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Splice of life

Researchers, bioethicists and regulators must contribute to transparent discussions on the risks and ethics of editing human embryos.

The news last month that scientists had edited the genomes of human embryos induced a predictable sharp intake of breath (see *Nature* http://doi.org/3xt; 2015). The work is notable because it altered the germ line, meaning that in a viable embryo, the genetic changes would have been passed on to all future offspring. What should be society's response to such research? How should the scientific community view other current and foreseeable experiments along similar lines, and what should it do about them?

Gene-editing tools have evolved to the point at which targeted changes to a genome can be made with unprecedented ease. In theory, gene editing allows specific genetic traits to be changed. The potential clinical applications, in which babies are engineered so that they no longer carry faulty, disease-causing genes that run in the family, might be attractive to many. But even such potentially legitimate clinical applications remain some way off. There are also longer-term ethical concerns that germline gene therapy might creep beyond eliminating deadly or debilitating heritable disorders to include disabilities, less serious conditions, and cosmetic and other supposed enhancements — leading to 'designer babies' and raising the spectre of eugenics.

Now is a good time for a public debate about such human germline editing — gene editing in sperm, eggs or embryos applied in ways that would allow changes to propagate to subsequent generations. Not only should voices from civil society outside the closeted worlds of science, bioethics and regulation be heard, but their highly diverse viewpoints must also help to set the terms of the debate. The accumulated knowledge and experience of the relevant academic disciplines and regulators needs to be taken into account. Ultimately, such debates should be resolved with international discussion, and regulation at national levels.

PRACTICAL CONSIDERATIONS

The latest research, published in *Protein & Cell*, demonstrates the issues (P. Liang *et al. Protein Cell* http://doi.org/34q; 2015). The researchers deliberately used embryos that were products of eggs fertilized by two sperm, and so could never grow into a baby. The details of the work highlight why attempting human germline gene therapy using editing techniques any time soon would be a terrible mistake. The efficiency of genetic modification turned out to be poor, and the technique generated many unintended mutations. It could be a long time before researchers can demonstrate that the benefits of the procedure would outweigh the risks. Until such a time, it is clear that no sensible laboratory, regulator or nation should even consider any attempt to implant and develop to birth an edited embryo.

The potential power and relative ease of gene editing offer compelling reasons to support such research, however. The latest work, for example, aimed to edit a gene that when mutated is responsible for the blood disorder β-thalassaemia. (The gene also helps to protect against *Plasmodium falciparum* malaria.) Extending the research could help us to understand and treat the blood disorder, forms of which can be severe. There is also a strong basic-science incentive for such experiments, which can help us to understand human development and perhaps be used to produce useful cell lines. A total ban on research would therefore seem counterproductive.

But there is also a need to keep germline gene therapy in perspective. Preimplantation genetic diagnosis and selection of healthy embryos during *in vitro* fertilization already provides a safer alternative for avoiding genetic disease in newborns — as can prenatal screening and abortion. The diseases for which gene editing would be superior are few.

"There is a need to keep germline gene therapy in perspective."

Many countries ban or restrict research that involves the destruction of human embryos, and moreover bar human germline modification. Even in countries with more-liberal laws, there is a de facto ban on gene editing as part of a human-reproduction technology, because the safety and efficacy of such work would not meet existing clinical-trial standards. Debates on other genetic-engineering topics such as recombinant DNA and somatic cloning have touched on many of the issues relevant to germline editing. What usually emerges from such discussions is a green light for properly regulated research, with tight restrictions on how that research could be applied. The same outcome seems the most sensible here, and probably the most likely, in light of the embryo-editing work.

But all involved must actively work to make that happen, and not passively assume that the field will simply evolve towards best practice. How should a more general discussion proceed? Whether in collaboration or separately, national governments need to step up on this issue. Scientists, companies and ethicists are already voicing their views and setting up further meetings.

Also helpful might be an official forum of experts to assist emergent policy discussions — an international meeting of scientists, regulators, ethicists and representatives of civil society, perhaps convened under the auspices of the World Health Organization (WHO). Such a meeting could take stock of the state of the science of gene editing, and articulate the regulatory and ethical landscapes. It could then quickly move to help close any gaps in legislation, and develop a regulatory framework for the inevitable germline-related advances in gene-editing techniques.

A model perhaps is a similar meeting convened by the WHO last year to rapidly assess the ethics of emergency clinical trials of Ebola drugs and vaccines that had not been fully tested for their safety. As with Ebola, any meeting on germline gene editing should also be given access to the unpublished results of ongoing experiments.

Transparent and inclusive discussion of issues raised by gene-editing technologies that could open the door to germline gene therapy is a must. Scientifically and ethically informed contributions would remind people that for the foreseeable future, science-fiction scenarios of 'designer babies' remain just that, while providing an articulation of the limitations of our scientific understanding. ■