THIS WEEK

EDITORIALS

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Ethical embryo editing

Progress in the use of CRISPR–Cas9 for human germline editing highlights some pressing ethical considerations for research on embryos.

This week, *Nature* publishes the results of experiments that used genome editing to modify the DNA of a human embryo. Kathy Niakan at the Francis Crick Institute in London and her colleagues have used the CRISPR–Cas9 technique to introduce mutations into a gene called *OCT4*, and show how the gene is required to steer cell fate as a fertilized egg starts to divide and proliferate (N. M. E. Fogarty *et al. Nature* http://dx.doi.org/10.1038/nature24033; 2017).

The research addresses a fundamental question of human biology, but understanding the events of early development could also help to refine culture conditions for embryos in future *in vitro* fertilization (IVF) treatments. It also provides crucial information about the mechanism that underpins the gene-editing technique. The embryos, which had been donated by couples who had undergone IVF treatment, were allowed to develop in the laboratory for only a few days.

Nature published a related paper last month, which explored how gene editing of embryos using CRISPR–Cas9 could correct a specific genetic mutation (H. Ma *et al. Nature* **548,** 413–419; 2017). Those experiments, by Shoukhrat Mitalipov at Oregon Health and Science University in Portland and his colleagues, did not use embryos from IVF clinics. Instead, the researchers made them in the lab by fertilizing donated eggs with sperm from a male donor who carries the mutated gene.

The publication of these studies seems a good time for all involved to take stock and discuss how they should navigate this type of research.

ETHICAL CONSENSUS

The development of CRISPR–Cas9 as an efficient genome-editing tool is under scrutiny because it brings with it the possibility that scientists could make permanent modifications to the human germ line. Specialist groups have charted these ethical challenges and made some recommendations about how best to take forward research that applies gene editing to human embryos. Consensus guidelines — such as those based on the efforts of an interdisciplinary ethics consortium called the Hinxton Group, as well as separate efforts by the US National Academies of Science, Engineering, and Medicine, the International Society for Stem Cell Research and others — have advised that editing the human germ line can be justified for the scientific purpose of research into fundamental biology.

But they also say that substantial basic research is needed to check the safety, accuracy and feasibility of genome editing as a potential clinical tool. Therefore, clinical applications can be considered only after strong research groundwork has been done, and only then for cases that are deemed acceptable after careful examination of alternatives and further societal debate.

Both research studies published in *Nature* aim to answer some fundamental scientific questions. And, in keeping with consensus guidelines, both studies have undergone strict and thorough ethical assessment during their inception, execution and peer review (as outlined in our policy; see go.nature.com/2xigr4g). Both studies were licensed by the relevant authorities, and had full ethical approval and consent from the couples who donated the embryos, eggs and sperm.

These studies are valuable on several counts. They provide important insights into the biology of human embryos, and the possible mechanisms of genome editing in this context. They also highlight technical and ethical issues that inform researchers, funders, journals and regulators as they plan and assess future projects in this field.

In particular, they show the importance of properly assessing the suitability of the type and number of embryos needed for research projects that explore different aspects of human germline editing.

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Using donated surplus embryos from IVF might be a better way to answer some research questions than using embryos fertilized in the lab. The inherent variability of donated embryos could offer a more rigorous and realistic testing ground for checking issues such as the rate of unintended 'off-target' genetic changes, which can occur when using CRISPR–Cas9 editing. But, for the time being, targeted correction of specific mutations will probably continue to rely on donated eggs and sperm that carry the mutated DNA and which are then used to make a fertilized egg in the research laboratory.

In both cases, *Nature* fully supports the principle that all donors should be informed of the details of the exact research to be carried out with their donated material — as described in the methods section of both papers.

In keeping with the sensitive nature of a donation, researchers must show that they have balanced scientific and ethical considerations to determine the appropriate number of embryos used. They must ensure that experiments will provide robust scientific answers, while minimizing the use of this precious material. This may imply, as was the case in both the published studies, that researchers must first perform the intended work in human pluripotent stem cells or mouse embryos to optimize the conditions. Journals, reviewers and editors should consider which questions arising during peer review can be answered using systems other than human embryos.

One point for the research community to consider is whether these initial studies might be peer reviewed and considered for publication before the hypothesis is tested in embryos. This independent peer review could happen in parallel with consideration of the project by the regulators, and could inform decisions on embryo provenance and the limits of experiments.

The particular requirements of studies will differ, but a strong framework for assessing them as early as possible seems the best way to ensure that they meet the highest standards. Regulators, funders, scientists and editors need to continue working together to define the details of the path forward for germline genome editing, so that the valuable resources and tools now at our disposal are used with good judgement. ■