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COMMENT

Gene editing of human embryos – more ethical questions to answer

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The short article by Robin Lovell-Badge entitled 'Editing human embryos' (see BioNews 799) addressing the work of Junjiu Huang and colleagues in China (1) on gene editing in human embryo - such as the use of the CRISPR/Cas9 system - raises a number of ethical questions (2). In this procedure, variants of genes are edited by removing or inserting genetic material into a developing embryo in order to see whether this could address a genetic disorder.

However, before such gene editing can be used in human reproduction, a number of biomedical challenges need to be addressed. For example, inserting or deleting specific DNA in the right place of the genome of a developing embryo without upsetting the biological equilibrium of cell is a difficult operation. A given gene may influence a number of different characteristics, which means that even if it were modified to influence a one dysfunction, this might give rise to unexpected consequences elsewhere. The overall result could be a modification that is actually harmful (3).

Another important difficulty is that gene editing of developing embryos represents a form of germline modification since changes would appear not only in the children resulting from the procedure but in all succeeding generations. In addition, gene-editing manipulations in early developing embryos are obviously eugenic, if this term is defined as 'strategies or decisions aimed at affecting, in a manner which is considered to be positive, the genetic heritage of a child, a community or humanity in general.' (4)

This is significant since international legislation clearly prohibits intentional germline modifications and eugenic practices. For example:

- UNESCO's Universal Declaration on the Human Genome and Human Rights indicates in Article 24 that germ-line interventions could be considered as a

practice that would be 'contrary to human dignity'.

- The Council of Europe Convention on Human Rights and Biomedicine (5), indicates in Article 13 regarding 'interventions on the human genome' that, '[an] intervention seeking to modify the human genome may only be undertaken for preventive, diagnostic or therapeutic purposes and only if its aim is not to introduce any modification in the genome of any descendants'.

- The EU Charter of Fundamental Rights which stresses in Article 3(2) that: 'In the fields of medicine and biology...the prohibition of eugenic practices, in particular those aiming at the selection of persons' must be respected.

Even in the UK, the use of gene-editing procedures would not be possible under the UK Human Fertilisation and Embryology Act 2008, which states in section 3(5) that any cell of an embryo used for human reproduction should not have been genetically altered. The only exception would be if the embryo has 'had applied to it in prescribed circumstances a prescribed process designed to prevent the transmission of serious mitochondrial disease'. Whether this would eventually result in new UK legislation enabling gene editing for mitochondrial disorders is an open question. Interestingly, a precedent for germline modifications has already been set by the UK's Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015. This legislation regulates the transfer of chromosomes from fertilised (or unfertilised) eggs, in which dysfunctional mitochondria are present, into healthy fertilised (or unfertilised) eggs that had been emptied of their own chromosomes.

Another ethical difficulty relating to the editing of a human embryo's genome is dependent upon the development stage at which this change occurs. If a genetic modification takes place on the gametes before they are used or during fertilisation - such as in the formation of pronuclear (one-cell) zygotes (6) - a new individual who would not otherwise have existed is brought into being. In other words, one could say that this individual should exist and not another, which has a clear eugenic element.

Alternatively, if gene editing takes place after fertilisation, another set of questions may arise. For example, if a certain gene in one of the cells of a two-cell embryo was edited, then the ethical concern would be whether any genetic changes would bring about a new individual while the original embryo would cease to exist (a form of death) or whether it would be possible to consider that the original embryo continues to exist and is simply modified (7).

In a way, this philosophical conundrum is not new and comes in many forms. It is similar to the one mentioned by the Greek historian Plutarch (c.46-120AD) in his 'Life of Theseus' (the mythical founder-king of Athens). Plutarch conducts as a thought experiment in which he asks whether a ship that is restored by replacing every one of its wooden parts remains the same ship. This is especially relevant if the old parts are used to build another ship. In the same way, it is possible to ask whether an embryo in which a certain number of genes have been edited remains the same embryo.

If the genetic modification does not give rise to any significant change in the already existing embryo, it would no doubt be seen as similar to any other form of medical treatment in which the original individual remains.

However, if a future procedure substantially modified the genome of a very early embryo, more questions relating to the continued existence of the original embryo could be asked. Genetic modification may then actually end the life of one embryo while creating another.

In summary, while it is clear that the safety and efficiency of gene-editing procedures on very early embryos give rise to significant biomedical challenges, a number of other ethical questions need to be addressed. These include aspects of germline modification and eugenic practices as well as looking at whether the existence of an embryo has been ended. Until such questions are answered, it would be appropriate for a common position to be taken by the international community. For example, countries could sign or support the Council of Europe Convention on Human Rights and Biomedicine, which can also be ratified by any non-European state.

SOURCES & REFERENCES

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5. Convention for the Protection of Human Rights and Dignity of the Human Being with Regard To The Application of Biology and Medicine, ETS – No. 164
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6. P.N. Ossorio, 'Inheritable Genetic Modifications' in Chapman and Frankel, Designing Our Descendants
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6. Pronuclear zygotes are not considered to be embryos in certain European legislations such as in Germany.

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