imprecisely and cause unwanted mutations. The use of CRISPR-Cas can also lead to off-target effects, i.e. changes to genes that lie outside the target sequence. Depending on where these changes occur in the DNA, they can go unnoticed or have serious consequences - in the worst case, they can lead to cancer. Another risk is genetic mosaics. Here, the desired changes are not present in all cells in the embryo, but only in some, as in a mosaic. This can also lead to health problems.

Dispute over recognition and money

When weighing the technical benefits vs. risks of genome editing, the economic context is often ignored. As the price of the gene therapy exa-cel shows, there is a lot of money at stake. In 2020, Jennifer Doudna and Emmanuelle Charpentier were awarded the Nobel Prize in Chemistry for the discovery and development of CRISPR-Cas in 2012. However, a second research team led by Feng Zhang was also working with the technology at the same time. There has been a patent dispute between the teams since 2016 for millions in license fees and recognition in the scientific community for the technology as a whole. In February 2022, the US Patent Office decided that Zhang would receive the patent for the use of CRISPR-Cas in higher organisms, as he was the first to use the technology in mice and human cells. In the meantime, other research teams around the world have also filed patent applications for various applications of the technique.

A global debate is necessary

Great financial interest from many sides exist to present CRSIPR-Cas as precise and safe tool and to develop it for a variety of profitable applications - one of which is the fertility sector. As the data on egg transfer and surrogacy abroad shows, national legislation cannot prevent many intended parents from using ethically controversial reproductive technologies. The regulation of research into and use of heritable genome editing must therefore be an international issue. This dossier therefore addresses the international debate on germline interventions from a critical feminist and anti-eugenic perspective.

Dr. Daniel Papillon, spokesperson for the International Coalition to Stop Designer Babies, outlines the evolution of global debate since the development of CRISPR-Cas. An interview with Dr. Gregor Wolbring, Professor of Disability and Ability Studies, underlines the importance of the disability rights perspective. Wolbring criticizes the focus of the debate on the safety of the technology, which civil society actors sometimes also fall prey to. In order to move away from this limited perspective, an international alliance has developed principles of human rights and social justice in relation to heritable genome editing. Dr. Katie Hasson from the US Center for Genetics and Society presents these guidelines. In the last article of the dossier, Dr. Isabelle Bartram draws a line back to the German debate, in which the legal ban on embryo research is currently being discussed. Scientists are trying to overturn the Embryo Protection Act with the dubious promise of „germline therapy". However, the debates taking place at the highest level are characterized by a striking lack of feminist and economically critical arguments. Once again, the focus is on purely scientific arguments and unrealistic promises, while social effects are ignored. A gap that this issue of GID aims to fill.

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JUST DO IT?

CURRENT LANDSCAPE OF INTERNATIONAL DEBATES ON HUMAN GENOME EDITING

The invention of CRISPR-Cas has sparked a debate around fundamental questions that should remain separated from the issue of the efficiency of the technology. While proponents dream of improving our species, others call for a ban on all research.

By Dr. Daniel Papillon,
biologist and spokesperson of the International Coalition to Stop Designer Babies, www.coalitionstopdesignerbabies.net.

Human genetic modification (HGM) is the deliberate manipulation of the DNA of human embryos, with the intention of leading to pregnancy.(1) Since the changes affect all the cells of the body, including the future eggs and sperm, the genetic changes are heritable, that is, they are passed on to the next generations. There is a strong international consensus against HGM, backed notably by international treaties such as the European Convention on Human Rights and Biomedicine and the Universal Declaration on the Human Genome and Human Rights, but also by national policies. In fact, of 96 countries that do have relevant policy documents, 70 prohibit the use of genetically modified in vitro embryos to initiate a pregnancy. More interestingly, no country specifically allows HGM.(2) Despite this overwhelming social consensus, civil society and human rights organisations, as well as many scientists, are worried about potential future implementation of HGM. Since the advent of CRISPR, a genetic modification technique deemed more powerful, safe, and precise than previous ones, the biotech and assisted reproduction technologies (ARTs) industries, associated with specific parts of the scientific community, are pushing for legalisation of HGM.

From theoretical discussions to practice

The emergence of CRISPR as a genome editing tool in 2012 stimulated an international debate: suddenly gene editing embryos for use in artificial reproduction stopped being science fiction and became a real possibility. Some organisations, ethics societies and concerned scientists reaffirmed that HGM should not be pursued (3,4) or that, at the very least, a moratorium should be put in place.(5,6) In 2015, the National Academies of Sciences from the USA, the UK, and China organised the first International Summit on Human Genome Editing (ISHGE). Hundreds of scientists from around the world gathered to discuss scientific, ethical, legal, social, and governance issues around human genetic editing. The summit's report acknowledged that due to technical safety reasons it would be irresponsible to proceed immediately with clinical use of HGM and deemed a "broad societal consensus" necessary to move forward with HGM. However, the proposal of a moratorium with the possibility of a ban put forward by some participants was overruled.(7) In 2017, a report by the US National Academy of Sciences concluded that while it was presently unsafe to create a human with a CRISPR-modified genome, it might one day be justified for compelling reasons.(8) This report was endorsed by the European Academies Science Advisory Council.(9)

In 2019, a second ISHGE was held in Hong Kong. While the summit was unfolding, a participating scientist, He Jiankui, revealed that he had used CRISPR to modify the genome of at least three embryos that lead to pregnancies – for medical reasons, he claimed. Interestingly to "He's ears, it was the [First 2015 ISHGE] report's fundamental conclusion that mattered. Despite many notes of caution, that report's message was clear […]: gene-edited children were ultimately permissible if the goal was to treat or prevent serious illnesses."(10) The tepid and ambiguous conclusions of the first ISHGE had served as a justification for He's experiment on humans. After a few years of debate on the controversial possibilities of HGM using CRISPR, He had brought the issue to a head by implementing its first application. Initially, the science community reacted with an uproar, inside and outside the summit. It was later revealed, however, that He was not a 'rogue' scientist but had been in contact with many of the leading CRISPR scientists in the US and China – none of whom raised alarm when He told them of his plans.

It is not surprising, therefore, that the organising committee of the second ISHGE issued a concluding statement that was even more permissive than the previous one: HGM was here to stay, it would be accepted in the future, so a 'translational pathway to germline editing [HGM]' should be designed from research to actual clinical use.(11) The statement simply mentioned in passing an "attention to societal effects" thus underscoring the shift from the previous demand of a "broad societal consensus" to the much narrower call for a "broad scientific consensus". The social and scientific conversations about HGM should thus be separated: scientists would keep working while society catches up to their decisions. Of course, not all stakeholders in the debate agreed – in the following I will describe the main positions on HGM that consolidated in the years after these early summits.

Image: A.I. generated (runwayml.com)

In context of an international summit in 2018, leading scientists recommended to created a „translational pathway to germline editing".

Position 1: Let's just do it

The first position is one that clearly embraces HGM. Proponents of this position, exemplified by the Nuffield Council On Bioethics in the UK, would not only argue that there is no ethical nor political case against HGM, but that there are "moral reasons to continue with the present lines of research and to secure the conditions under which heritable genome editing interventions would be permissible".(12) This was echoed by another report from the US-American National Academies of Sciences, that clearly set out this 'translational pathway' to start implementing HGM in clinical context, i.e., on real people.(13) Both reports went beyond its use for therapeutic needs to consider genetic enhancements.(14)

The scientific enthusiasm for human enhancements shouldn't come as a surprise. Since the birth of modern biology, scientists have entertained a vision of science finally reigning over the messiness and unpredictability of nature. This is iterated by, Francis Galton, the 19th century British polymath who invented eugenics – „What nature does blindly, slowly, and ruthlessly, man may do providently, quickly, and kindly. As it lies within his power, so it becomes his duty to work in that direction".(15) This view found a more recent formulation by Jennifer Doudna, the Nobel Prize winning scientist for her contribution in the development of CRISPR: „Indeed, we are already supplanting the deaf, dumb, and blind system that has shaped genetic material on our planet for eons and replacing it with a conscious, intentional system of human-directed evolution."(16). On a more militaristic example, British researcher Robin Lovell Badge affirmed: "You could also contemplate altering humans so they could see in the infrared or the ultraviolet range, as some animals can do. Such enhancements would be ideal for troops fighting at night or in other hostile conditions."(17) As Lovell Badge is a key player in the debate as the chair of ISHGE summits and part of British regulatory bodies, this gruesome outlook on the use of HGM on cannot be dismissed as a fringe position.

These proponents find moral support in the work of philosophers like Savulescu and Singer, for whom an ethically justifiable translational pathway to HGM should look like this: "catastrophic single gene disorders (like Tay–Sachs disease), then severe single gene disorders (like Huntington's disease), then reduction in the genetic contribution to common diseases (like diabetes and cardiovascular disease), then enhanced immunity and perhaps even delaying ageing … Further into the future, gene editing could be used for enhancement of the genetic contribution to general intelligence."(18)

Position 2: Let's do it, but safety first

An intermediate position is embodied by the World Health Organisation (WHO), which adopted an ambiguous stance recognizing that it is still "irresponsible at this time to proceed" with HGM and advised refraining from approving clinical trial application. But it did not call for a moratorium.(19, 20) A similar ambiguity emerged from the third ISHGE in 2023. Critics like the US-based NGO Alliance for Humane Biotechnology noted an interesting recasting of terminology. What previously was termed 'Human germline genetic editing' was split into 'Heritable human genetic editing' (HHGE) and 'Non-heritable human genetic editing'. In other words, there was human genetic

engineering 'for reproduction' and 'not for reproduction'. This allowed the germline research and manipulation (such as in vitro gametogenesis and its possibilities) to be recast as "non-heritable", and therefore, presumably, less ethically controversial and easily bracketed out of the social conversation.(21a)

Planning for the third ISHGE started out with an ostensible effort to be more inclusive and some critics did get the chance to lay out arguments against HGM. But some voices, i.e. from the disability rights movement, were still missing. Despite such exclusions, the criticism of civil society organisations and some scientists was reflected in the concluding statement: "Heritable human genome editing remains unacceptable at this time. Public discussions and policy debates continue and are important for resolving whether this technology should be used."(22, emphasis added). This position was the result of intense efforts to change the framing of the debate from one that tended mostly to be about how to implement HGM, to go back to actually considering whether we wanted it to be implemented at all.

Indeed, focusing narrowly on safety reduces the permissibility of HGM to technical and scientific criteria.(23) From such a truncated framing, technologies simply need to be developed further and, presuming that safety will be reached, the ethical and political issues of HGM will therefore fall away. Addressing the question at the root of the issue, however, should not be influenced by the efficiency of a technology: does HGM constitute an ethical and moral human 'red line'? Do we actually want to go ahead with it? How will the implementation of HGM unfold in our highly unequal societies blighted by racism, sexism, and ableism?

Position 3: We shouldn't do it

These questions are at the heart of the third position on HGM. It is illustrated by the 2019 call for a moratorium on HGM written by some concerned scientists (24), which was subsequently backed by numerous organisations.(25-29) Additionally, public interest advocates, policy experts, bioethicists, and scientists issued the Geneva statement to demand a "course correction" on HGM.(30) Several Civil society organisations also backed the idea of a moratorium or even a ban on HGM (31,21b), as well as some scientists.(32) In 2023, various national civil society organisations and initiatives formed the International Coalition to Stop Designer Babies. Right at the start of the third ISHGE, this coalition, which included 44 organisations and over 1600 signatories from around the globe, published the International Declaration Against Legalisation of Human Genetic Modification, calling for an international ban on HGM.(33) The Missing Voices Initiative from the US-based organisation Center for Genetics and Society shares a similar position. It aims to amplify "social justice and human rights voices and perspectives in debates about heritable genome editing".(34) There are also some more academic initiatives, which are not necessarily displaying a clear position on the matter, like the Global Observatory for Genome Editing that "seeks to expand the range of questions arising at the frontiers of emerging biotechnologies and explore and encourage alternatives", a somehow mysterious endeavour.(35) The observatory called for a "Democratic Governance of Human Germline Genome Editing" in 2019, with unclear results.(36) Other projects like the Global Citizens' Assembly on Genome Editing, spearheaded by scientists from the University of Canberra in Australia, try to develop methods to reach the "broad societal consensus" the first summit proposed as needed for HGM. Related to this initiative, citizen assemblies and juries were organised in Australia, France, the USA and the UK to discuss issues around HGM, with the aim of organising an eventual worldwide Global Citizen Assembly.(37) As the outcomes of these formats are very sensitive to what arguments are presented and whose voices are heard, the result of this process remains to be seen. The outcome of the UK version were used by the media to justify the implementation of HGM.(38)

Conclusion

Other articles in this issue are making the case against HGM. But from my very summarised picture of the ISHGE process and the various positions regarding HGM in the scientific community and civil society, we can conclude that despite the framing of HGM as only a matter of technical safety in the mainstream debate, much is left in the open. The global legal landscape of the rejection of HGM is often ignored while crucial issues of equity and human rights are not given the importance they deserve.

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"THE SECURITY DEBATE IS A RED HERRING"

A DISABILITY RIGHTS PERSPECTIVE ON HUMAN GENOME EDITING

Photo: © private

In various reports and recommendations, ethics and scientific bodies promote a problematic image of disability as something worth avoiding. Even critics of germline interventions are often unable to free themselves from this ableist perspective.

Interview with Prof. Dr. Gregor Wolbring,
since 2008 Professor for Disability Studies at the University of Calgary. He conducts research in the fields of Science and Technology Governance, Sustainability Studies, Disability Studies, Ability Studies, and Sport.
Dr. Isabelle Bartram conducted the interview.

Dr. Wolbring, you are a professor for Disability Studies, what does that mean for people who have not yet heard of it?

I use Disability Studies, but also Ability Studies, as an analytical framework in the various fields of research in which I work. Disability studies, in a nutshell, is the critique of the social reality of people who are treated in a disabling way because they don't fit the prevailing ability norms. Ability studies is about who promotes and can decide which abilities are important. Ableism is often used as a shorthand term for discrimination against disabled people. I see ableism as a general social reality in which all people are judged on the basis of their abilities. The people and social groups in positions of power can then decide which abilities are important and which are not. Genetics naturally constantly plays a role in this, as genes are often discursively linked to abilities.

What is the difference between the medical and social model of disability?

The German word „Behinderung" - just like the English word „disability" - is used for very different things. On the one hand to describe a body, and on the other hand to describe what disables a person.
When you look at the body, you have two options: You can describe the body as deficient or as a variation within human diversity. When dealing with what disables a person, you have three options: You can identify the body or society or both as the cause of the disablement. Viewing the body as deficient and as the cause of the disablement is the traditional medical model - from this perspective, the main solutions are elimination or treatment.
As a second option, you can also say that my body is deficient, but I am also socially disabled and demand that this social disablement ends. Just because you perceive your body as deficient doesn't mean that you don't experience social discrimination. This is a fusion of the medical model of the body and the social model of disability.
Thirdly, you have deaf culture, the neurodiverse community (1) and others who do not see their body as deficient and therefore do not see the body as the cause of their disablement, but only the social structure. This is the social model of the body and the social model of disability.
Many people use the word disability without defining it precisely, so that it remains unclear exactly what they mean.

This issue of GID focuses on germline interventions - what would a Disability or Ability Studies perspective on the topic look like?

Disability Studies would examine how the need is justified and ask why we are jumping to "fix". According to Disability Studies, the genome editing discourse has the same problems as the genetic testing debate, although the modes of intervention in genome editing are more diverse: at the somatic level (2), in the germline, prenatally or after birth.
Genome editing allows not only the modification of genes associated with so-called diseases, but also of genes that lead to somatic and heritable enhancement beyond the norm - i.e. "the enhancement" of traits beyond the species-typical. The 'safer' genome editing is considered to be, the more genes that are not associated with disease will be targeted - a goal that transhumanists are clearly pushing for. Thus, people who are considered to be ill will be treated first and if no major problems arise there, then other traits will also be tackled.
Here, disability studies ask what the social consequences of enhancement would be for the untreated disabled. Ability studies ask who is pushing which enhancements towards a new ability norm and why.

Since you mentioned enhancement – in reports by ethics committees and science bodies, a distinction is always made between therapy and enhancement. What do you think about this differentiation?

This distinction has been questioned for a long time, even outside of genome editing. In 2013, we conducted a survey with people from the deaf culture and asked them whether they would prefer a cochlear implant that gives them average hearing or an implant that goes beyond normal hearing. Most respondents answered that they would choose an implant that gives them above average hearing if they are forced to change, because they are not accepted as they are and their ability differences lead to many social disablements. I think the preference for enhancements applies to most people. It will be the same with genome editing once it is considered 'safe'. Ultimately, the concept of illness will change and many „normal" people will be labeled as ill if they cannot keep up with people with enhancements.

What are your thoughts on how people with disabilities are currently portrayed in the debate on human genome editing?

They are portrayed within the medical model of body and disability/disablement, otherwise you can't promote genome editing. At the moment, germline interventions are portrayed in the debate as something bad, but somatic gene therapy and other interventions such as genetic testing are unfortunately often portrayed as okay, as 'safe'. From a disability studies perspective, I think disabled people are thrown under the bus when the argument is made on the level of safety. Because many „safe" methods are seen as problematic by many disabled people.(3)

Let me give you another example of a controversial method: In Alberta, disabled people were not gassed as in Germany in the time of World War II, but many were sterilized. In 1996, Leilani Muir sued the Alberta government as a person affected. In the lawsuit, the Eugenics Commission's decision at the time was defended by the argument that "some causes of learning disabilities were hereditary and that at the time the Commission was established, there was a risk of passing them on because the choice of contraceptives was limited. Today, people have the pill and other contraceptives, they can get genetic counseling and have an abortion before a disabled child is born." This is not about safety, but again the argument is that they should have used this method because the others did not exist. In both cases, the idea behind it is „disabled people must be prevented".(4)

So, you wouldn't make this distinction between somatic genome editing and germline modifications?

People argue that germline interventions have consequences for society that we cannot foresee. If something goes wrong with somatic gene therapy, it would only affect one person; if something goes wrong with germline modifications, it would have consequences for many more people. This is a safety debate and, for me, a red herring. Because the risk-benefit assessment totally depends on how widespread an intervention is - the more it is used, the more people see it as safe and the more it is then used. The more an application is seen as technically unproblematic, the more it will be used. If somatic gene therapies are carried out without negative consequences, germline interventions will follow.

At the moment, somatic gene therapies are a major intervention, like a stem cell transplantation, so that they are only considered in very rare cases. Do you think it will be developed to be just like an injection at some point?

Whether somatic interventions become consumer goods depends on how successful the previous interventions are, which are limited to certain diseases, and whether there are

Whether an enhancement becomes a consumer good, depends on how great the social advantage is, that it offers.

Image: A.I. generated (runwayml.com)

traits apart from diseases that are desirable and linked to genetics. I think with regard to the enhancement of abilities, non-genetic possibilities will be exhausted first, as only for a few enhancements there are clear genetic targets.
Which enhancements you want depends on the level of advantage they bring. If you get a better job because you gain certain abilities, for example because you have sensors that give you certain abilities, many people who can afford it will use the sensors. We constantly expect people to change their skills. For example, in Canada you now have to have a smartphone and be able to use it. It is mandatory to verify accounts for many applications. And many of the apps you need are only available on smartphones and not on computers. Thus, we expect more and more and also different skills, I call this Ability Expectation Creep.
There are many things that people have to adapt to if they want to continue to participate in society. This will also happen with enhancement if it is seen as safe and cheap and is widespread enough - it's just a question of time.

Only very few people with disabilities participate on all these committees. For example, there was one person with cystic fibrosis on the German Ethics Council who took part in the discussions, but otherwise all other members are able-bodied - at least publicly. Why is that?

I think that, on the one hand, it's a capacity problem. We haven't yet solved previous issues like access and new problems keep cropping up. People can't be experts in everything. Genetics, access, enhancement and now artificial intelligence as the latest aspect. Thus, priorities are set as to which issues you can influence. For example, when legislation against genetic discrimination was being discussed in North America, the only stakeholders who took part were the patient groups. They wanted an anti-discrimination law against discrimination by health insurance companies, for example. But that doesn't protect you from being eliminated before you show symptoms - that's not part of the laws against genetic discrimination, it's just about making sure you're not discriminated against in the workplace or by insurance companies. The debates on genetic testing have been going on for so many years, and the disability rights arguments have been ignored or rejected for so long, that now nearly no disability rights group in North America is working on the issue.

How could the capacity of people from the disability rights movement be increased to participate in debates and decision-making processes?

First, the drivers of activist burnout, like those that have been described for disabled climate activists, need to be addressed: Stressors that deteriorate activists' physical or emotional health and affect their sense of connection to the movement and their ability to stay engaged. Worse, burnout begets burnout: when movement work is taken on by fewer people, they begin to burn out, engage less effectively and take out their hopelessness on other activists.
Relevant factors can include unreasonable expectations placed on disabled activists, too much workload, working on issues around identity, sexism, racism and other additional forms of discrimination, the life situation of disabled people outside of activism and how activists are treated in organizations.(5a) A part of burnout is not even daring to be who you are: autistic burnout, for example, is triggered by the stress of „masking", or suppressing autistic behaviors, that comes with living in a non-inclusive neurotypical world.(5b)
Most disabled people live very precariously. And if we always say „and with disabled people", then it's not that simple. Disabled people have to be in a life situation where they have the space to engage with the issues and learn enough on the topic so that they can challenge the system. How can you do that if you're poor and cannot access transportation and venues where the discussions take place and you don't have a job - that means you get a few privileged people like me who often appear somewhere.
Then there's the hierarchy between social movements, where the disability rights movement is often at the bottom. In relation to the debate on genome editing - why should the disability rights movement support moves in the gene editing discussions that only oppose germline interventions today and accept when methods such as pre-implantation genetic diagnosis or non-invasive prenatal tests, which are also problematic from a disability rights perspective, are presented as justifiable alternatives or are not even discussed in the gene editing discussions? Disability rights groups have questioned many genetic technologies and their aims over the years - unfortunately with little success. Why should disability rights groups get involved if only germline interventions are being questioned when there are so many issues that make life difficult for disabled people today?

Thank you very much for the interview!

Notes and references:

(1) The concept of neurodiversity views neurobiological differences as a human disposition among others and rejects a pathological perspective on characteristics of people i.e. autistic people or people with attention deficit/hyperactivity disorder (ADHD).

(2) In somatic genome editing, individual cells of an existing person are changed and the change is not passed on to the next generation.

(3) Wolbring, G./Diep, L. (2016): The Discussions around Precision Genetic Engineering: Role of and Impact on Disabled People. In: Laws, 5, 3, www.doi.org/10.3390/laws5030037.

(4) Thomas, D. (29.06.1995): Geneticist defends sterilization in era before the pill. In: Calgary Herald.

(5a,b) Wolbring, G./Lillywhite, A. (2023): Burnout through the Lenses of Equity/Equality, Diversity and Inclusion and Disabled People: A Scoping Review. In: Societies, 13, www.doi.org/10.3390/soc13050131.

SOCIAL JUSTICE AND HUMAN RIGHTS

PRINCIPLES FOR GLOBAL DELIBERATIONS ON HERITABLE HUMAN GENOME EDITING

Current debates around genetic changes to the human germline are often centered on the safety of the technology. In an effort to shift the focus toward social justice and human rights issues, an international coalition of civil society advocates and academics has developed a set of principles.

By Dr. Katie Hasson,
sociologist and Associate Director of the Center for Genetics and Society (USA), www.geneticsandsociety.org.

Heritable human genome editing – using genetic modification tools such as CRISPR on embryos or gametes and using them for reproductive purposes – would alter the genes and traits of future generations. Despite the dire effects that this technology could have on society, it is rarely considered a social justice or human rights issue. Too often, public and policy discussions assume heritable genome editing is an issue for scientists or ethicists to decide. There is an urgent need for the voices and perspectives of advocates and scholars committed to social justice in deliberations about whether heritable genome editing should ever be used at all.

That is the purpose of the Missing Voices Initiative (MVI), a project organized by the US-based organization Center for Genetics and Society (CGS). MVI brings together civil society advocates and socially engaged scholars to model meaningful inclusion and amplify social justice and human rights perspectives in debates about heritable human genome editing.

The Gender Justice and Disability Rights Coalition (initiated as part of CGS' Commitment to UN Women's Generation Equality Forum, and later brought under the MVI umbrella) was formed to develop principles, model policies, and tools for advocacy to center gender, reproductive, and disability justice in policy-making on heritable genome editing.(1) The Coalition is made up of 16 advocates and scholars from 10 countries working in a range of civil society organizations and academic institutions who are committed to feminist, disability rights, anti-eugenic, and intersecting justice-oriented perspectives.

The Coalition developed a comprehensive set of governance principles based in intersectional social justice perspectives to guide policy-making and public engagement on heritable genome editing. The 11 principles that make up the Coalition's Social Justice and Human Rights Principles for Global Deliberations on Heritable Human Genome Editing "center women and pregnant people's health, rights, and freedom from exploitation, and affirm the full inclusion and worth of all people with disabilities." The principles prioritize gender, reproductive, and disability justice, while addressing the ways they are intertwined with racial, LGBTQ+, economic, intergenerational, and environmental justice and Indigenous sovereignty. The Coalition's conclusion is that there is no case for pursuing heritable human genome editing that is consistent with feminist and anti-eugenic principles.

Changing the conversation on heritable genome editing

Our Coalition is not alone in recognizing the ways that heritable genome editing would be dangerous to society. In fact, there is a widespread global policy consensus on prohibiting its use. At least 70 countries categorically prohibit heritable genome editing—including the 29 that have signed and ratified the Council of Europe's Oviedo Convention—and no country in the world explicitly permits it. This fact is frequently downplayed or ignored in governance discussions that assume policy making on heritable genome editing can start with a blank slate.

The Principles create space for civil society advocates to bring social justice—particularly gender justice and disability rights—to the forefront of public and policy conversations on heritable genome editing. Prominent scientists, bioethicists, national science academies, international bodies such as the Council of Europe and the World Health Organization, and many others are in agreement that decisions about heritable genome editing cannot be made by scientists alone and should be influenced by the broader public. But there are varying ideas about what public participation would entail.

The scientists and bioethicists who have taken the lead in organizing high profile science policy conversations seem committed to limiting the role the public could play. Exercises in "public consultation," which may seem to fulfill calls for public engagement, can also be manipulated to engineer public acceptance of heritable genome editing. The Principles therefore lay out in detail the necessary elements for robust, meaningful, and legitimate public deliberation that approaches true public empowerment.

One element highlighted in the Principles is the importance of accurate and unbiased information on heritable genome editing—for example, the significant distinction between somatic and heritable genome editing, and acknowledgment that it is not a medical treatment.

Image: A.I. generated (runwayml.com)

A global process is needed, if the existing social consensus against heritable genome editing is to be renegotiated.

The Principles also stress the importance of including representatives from across social change sectors. In particular, those that highlight feminist and anti-eugenic perspectives bring unique perspectives on the broader political, economic, and societal context in which this technology would be researched, developed, and used. Drawing on lived experience and their work to build a fair and inclusive society, civil society advocates are well situated to anticipate how heritable genome editing would interact with existing inequalities, causing harm to marginalized communities and society as a whole. Centering voices and perspectives that are seriously engaging with disability rights, reproductive rights and justice, racial justice, health equity, and Indigenous sovereignty would fundamentally change the conversation. The Social Justice and Human Rights Principles for Global Deliberations on Heritable Human Genome Editing make the case that this intersectional approach must be the starting point for discussions of heritable genome editing.

The Principles

These Principles lay out a vision for the world we want to live in, and ground our claim that there is no argument for pursuing heritable genome editing. The brief summary below outlines key points from each of the 11 principles. Learn more about each principle in the full document.(2)

Principle 1 calls for an inclusive global process to consider whether heritable genome editing should ever be pursued, based in acknowledgment of the potential harms of human experimentation required to develop this technology, particularly on women and pregnant people.

Principle 2 calls for women and gender expansive people from diverse backgrounds and contexts to lead policy making processes relating to heritable genome editing, acknowledging the ways that they have been prevented from controlling their reproductive lives.

Principle 3 affirms that decisions about using biotechnologies like heritable genome editing must be based in a stance that values all lives and diversity in bodies, intellect, and ability.

Principle 4 acknowledges the harmful history of eugenics and calls for science and medicine to reckon with its continuing legacies through education, policies on genetic non-discrimination, and comprehensive information and counseling about disability to parents undergoing reproductive genetic screening.

Principle 5 seeks to end disability discrimination by promoting a broader concept of health and pursuing solutions articulated by people with disabilities, rather than imposed technofixes like heritable genome editing.

Principle 6 acknowledges that health inequities would not be addressed by heritable genome editing, and calls for policies that ensure access to comprehensive health care and eliminate the structural and social roots of health inequity.

Principle 7 calls for policy that safeguards the rights, interests, dignity, and health of future generations, including anyone born through heritable genome editing.

Principle 8 seeks to ensure the right to self-govern genetic material and biological data and for communities participating in research to share in its benefits, supporting calls by Indigenous peoples and ethnic minorities.

Image: A.I. generated (runwayml.com)

The rights, interests, dignity, and health of future generations, including anyone born through heritable genome editing, must be protected.

Principle 9 calls for a precautionary approach in policy making, recognizing the unknown and unpredictable harms of heritable genome editing on future generations.

Principle 10 calls for regulation that prioritizes health, well-being, justice, equity, and human rights, in the face of rapid commercialization of biotechnologies and financial conflicts of interest that undermine this goal.

Principle 11 calls for implementation of programs for public empowerment, emphasizing the importance of engaging diverse perspectives, particularly from those who would be most affected by heritable genome editing and its potential harms.

As the Principles document declares: "It is essential to apply the frameworks of gender, disability, racial, reproductive, economic, environmental, and LGBTQ rights and justice, human rights, Indigenous sovereignty, and the rights of children and future generations in all policy concerning heritable human genome editing. Our future depends on it."

The Gender Justice and Disability Rights Coalition on Heritable Genome Editing calls for governments to prioritize these social justice and human rights principles in policy making on heritable genome editing. There is no justification for pursuing heritable genome editing that conforms with these principles.

Next steps

The Principles have been endorsed by a range of organizations, advocates, and scholars. We plan to circulate them within Coalition members' communities and networks, and distribute them widely to the media, policymakers, and members of influential committees and international bodies. We hope that the Principles will be translated into multiple languages and adapted for use in a variety of country, regional, and international contexts.

Based on these Principles, the Coalition is drafting model policy language that explicitly opposes heritable genome editing. We will also develop tools and resources to encourage advocates around the world to learn more about heritable genome editing as a social justice and human rights issue; to engage with and adapt the principles and model policies to their own national context; and to advocate for adoption of the proposed policies.

We encourage you to read the full Principles document and to stay tuned for the forthcoming model policy language and resources. Your participation and perspectives are urgently needed in the consequential public and policy debates about heritable genome editing.

Notes and und References:

(1) Gender Justice and Disability Rights Coalition, Online: www.kurzelinks.de/gender-justice oder www.geneticsandsociety.org.

(2) The full document will soon be published on the Coalition website (see 1) and also translated to German on the Website of Gen-ethical Network.

GERMLINE EDITING MADE IN GERMANY?

CALLS FOR GERMAN EMBRYO RESEARCH

Pressure on the German Embryo Protection Act is growing. The scientific community is launching a renewed attack on the controversial law and demands access to embryos for so-called high-ranking research objectives. „Germline therapies" are among the boastful promises of the proponents.

By Dr. Isabelle Bartram,
program director of Gen-ethical Network, www.gen-ethisches-netzwerk.de

The German Embryo Protection Act (ESchG) prohibits not only controversial reproductive technologies such as oocyte transfer and surrogacy, but also research on human embryos. It became effective in 1991 as a criminal law passed on the grounds of "pro-life" arguments. The legislators referred to article 2 para. 2 sentence 1 of German Basic Law: „Everyone has the right to life and physical integrity". Human life must „not be made an object for the benefit of others" and this must „also apply to human life at the stage of its earliest embryonic development"(1).

Since its adoption, the ESchG has attracted the displeasure of some German scientists who disagree with its moral-theological justification and seemingly irrational unequal treatment of embryos before the law. After all, although abortion is prohibited, it can - unlike embryo research - be carried out by those involved under certain circumstances with impunity. And as researchers have not tired of pointing out for more than three decades, embryos produced by artificial insemination (in vitro fertilization = IVF), which is now carried out tens of thousands of times a year, are regularly discarded if they are not used, effectively „killed".

Around the turn of the millennium, the pressure on legislators grew due to the international stem cell hype. In 1997, the cloned sheep Dolly was born and research promised the development of therapies for all kinds of diseases from embryonic stem cells. Scientists imagined a gloomy scenario in which Germany would not be able to keep up with the international research competition and German patients would be left empty-handed if research could not use embryos. As a compromise, the Stem Cell Act was passed in 2002, allowing the import of embryonic stem cells that were produced abroad before a certain date in the past (currently May 1, 2007). This may only happen if a research question can only be resolved using embryonic cells and if it serves „high-ranking research objectives" - the responsible authorities decide on the basis of an individual assessment by the Central Ethics Committee for Stem Cell Research set up for this purpose.

A new attempt

Making use of the current public and political debate on the legalization of some reproductive technologies, proponents have engaged in a renewed push for embryo research in Germany. In October last year, the Federal Ministry of Education and Research (BMBF), currently led by the German Free Democratic Party (FDP) organized an ELSA (Ethical, Legal, Social Aspects) conference entitled „Human embryos in medical research: Taboo? - Justifiable? - Opportunity?".(2) The introductory speech by Federal Minister of Education and Research Bettina Stark-Watzinger emphasized the latter: „We should seize opportunities that we can seize,". She promised that stem cell research would make it possible to understand and cure diseases. The statements from the scientific community were clear, she said, and it was an issue of freedom of research. If we limit it, we would have to justify it well. However, her announcement that „we will not sweep risks under the carpet, no argument should go unheard" was barely fulfilled. With few exceptions, the invited speakers were all in support of embryo research. These included members of the German science lobby organization Academy of Sciences Leopoldina, which has long advocated for the legalization of embryo research, as it would „help to better identify and treat infertility, improve the survival and healthy development of embryos and fetuses during pregnancy and prevent miscarriages and premature births".(3) At the BMBF conference, the speakers repeatedly mentioned the statistic that approximately 30 percent of natural pregnancies end in premature miscarriage and the unexplained death of many embryos in IVF, and suggested that these could be prevented through research. The finding that many early miscarriages are caused by lethal chromosomal aberrations in the embryo was not mentioned, but makes the fulfillment of this promise questionable.

Surplus embryos and old promises

Physician and Leopoldina member Claudia Wiesemann cited the development of elective single embryo transfer (eSET) as an example of the successful improvement of reproductive medicine through embryo research.(4) In this method, a larger number of egg cells are fertilized and the embryo with the highest chance of development is transferred. The selection criteria are morphological characteristics. In Germany, this method is prohibited; the ESchG makes it illegal to fertilize more eggs from one person within an IVF cycle than planned embryo transfers. The medical advantage: eSET can reduce the rate of multiple pregnancies, which are dangerous for pregnant people and developing children. The method also has a beneficial side effect for research, as many surplus embryos are produced which would then be available for experiments. As Leopoldina President Gerald H. Haug reported at the BMBF conference, the government has planned to legalize eSET, meaning that more embryos than are needed for IVF would soon be intentionally produced, which could then be used for research. Law expert and Leopoldina member Jochen Taupitz also referred to the fact that currently around 50,000 surplus frozen embryos exist, a number that would increase when using eSET.

Proponents also keep the several decade old promise of a therapeutic use of human embryonic stem cells (hES) alive. Due to their ability to mature into all possible tissue types, hES would hold „great potential for regenerative and personalized medicine", writes Leopoldina on its website. Unmentioned remains that this potential has not yet been realized, although a great deal of money has been invested in this field of research in other countries such as the USA in recent decades. Many clinical studies have been carried out, but no treatment has yet been successful enough to be established as a routine therapy. In the same line, stem cell researcher Fredrik Lanner from the Swedish Karolinska Institute only presented his research group's plans for clinical trials for hES-based therapies for age-related macular degeneration at the BMBF conference.

Genome editing as a new opportunity

However, a relatively new argument put forward by proponents of embryo research is claiming a need for the further development of new genome editing technologies such as CRISPR-Cas with regard to reproductive applications. In 2017, Leopoldina members published a discussion paper in which they spoke out in favor of a general acceptance of „germline therapy".(5) Although the content of the paper is only intended to reflect the opinion of the authors and not Leopoldina, the editor is then Leopoldina president Jörg Hacker. According to the authors, the new technology enables „interventions of such unprecedented precision and efficiency that a reappraisal of the situation is required". Why germline interventions are ethically justifiable was not even discussed. As co-author Jochen Taupitz explained in his talk at an event organized by the German Ethics Council in 2016, from an ethical and moral point of view there is even a requirement to approve the technology in order to prevent serious diseases and disabilities.(6) According to the discussion paper, the only decisive factor is technical safety: an „acceptably low risk" of a germline intervention „in comparison to the hereditary disease it seeks to prevent" must be achieved. And in order to gain „the empirical bases for such a risk assessment and the subsequent normative evaluation of the risks and opportunities", it is necessary to allow conducting research with human embryos in Germany.

Subsequently, the Leopoldina advocated the legalization of embryo research for „high-ranking research objectives" in a 2021 statement.(7) For the authors, this means, among other things, being able to „critically review and evaluate the opportunities and risks of this form of gene therapy", referring to heritable genome editing. Although they note an insufficient justification of the necessity of germline interventions and mention the risk of „enhancement of biological traits", research should still be carried out.

The description of germline interventions as „genome surgery", „germline therapy" and „gene therapy" in the Leopoldina's publications is astonishingly imprecise for scientists, as no existing humans are being treated, but embryos are being created in the laboratory specifically for this purpose. This rhetorical trick was also used at the BMBF conference when in a discussion about germline interventions, Jan Ellenberg, co-author of the statement, claimed that the life of a patient with sickle cell anemia was saved by the technology. Being a biologist Ellenberg is probably aware that the patient's treatment with a CRISPR-based somatic gene therapy had nothing to do with germline interventions, as it was applied in adulthood.

The Leopoldina authors refer to a report of the German Ethics Council in which a majority of members affirmed the ethical permissibility of research on early human embryos in vitro. At the BMBF conference, the Chair of the German Ethics Council, Alena Buyx, also pointed out that in its statement on heritable human genome editing the council had spoken out in favor of embryo research for the first time, as it is needed for the further development of germline interventions to prevent monogenetic diseases. According to Buyx, this research is not only permissible, but also necessary.

Ignoring the consequences

Thus, technological possibilities alone are proposed to guide legislation on research with human embryos. However, instead of reducing the debate - as seen at the BMBF conference - purely to two opposing poles of „dignity of the embryo vs. supposed scientific rationality", a nuanced consideration of possible consequences could also be applied. This approach has been voiced by feminists for decades. An analysis of research embedded within an economized science and healthcare system and social inequalities, in which germ cells and embryos become a commodity, could also underline the necessity of maintaining the ESchG, without resorting to moral-theological „pro-life" arguments. From a very practical point of view: How would the surplus embryos make their way from medical practice to research? Would fertility clinics receive financial compensation for the „production" of the supplied research resource? Would there be incentives to remove as many eggs as possible from patients so that some remain for research?

Egg retrievals always carry a medical risk, and the more hormonal stimulation is used, the greater the risk. Even if there are no direct financial conflicts of interest, research interests and the associated pressure to obtain research funding could

also create conflicts of interest between patient welfare and the scientific goals of reproductive medicine researchers. And what happens if the „surplus“ embryos are not enough? Will advocates then call for further changes to reproductive medicine legislation to allow egg „donations“ purely for research purposes? Would a market emerge in which economically disadvantaged people „donate“ eggs, e.g. in order to be able to afford their own reproductive medical treatment?

In addition, the unrealistic promises described above with regard to research results for therapeutic purposes could be critically analyzed. Not to mention the many arguments against further research into germline interventions that arise when social consequences are included in the considerations. Unfortunately, all these aspects represent a gaping hole in the public debate.

Notes and references:

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(2) Interdisziplinäre Konferenz, ausgerichtet vom Bundesministerium für Bildung und Forschung (BMBF), 9.-10.10.23, Online: www.kurzelinks.de/gid268-bd.
(3) Leopoldina (2021): Erkenntnisse und Nutzen der Embryonenforschung, Online: www.kurzelinks.de/gid268-be.
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(5) Hacker, J. (Hg.) (2021): Ethische und rechtliche Beurteilung des genome editing in der Forschung an humanen Zellen. In: Leopoldina Diskussion Nr. 10, Online: www.kurzelinks.de/gid268-bb.
(6) Achtelik, K. (2016): Ethische Gespensterdebatte. GID 237, S.33. Online: www.gen-ethisches-netzwerk.de/node/3367.
(7) Leopoldina (Hg.) (2021) Neubewertung des Schutzes von In-vitro-Embryonen in Deutschland, Online: www.kurzelinks.de/gid268-bc.

Embryo research is supposed to create the possibility, to study opportunities and risks of germline interventions – social risks are not part of this proposed assessment.

Image: A.I. generated (runwayml.com)

GEN-ETHISCHES NETZWERK
(GEN-ETHICAL NETWORK)

Gen-ethisches Netzwerk (GeN) was founded in 1986 in reaction to the rapid developments in biotechnological research. Since then we have observed and reported on research and industry trends in the fields of biotechnology, genetics and reproductive technology for the public. Our goal is to make the developments in these fields accessible for emancipatory, socially focused debates in Germany. As a non-profit grassroots organisation we promote independent knowledge generation.

Our vision is:
- a just and sustainable and solidary future for all.
- a society that uses biotechnology, genetics and reproductive technology responsibly and for the common good.
- politics, science and research that include diverse perspectives and reflect social diversity.

How we work
In order to counterbalance the self-promotion of academia, industry and politics, we engage in critical science communication with a focus on the social implications of biotechnological and reproductive technology research. Our expertise is generated in cooperation with critical scientists, activist groups and initiatives of people affected by technologies. By joining or initiating campaigns and protests, we also actively advocate for transparency and responsibility in science, and ultimately a just and non-discriminatory society.
Our office in Berlin is managed by a small team of scientists and activists that work together with the members of our management board on our political and editorial work. Our advisory board meets once a year to discuss scientific and strategic questions. Since its establishment GeN publishes the quarterly German-language journal Gen-ethischer Informationsdienst (GID) which reports on our current work and the newest technological developments. As a non-profit organisation we are financed nearly exclusively by membership fees, GID subscriptions and individual donations. Our donors give us the basis for our political independence.

What we want
Our criticism of genetic engineering in agriculture and medicine is linked through the objective to promote a democratisation of science and technology policy. We advocate for pushing back capitalist dynamics of economisation in the different fields of biopolitics.

We strive for
- democratic and transparent sciences

In agriculture
- adherence to the precautionary principle
- sustainable and ecological agriculture
- food sovereignty for all
- regulation of genetic engineering that includes risk assessment and mandatory labeling
- consistent and transparent implementation of the polluter pays principle
- the prevention of biopiracy
- no patents on animals and plants
- no release of genetically modified wild species

In medicine
- a health care system without profit interests based on solidarity
- long-term data protection of genetic and biological samples from research volunteers and patients
- sexual, reproductive and physical self-determination
- evidence-based and ethical use of reproductive technologies
- maintaining the ban on egg "donation" and surrogacy in Germany
- no selective prenatal diagnostics
- no heritable genome editing in humans

We publish mainly in German, but we speak English and invite international journalists, researchers and potential cooperation partners to get in touch with us: gen[at]gen-ethisches-netzwerk.de or phone 0049-30-6841183.

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