GENETICS

Embryo editing divides scientists

Researchers disagree over whether making heritable changes to genes crosses an ethical line.

BY DAVID CYRANOSKI

Research that uses powerful gene-editing techniques on human embryos needs to be restricted, scientists agree — but they are split over why.

Some say that if safety fears can be allayed, such applications could have a bright future, and could help to eradicate devastating diseases. Others say that modifying the DNA of embryos, which means that the changes could be passed on to future generations, is an ethical line that should not be crossed.

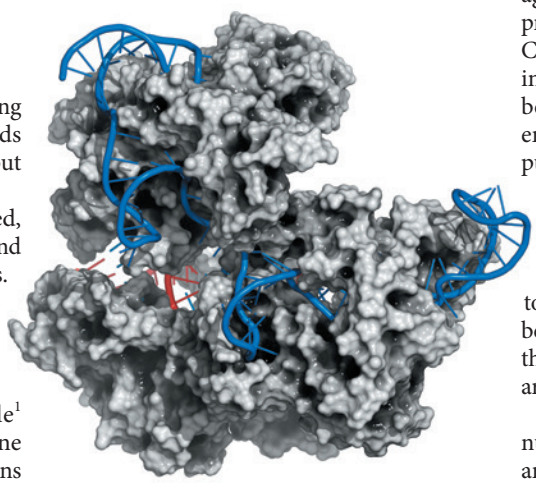
The concerns are laid out in an article[1] published in *Nature* on 12 March and in one expected to appear in *Science*, amid suspicions that scientists have already edited the genes of human embryos.

Gene-editing techniques use enzymes called nucleases to snip DNA at specific points and then delete or rewrite the genetic information at those locations. Most recently, excitement has focused on a technique called CRISPR/Cas9, which is particularly easy to use. Current applications of the technology are in non-reproductive, or somatic, cells: for example, Sangamo BioSciences of Richmond, California, has used zinc-finger nucleases, an older gene-editing technology, to remove a gene from white-blood cells that encodes the receptor to which HIV binds to enter the cells.

But concerns focus on the use of gene editing to modify the genomes of eggs and fertilized eggs — a process known as germline modification.

Edward Lanphier, president of Sangamo and chairman of the Alliance for Regenerative Medicine in Washington DC, together with colleagues from both organizations, wrote the Comment article[1] in *Nature* calling on scientists not to modify human embryos, even in research. The authors warn that such work could be exploited for "non-therapeutic modifications" — to change a child's eye colour, for example — and that a public outcry about such an "ethical breach" could hinder the use of gene editing in somatic cells.

They also have more basic objections. "We are humans, not transgenic rats," says Lanphier. "We believe there is a fundamental ethical issue in crossing the boundary to modifying the human germ line."



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CRISPR/Cas9 makes precisely targeted gene edits.

George Church, a geneticist at Harvard Medical School in Boston, Massachusetts, agrees that there should be a moratorium on embryo editing, but only "until safety issues are cleared up and there is general consensus that it is OK". Church, along with a group of scientists who met in Napa, California, in January to discuss the ethics and potential of the procedure, authored the piece for publication in *Science* detailing their concerns.

One concern is that nucleases could make mutations at locations other than those targeted, potentially causing disease. Church says that gene editing in animals is likely to reveal how to understand and avoid this complication. In one application, his group is editing genes related to the immune system in pig embryos to 'humanize' them, potentially allowing the pig's organs to be transplanted into people.

Other indications of safety will come from trials on somatic cells. Sangamo has already demonstrated the safety of its modified white-blood cells in a trial of people with HIV[2].

Church sees no fundamental problem with editing the germ line — he notes that even the somatic-cell therapies are still a form of artificial modification. He compares gene editing in embryos to *in vitro* fertilization, which people objected to until it was shown to be safe.

"In the distant future, I could imagine that altered germ lines would protect humans against cancer, diabetes and other age-related problems," says Nobel-prizewinning geneticist Craig Mello of the University of Massachusetts in Worcester. In the nearer term, "there could be good reason to experiment with discarded embryos or embryonic stem cells for research purposes", he says.

But Lanphier says that for most cases in which parents carry disease-causing genes, not all of a couple's embryos will carry the faulty gene. Existing technology can be used to genetically screen and select healthy embryos before transplantation into the uterus, negating the need for permanent germline repair. "There are almost always alternatives," he says.

Church, however, says that for the growing number of known cases in which several genes are involved in a disease, most embryos need to be discarded. Editing would greatly increase the odds of getting a healthy embryo.

Dana Carroll, a geneticist at the University of Utah in Salt Lake City who was at the Napa meeting, says that a national agency such as the US National Academy of Sciences should convene a conference that includes medical professionals and the interested public to weigh up the positive and negative aspects of germline editing. They had better hurry: several researchers who do not want to be named told *Nature*'s news team that papers describing such work are currently being considered for publication in journals.

Carroll also cites the importance of educating the next generation of physicians about gene editing. "They should be learning now what the technology is able to do and what the social, as well as clinical, concerns are." ■

1. Lanphier, E. *et al. Nature* **519,** 410–411 (2015).
2. Tebas, P. *et al. N. Engl. J. Med.* **370,** 901–910 (2014).

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