

Germline gene editing of human embryos is wrong

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Over the last few decades, the international community has developed a position, expressed in several international ethical guidelines and legally binding documents, ranging from UN Conventions to regional Charters to national legislation, that all research practices which are named as contrary to human dignity are prohibited. Until 2015, germline modification belonged into this group, though – as is always the case in questions of human rights and dignity – some bioethicists began to argue against this position since the early 2000s. Apparently, their voices dominate the position papers concerning germline gene editing. These do not engage the documents in a comprehensive way, regarding them apparently irrelevant for the current debate – a striking departure from many other debates.¹ This is a big mistake, because it ignores decades of interdisciplinary work in bioethics and medical ethics; after all, the governance positions rest upon academic and scholarly work that had been published together with public deliberations that has made bioethics a prominent area of democratic deliberation – this governance framework should have served as the starting point for the actual discussion.

Apart from this lack of engagement with the governance framework of bioethics, the underlying normative framework of political liberalism that dominates the national academies' reports is not questioned, although liberal bioethics is but one approach within the wider field of bioethics.² This is unfortunate.

Two ethical perspectives have informed the discussions so far:

First, it is said that germline gene editing may offer, for the first time, a reproductive option for couples that are faced with no other alternative to have a genetically related child than this new method. Hence, this new possibility should *in principle* be *welcomed* as one further progress of reproductive medicine, albeit under conditions that must be determined by the scientific community, ethicists, and policy-makers, and discussed by the broader international public.

¹Most importantly for my discussion here are the Nuffield Council on Bioethics. Genome Editing – An ethical review. September 2016.

Available at: <http://www.nationalacademies.org/gene-editing/Gene-Edit-Summit/Slide-Presentations/index.htm> (last seen: May 2nd, 2017); and the National Academy of Science & National Academy of Medicine. Human Genome Editing: Science, Ethics, and Governance. 2016.

Available at:

<http://nationalacademies.org/gene-editing/consensus-study/> (last seen: May 2nd, 2017).

² Hille Haker, "On the Limits of Liberal Bioethics," in *The Contingent Nature of Life*, ed. Marcus Düwell, Rehmann-Sutter, Christoph, Mieth, Dietmar, Publication of the European Science Foundation Conference (Berlin et al.: Springer, 2008).

Second, genome editing may in the future bring about new possibilities to germline genetic enhancement. While this is not a scenario for the near future, enhancement, too, should not be ruled out in principle, because it enables human beings to “enhance” their capabilities to live a good life.

Both perspectives are contested in the bioethics community and, given the history of bioethics debates around reproductive medicine, most likely, they are also contested in the public. The scientific position papers, in contrast, have embraced them with few variations. Yet, both perspectives are presented in a way that conceals rather than reveals their underlying premises.

Unfortunately, this is the case, too, in the present Nuffield Council Survey that is part of a public consultation process.

Germline Gene Editing – Just Another Method of Assisted Reproduction?

As several scientists have stated repeatedly, there are, except for (perhaps) some very rare cases, no therapeutic scenarios for reproductive gene editing. In fact, there are medical alternatives that by now all interested (affluent) couples concerned about the health of their future children are offered, although especially Preimplantation Genetic Diagnosis is not unproblematic.³

Scientific academies and proponents argue that there will still be (some) couples who cannot be helped by the current methods. These will be able to have genetically related, healthy children by using the technology of germline gene editing.

The ethical debate on germline gene editing was shifted almost immediately from the debate on a research agenda – its broader context, its motivation and purpose, the means, the actors, and institutional and economic settings – to one aspect only, namely the clinical context of assisted reproduction. While this ethical debate is continued, the public is assured that *at present* most of the research entails basic research, and any application would be feasible only in the future. The position of scientists concerning this application is either apologetic or enthusiastic: either it is argued that couples have the right to the best available technology to realize their wishes, or it is argued that genome editing is the ultimate opportunity to overcome the constraints of human nature. The first position argues for the exceptional application of germline modification, while the second position argues to proceed more aggressively to enable germline genetic enhancement.

The contested issue for the more cautious position is whether reproductive autonomy includes the right to a genetically related child, and if so, under which conditions. But even this seemingly cautious approach misleads the public about the alternatives at hand: it does not emphasize that if couples were to refrain from their ideal of genetic kinship they could be helped

³ I have discussed the issue of Preimplantation Genetic Diagnosis as a question of social ethics and responsibility in: *Ethik Der Genetischen Frühdiagnostik. Sozialethische Reflexionen Zur Verantwortung Am Menschlichen Lebensbeginn* (Paderborn: mentis, 2002).

via the current technologies. To skip over this important condition – genetic kinship is a desire that medicine cannot question – renders the whole argumentation conditional on a premise that is not justified on its own terms. Taking the desire as premise, the ethical issue is reduced to the technical safety of the procedure.

Genetic kinship, however, is only one among several forms how parenthood can be conceived of: adoption is a well-known kind of parenthood, and like any other society, too, modern societies have created many kinds of parenting beyond genetic kinship. Obviously, in other constellations, reproductive medicine offers sperm or egg donation. Why is genetic kinship not important for the ethical discussion but taken as the unquestioned premise? This discussion is pushed to the background, in the position papers as well as in the Nuffield Council Survey.

Once the framing of reproductive autonomy is adopted, couples seem to be at the center of the inquiry – though they are immediately rendered merely the *recipients* of the new technology rather than being conversation partners. The main concern that the scientific community sees is not centered on the social issue of assisted reproduction but centered on the technical questions. This puts the scientists in the driver's seat; it is up to medical science to decide when a procedure is safe enough to move on to clinical trials. But if this is so, what can the public contribute? The public is consulted, but it is not given the full picture that would be necessary for an informed contribution to the debate. Any information about the research battle surrounding gene editing, the race for patents, the economic interests of the reproductive medicine market is left out of the discussion; the public is not even given any context of the diseases germline gene editing is targeting; and it is not informed about the general shape of reproductive healthcare of which germline gene editing is a part.

Medical ethics speaks of 'minimal harm' and 'minimal burden' for those who participate in medical research. In the case of germline gene editing, this does not only concern the parents but also their children and the following generations. Safety is important, the scientists say, but the same questions, they claim, have been raised in the beginning of In Vitro Fertilization: safety issues were raised, and they, too, concerned the health and well-being of the future children. Over the last decades, long-term studies have been published, which are at times conflicting with respect to health issues of IVF-children, but in general, they have not raised red flags within the scientific community: assisted reproduction is considered a safe medical procedure. The same outcome, it seems, is anticipated for the case of germline gene editing.

Germline gene editing, however, is not merely a matter of minimal risks that nobody can anticipate. The off-target effects, studied thoroughly in other fields, are 'real possibilities', more likely to happen than not. One can doubt whether the safety standard of minimal harm and minimal burden for the future child can ever be met. But the more important question is: should safety concerns dominate the discussion?

The ethical issue is far from being "one issue only". Even if we were to exclusively address individual rights only – which is a mistake that must be corrected by a social ethics approach – germline gene editing concerns not only health rights but also freedom rights, *including the*

reproductive freedom rights of future generations. These cannot be translated into safety questions. They create a conflict between rights of parents and rights of future children, and it is must be argued for – not merely be presupposed – why the one group should win out over the other.⁴

Perhaps the position papers presuppose that the children’s ‘health rights’ must take priority over their freedom rights. But if health is so central in the prospective parents’ choice, it raises the question again about the alternative options that would better “secure” the health of a future child. If health is the greatest priority for prospective parents – and I believe it is at least a very high value – then this should be discussed in comparison to the value of genetic kinship; in other words: what kind of parental responsibility is presupposed in the position papers?

Parental Freedom and Responsibility

Illnesses often mentioned in the literature, such as Cystic Fibrosis, are among the “exceptional” cases all position papers mention. CF is interesting in Western populations, because it a predominantly “Caucasian” genetic disease:

The US *Cystic Fibrosis Foundation*, with numbers from 2004, states the risk to be a *carrier* of Cystic Fibrosis

- 1 in 29 Caucasian-Americans
- 1 in 46 Hispanic-Americans
- 1 in 65 African-Americans
- 1 in 90 Asian-Americans

The risk to have the *sickness* is

- 1 in 2,500-3,500 Caucasian-Americans
- 1 in 4,000-10,000 Hispanic-Americans
- 1 in 15,000-20,000 African-Americans
- 1 in 100,000 Asian-Americans .⁵

⁴ This clash of rights is, of course, an effect of the underlying framework of liberal ethics; I am not arguing that this reflects necessarily how parents relate to their children. In fact, I find it counter-intuitive to think of parents and children fighting for their respective rights. But I am committed here to argue from within the framework that the reports use, and to demonstrate that even within this framework, the conclusions they draw are questionable.

⁵ <https://www.cff.org/What-is-CF/Testing/Carrier-Testing-for-CF/> Note that population genetics cannot but generalize – using the racial framework it inherited from the early genetics – which themselves are deeply correlated to race theory. I am referring to this website because it is the official site for the CF Foundation so that one can assume that more people consult it than going to medical databases.

These population statistics are of relevance, for example, for companies who develop tests or, potentially, the tools for genome editing. It is indeed not unlikely that there will be couples who both suffer from CF. If they seek assisted reproductive services, genetic counseling must communicate some basic facts of the given genetic illness in question. For the more general public discussion, however, it is important to know that life expectancy in the case of CF is currently below the age of 40, that is 38,7 for men and 36 for women, with male subfertility above the average population. Assisted Reproduction is more than a technology; it entails also information and counseling. The latter must certainly include the information about the very likely possibility that if both parents suffer from Cystic Fibrosis *and* opt for assisted reproduction of any kind, they may risk both die before their child has grown up. Safety of a technology can certainly not be the only issue at stake – the most important, if not constitutive element of parenthood that one is able – or, more radically, alive – to care for a child. If that is not likely – after all, assisted reproduction is rarely offered to couples in late adolescence but rather in their thirties or early forties – the concept of reproductive autonomy and responsibility is reduced to the issue of health, ignoring any other factors that also inform “responsible parenthood”.

Germline gene editing presupposes such “exceptional” cases against all such odds. But germline gene editing comes with *severe* potential risks and burdens for future children. In the parent-child relationship, this is odd: no parent can *reasonably*, i.e. *responsibly* wish to leave the burden of a procedure entirely to the children when there are alternatives that would reduce such a burden.

Ethically speaking, however, germline gene editing infringes upon the future children’s freedom, more precisely, on children’s freedom *rights*; for the sake of the long-term clinical trial (that spreads over more than one generation), the children must take part in a life-long trial that involves monitoring and recommends assisted reproduction for this generation, too. Even if the children (may) act against the recommendations (the 2017 NAS report explicitly states that a long-term plan is needed before the first clinical application would start) and opt out of these programs, they will still have the knowledge that their children, too, face the risks of off-target mutations. Their right not to know that is granted all other couples as part of the voluntary service of prenatal diagnosis, for example, is impossible to uphold – the children must be informed that the side-effects of germline gene editing may only show up in the second generation. This is not merely a question of whether children could have or would have consented to their birth or to the procedure – no child can. It is a question of whether this specific infringement upon their rights, in view of the alternative options, is justified. The closer one looks at the given scenarios, the more ethical questions arise. Safety, because it is an ultimately technical question of risk assessment, is not the most important ethical question at all.

The way the discussion has been framed by ‘liberal’ or ‘libertarian’ bioethicists, is this: parents are faced with the *dilemma* of either passively accepting the transmission of a genetic health risk to their children, or actively taking the safety risk of gene editing. Once they are assured that the safety risk is low, action (medical intervention) seems to outweigh non-action. The problem with this scenario is that the depicted dilemma is not unavoidable and hence, it is *not* a dilemma – it is a constructed one, because genetic kinship is taken as an absolute good. This naturally reduces

the options to intervention on the germline or non-intervention, which means the genetic trait is passed on to the next generation.

Finally, while ethics can (and should) affirm personal freedom and responsibility, the way it is framed in the ethical and public discussion matters. Neither freedom nor responsibility are 'individualized' concepts; both are socially mediated. They cannot be discussed or constructed as if they were not situated in a social context in which research takes place: In the US, for example, the racial and class disparity of healthcare services, most basic reproductive services, and even child mortality – not to speak of disparities concerning poverty, education, and social status – is so overwhelming that the talk of parental freedom and responsibility cannot be aimed at these couples whose "reproductive autonomy" is very much limited. While it is ethically impossible to *simply* compare one practice to another, it is likewise wrong not to connect and compare services in the same field *at all*.

Thus, reproductive medicine is not offered outside the general social institution of healthcare. What is offered to couples must be determined by the individual circumstances; the more general – public – discussion, however, must include the social requirements and priorities within the field of reproductive healthcare. Assisted reproduction services may well be offered, and there may still be some flexibility with respect to different services available to different groups, but to *exclude* the different reproductive health care contexts – and histories – from the discussion altogether reveals a flawed ethical method.

Here are some of the issues to be considered under the headline of reproductive autonomy and responsibility:

1. **Gene editing creates other health risks than the genetic risks targeted by gene editing for the future children.** Consenting to gene editing, *parents* opt against safer alternatives.
2. The main motivation to take the risk of germline gene editing is a scenario that assumes **couples 'affected' by a specific genetic trait who want a genetically-related child. But in most cases, couples could opt for preimplantation genetic diagnosis to achieve the same goal.** However, scientists claim, "some couples" oppose PGD; they claim that gene editing would reduce the selection of human embryos and/or abortions – but it is hardly feasible that modified embryos would not also be tested before implantation. In fact, this would be medically irresponsible and create greater risks of abortions. It should be noted, however, that already the cautious position is broadened to anybody opposing PGD. Once this step is taken, any limitation to couples within assisted reproduction services may not be justifiable – the result is a much broader application than the one that is currently discussed.
3. **The desire to have a genetically related child is certainly a strong *motive* – but it is not necessarily a *reason*** that justifies the risk it may involve for future generations.

4. Confronted with these alternatives, **scientists and physicians claim they are the patients' advocates – but at the same time, they put the burden of responsibility entirely on the couples.** Scientists claim it would be paternalistic to exclude germline gene editing from parents' choices, but they do not hesitate to propose limitations, i.e. restricting the applications to “exceptional” cases.
5. **Because germline gene editing affects all future generation, genetic intervention puts a major burden on the future children. They will be recommended to participate in long-term medical research, and most likely, their condition will affect their own reproductive choices.** This is a violation of their reproductive freedom rights that cannot be resolved.
6. As for **enhancement** of genetic traits that some bioethics promote as justified path forward: this clearly goes beyond parental liberty and responsibility, and it goes beyond the purpose of medicine, namely to prevent or cure illnesses. Enhancement is an ethical issue of public health and social ethics, going far beyond the framework of individual liberty.
7. From the perspective of **social justice**, we cannot ignore that the resources potentially spent on research in germline gene editing *could* in theory be spent on research and programs to secure the social conditions for those living with the same condition – or other healthcare issues. If this is not the interest of biomedical research and reproductive medicine institutions, this should be a major concern for the public.

Social ethics

Germline Gene Editing is about Enhancement

In the case of embryo modification, the second perspective to proceed with research on germline gene editing is not the cautious, exceptional *prevention* of genetic mutations but genetic *enhancement* of the human genome. No matter how ‘individualistic’ the debate is framed, enhancement is *not* based upon an abstract, individual or ‘atomistic’ concept of self-fulfillment; rather, it works against the foil of social positions. To enhance an embryo’s genetic dispositions via technologies is not merely a “human dream” of self-perfection. It is situated within social relations and structures in which better traits are intended to serve as an advantage over others.

In its new shape, enhancement theory must be the return of a naturalistic social theory that was first put forward at the end of the 19th century, albeit with better technologies. It is the return of social Darwinism that assumes competition for the best character traits among human beings as driving force for individuals who assumedly struggle for the best possible position in societies. In fact, the historical study of the 20th century should teach us a lesson about how the dream of human perfection was used within a broader framework of race and class – starting with an

individualized, “non-coercive but recommended” reproductive agenda. If a certain group within reproductive medicine wishes to promote this social vision, it should at least be explicit about it and not hide behind the veil of an altruistic, patient-centered medicine.

Enhancement is Eugenics

No matter what words are used - ‘germline gene editing’, ‘genome editing’, or ‘hereditary genetic modification’ – enhancement is tied to what historically was called eugenics. Eugenics – either in the negative form of preventing the births of seemingly ‘unfit’ children, or in the positive form of enhancement, i.e. ‘making children fit’ for the societal battle they will encounter – is a dramatic departure from the international Human Rights Framework that has been established over the last seventy years. The burden of proof that a return to the alternative normative vision of genetic perfection for some that strives for inequality (why else should one enhance one’s child if not for their advantage) over against the normative vision of social freedom and equality, must therefore be on those who want to promote it – and not on those who argue against it.

Apart from its underlying imagery of society, reproductive gene modification sends – to say the least – a clear message to persons with disabilities: their DNA falls under the category of requiring ‘modification’. Since specific research is necessary for every genetic trait that is to be modified – and even a monogenetic trait like Cystic Fibrosis comes in thousands of variations – it has been mostly left to biomedical companies to decide which conditions are to be modified. The discussion of a list of genetic traits that should be detected is well-known from the area of genetic diagnosis. It has never been resolved, and many groups, including advocates for disabilities rights, are (rightly) concerned that gene editing involves yet another (negative) value statement about their life and identities.

The underlying social imagery of genetic enhancement clashes with the social anthropology and vision of the human condition that is reflected in the Human Rights tradition. This tradition clearly states the dignity of every human being independent of their biological heritage, social status, or sexual orientation. The other side of the coin of Human Rights is Human Responsibility – duties that societies must guarantee so that *everyone*, not only the ‘abled’ or ‘most-abled’ or ‘best-equipped’ children can indeed flourish.

Medicine and Society: The Nuffield Council Survey

The disconnect and the gap between science and society is, in my view, dangerous for both sides, because it leaves societies without a context of the debate, and without a voice about the direction science is already taking; it is not only the ultimate step of the application that is contested and potentially irresponsible but already the first step of research in this area: it leaves the scientists without the necessary corrective of and by the public, and the public without a proper information of the course that science is taking – here and now.

The public consultation – as offered in the **Nuffield Council Survey** – legitimizes the ‘order of thought’ that dominates the scientific and ethical discourse so far: it narrows the societal discussion in such a way that the overall framework – the individual choice with the assistance of reproductive medicine or the genetic enhancement of the human embryos – is promoted even when respondents opt not to choose one of the given options.

The survey is a shockingly naïve document that aims to promote the public discussion while implicitly assuming that the way science & medicine (and some parts of ethics) have framed the discussion is the only possible approach.

Public Discourse Revisited

The first gene editing research projects on human embryos having already begun.

The two options we have seen so far from scientific societies’ reports (clearly underrepresenting a diverse group of participants and certainly not meeting the standards of public, democratic deliberation) are either not to hinder the scientific projects or to promote germline gene editing full-heartedly, including the genetic enhancement of human embryos. Both positions, however, risk to erode public trust that is already fragile when it comes to genetic research.

While many areas of somatic human gene editing are ethically well covered by current regulations and ethical guidelines, the presently discussed field of research – basic research of infertility and genetic causes of particular diseases – would be easier to justify if scientists and the public could agree to maintain the prohibition on germline gene modification.

Short of this, reproductive gene editing not only risks becoming the symbol of gene editing in general, moreover, the non-reproductive research will necessarily be considered as the first step to reproductive gene editing.

In sum, I want to raise three objections:

First: while health rights might be, in principle, met by safety requirements, the violation of the (reproductive) freedom of future children cannot be overcome *in principle*; it is an inherent part of the procedure of germline gene editing.

Second: Germline gene editing is yet another practice that disrespects persons with disabilities as a group. Discrimination is built into the premises of genetic modification that some genes (and some children, and some adults) are just not “good enough” “genetically”. Disability studies have demonstrated well enough that this attitude is, if nothing else, the effect of an intellectual and ethical *lack of imagination*, ignoring all biographical, relational, and social elements that constitute the life of a human being.

Third: The seemingly individual solution to genetic diseases that is promoted through and with germline gene editing cannot be abstracted from its social vision that resembles (or echoes) the Social Darwinism, a well-known social theory that contradicts the UN human rights framework. Prioritizing an assumedly atomistic individual autonomy, medicine ignores its own historical

contribution to the scientific and social movement of eugenics, including its underlying racism and discrimination against several groups and minorities. Furthermore, in emphasizing individual freedom, it ignores that human freedom rights *require* the commitment of both science and society to the concept of social freedom, rendering any atomistic depiction of the individual flawed anthropology, flawed social science and flawed ethics.⁶

Germline gene editing is not the right response to the desire to have a (healthy) child. Genome enhancement is not the right response in and for societies that struggle with injustices on many levels. But today, we are facing scientific academies who demand of societies to depart from a long ban on germline modification. Because I do not see how the three objections can be overcome – violation of freedom rights of future children, violation of disability rights, and the return of eugenics – I oppose any research that is oriented towards the clinical application of germline gene editing, be it projects in basic research, applied research, or the grey area in-between where basic research and applied research cannot be distinguished sharply.

The Nuffield Council Survey does not give any information on the regulatory system that is in place. It suggests that there is no need to discuss the research itself – its scientific, economic, national and international contexts. It suggests that individual cases reveal ethical values and inform us of social values. “The” public should demand more of ethics, and more of a public consultation process than what is offered so far.

Haker, Hille. *Ethik Der Genetischen Frühdiagnostik. Sozialethische Reflexionen Zur Verantwortung Am Menschlichen Lebensbeginn*. Paderborn: mentis, 2002.

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Honneth, Axel. *Freedom's Right. The Social Foundations of Democratic Life*. New York: Columbia University Press, 2014.

⁶ Axel Honneth, *Freedom's Right. The Social Foundations of Democratic Life* (New York: Columbia University Press, 2014).