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Editing the genome of human embryos: German perspectives

The legal situation in Germany

Art. 5 Embryo Protection Act (EPA) of 1990

(1) A person who artificially alters the genetic information of a human germline cell commits an offence and shall be punished by imprisonment up to five years or by a fine.

(2) The same applies to a person who uses a human germ cell with artificially altered genetic information for the purpose of fertilisation.

(3) An attempt to commit one of the aforementioned offences is punishable.

These norms obviously state an in-principle prohibition of germline interventions. The law does, however, grant certain exceptions.

Art. 5 subsection 4 EPA

Paras. 1 and 2 of this subsection state (in a somewhat intricate manner) that

- ⇨ the artificial alteration of a germ cell is not illicit if it is excluded that the cell will be used for fertilisation purposes;
- ⇨ the artificial alteration of a germline cell is not illicit if it is excluded that it will be transferred to an embryo, a fetus, or a (born) human being, or that it will be transformed into a germ cell (*the latter being somewhat inconsistent with the above provision*).

Hence, genetic experiments on *in-vitro* cells are permissible if provisions are made that ensure that no embryo will result from the experiments and no born human will be affected.

Art. 5 subsection 4, para. 3 EPA

In addition, paragraph 3 states exceptions to the general prohibition in cases of vaccination, chemotherapy, radiation or any other medical treatment that might involve a risk of genetically modifying germ cells but is not intended to do so. In short:

⇨ No prohibition of unintentionally causing germline mutations through medical treatment.

⇨ This applies to measures of a somatic gene therapy too, be they provided for born or unborn humans (embryos).

In very early embryos, however, it may not be possible to discern somatic cells from germline cells. In that case, the general prohibition of genetic alterations prevails.

Legal loopholes in Art. 5 EPA

There are some (unintended) loopholes in the overall prohibitive architecture of the law, having to do with recent developments in biotechnology that the legislature of 1990 could not possibly have dreamt off, such as the exchange of mitochondria of oocytes by transferring the nucleus of the one into the enucleated other.

And with respect to gene editing: A germline intervention is currently not prohibited if it is done in the following way:

(1) Alter the genome of an iPS cell, (2) transmute it into a germ cell and (3) use it for reproduction.

For if the iPS cell was created from a non-germ(line) cell, then no artificial alteration of the genetic information of a human germ-(line) cell has occurred – and *that alone* is what is illicit.

Normative perspectives

It seems, therefore, that we are at the brink of a new debate about readjusting the law of embryo protection – above all with regard to the new CRISPR technique and what it promises (or threatens).

Many (including our Constitutional Court) claim that legal embryo protection is based on fundamental constitutional rights, just as much as the protection of born human beings is.

If that is so, we should certainly try to come to grips with the basic ethical problems first, i.e., with the famous Kantian question: What ought we to do?

To initiate a public debate about these problems was the idea behind our annual public conference held in June this year in Berlin.

So let me sketch some reverberations of our discussions there.

The ethical controversy: basic distinctions of possible objections

- ⇨ Objections referring to the current lack of sufficient safety of the procedure and the corresponding high risk of harm, especially via uncontrollable *off-target* effects.
- ⇨ Objections of an in-principle kind that morally reject any and every genome editing with heritable effects *as such*, i.e., even if the procedure might become sufficiently safe one day.

Concerns about the biotechnical risks presently associated with the procedure might possibly be overcome by future research and scientific development; the in-principle objections obviously not.

Four (common) principled objections

1. Violation of human dignity.
2. No consent obtainable from any and all of the future individuals born with the altered genome.
3. Needlessness of the whole technique as its desired effects – prevention of genetically ill children – can be achieved entirely by PGD, hence by a far less risky procedure (with intended effects of a purely *enhancing* nature being morally reprehensible anyway).
4. Violation of principles of social justice, as potential benefits would foreseeably be subject to unequal distribution.

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Violation of human dignity?

Query of the objector: whose dignity?

- That of the genetically modified embryo (*this being the pre-dominant claim*)? – Hardly. It is difficult to see how the human dignity (of all things) of a particular embryo could possibly mandate to allow this embryo to be born with a severe genetic impairment, namely its defective "natural" genome, if this could be medically corrected so as to be healthy.
- The dignity of all of humanity? – Even if one would (with little plausibility) raise this claim, it would not pertain to the highest ("inviolable") individual right of persons but to a *collectice good*. The protection of such a good follows utilitarian maxims, meaning that it can and must be balanced against competing interests. It would certainly have to yield to the fundamental interest of the affected embryo not to be born in a severely harmed genetic state.

Lack of consent of all future individuals born with the altered genome?

Objection: unconvincing for two reasons:

1. For the intervention into the bodily sphere of *another*, long before one is even conceived, and with the consequence that one is born with a healthy, in lieu of a severely impaired, genome, one's consent is not required at all.

2. Furthermore, if the genome of embryo $\mathbf{E_1}$ is artificially corrected (or if $\mathbf{E_1}$ is created from genetically corrected germ cells), and, years later, the adult person $\mathbf{E_1}$ begets the now genetically healthy embryo $\mathbf{E_2}$, then it is simply incomprehensible what claim $\mathbf{E_2}$ could possibly have to inherit the (impaired!) genome of one of her grandparents instead of the healthy one of her father $\mathbf{E_1}$. Unless she had such a claim, however, the talk of a necessity to obtain consent from her does not make sense in the first place.

Needlessness of the entire risky procedure because of the availibilty of PGD?

Objection: the assertion that the goals of *genome editing* – to prevent the birth of genetically ill children – could be achieved entirely through the almost risk-free PGD is incorrect.

⇨ It is false in all, though admittedly very rare, cases in which every individual in a progeny will definitely be affected by the parental genetic disease.

⇨ Moreover, basically it pertains to monogenetic diseases (such as chorea Huntington or cystic fibrosis) only, but not to poly-genetically influenced illnessess (such as schizophrenia or Alzheimer's) oder polygenetic dispositions to other diseases (such as numerous types of cancer).

Needlessness … ?

- ⇨ In cases of such dispositions (say, with 20 defective genes involved), large numbers of *in-vitro* embryos would have to be created in order to have a chance to even get one single healthy one. (Whereas *genome editing* might one day be fit to provide a full remedy for such situations.)
- ⇨ Moreover, in Germany PGD is permissible within narrow boundaries only: in cases of "high risks of a severe hereditary disease" or "a high probability of misscarriage or stillbirth" (Art. 3a, subsection 2 EPA).

  It is hard to see why in cases of slightly less severe genetic diseases no remedy should be allowed, provided that it became available one day in the form of a sufficiently low-risk method of future *genome editing*.

Results of our debate

Unsurprisingly, we were not able to reach a consensus on these matters.

Some of us hold that basic research on inheritable forms of genome editing should be allowed and, for moral reasons, be continued. Others are of the opposite opinion claiming that such research should be subject to, at least, an indefinite moratorium if not a permanent ban.

There was, however, a firm consensus on one point: In its current and somewhat opaque state, the method of editing the human germline by CRISPR, if applied for reproductive purposes, would be morally reprehensible and should, for the time being, remain illicit – subject, as it were, to a moratorium of application.

Thank you and
vielen Dank!