DNA editing of human embryos reignites debate over designer babies

Base editing, the process used to make the changes, only nicks one strand of DNA, avoiding the major DNA errors that made CRISPR unsafe.

Scientists have announced the successful use of a next-generation tool to precisely edit human embryos' DNA, highlighting a major advance in the ability to tweak genes as life takes shape — and fueling the ongoing debate over the ethics and safety of "designer babies."

Two separate teams deployed base editing, which allows scientists to swap one letter of DNA for another to make targeted changes to the 3 billion letters of the genome, the biological instructional manual for a human being.

In a study released Thursday, a group in the United Kingdom used base editing to probe the role a gene called NANOG plays in the first week of embryonic development, helping illuminate one of the most consequential black boxes in human biology. In a different study released this month and undergoing peer review, a team at Columbia University made edits to a gene that lowers "bad" LDL cholesterol and another that can be used to treat sickle cell disease.

Each experiment was designed with very different goals. But together, the results underscore the power and limitations of the technology, a newer version of CRISPR gene editing that won the Nobel Prize in 2020. They show how broadly this approach could be used — to probe basic science questions about human reproduction and, more contentiously, possibly change it.

Gene editing is already being used to treat people suffering from sickle cell or inherited metabolic disorders. But editing embryos fundamentally alters and raises the ethical stakes.

The prospect of using gene editing to create babies exploded into the public consciousness in 2018, when a Chinese scientist named He Jiankui used CRISPR to create gene-edited babies. He was widely denounced as a rogue by other scientists and put in prison. Those genetic changes, and any unintended errors, will be passed down to the next generation if those embryos are used — essentially tinkering with what it means to be human.

Editing embryos for human reproductive use is effectively banned in the United States, and federal funding cannot be used in research that creates or destroys human embryos, limiting the research.

"Studying the role of genes and studying human development will undoubtedly advance our understanding of our own biology, and that, in turn, the knowledge will lead to improvements in stem cell biology and will lead to improvements in treatments for infertility," said Kathy Niakan, a developmental biologist at the University of Cambridge Loke Centre for Trophoblast Research, who led one of the studies, published Thursday in the journal Nature.

A second paper, published to a preprint server in early June, made edits to embryo genes that mirror therapeutic approaches to address high cholesterol and sickle cell disease. Those scientists hope their work will lead ultimately to being able to correct genetic mutations that cause devastating diseases.

"These base editors are compatible with development, and that's new both from our study and the new one," said Dieter Egli, a stem cell biologist at Columbia University whose lab led the work on the preprint, which is now undergoing peer review at Nature.

The “whither humanity” thought experiments sparked by these recent studies overshadow the actual advances, which are incremental in many ways. Both papers show the current state-of-the-art gene editing technology represents a big step up in accuracy from CRISPR, which often jumbled up chromosomes and caused genetic errors. Base-editing has been reported before on human embryos by research groups in China.

But the new papers also reveal unresolved safety and technical issues — including the existence of stray “bystander” edits to nearby areas of the genome. Resulting embryos are often a mosaic, including both edited and unedited cells.

“I think we all agree, we are not at the stage of discussing clinical application,” said Thanos Papathanasiou, an author of the Nature paper and medical director of Bourn Hall Clinic, the world’s first IVF clinic, in the United Kingdom.

“There are lots of limitations here, and I think some of them are worth pointing out, otherwise the public will anticipate: Next year my neighbor will use this to have a blue-eyed baby,” Egli added.

Nevertheless, the work edges the field closer to questions that have no easy answers and have been roiling the scientific community for years. Can and should this type of technology be used in human reproduction? When and why?

“The more that we begin to chip away at the concerns around safety and efficacy, the more we are forced to confront the more fundamental questions about why this can and should be done, for what indications, what are the so-called use cases?” said R. Alta Charo, a professor emerita of law and bioethics at the University of Wisconsin at Madison. “And is there a fundamental ethical objection to doing it for those use cases? There is a genuine split of opinion.”

I. Glenn Cohen, a bioethicist at Harvard Law School, said in an email that there is a concept in moral philosophy called “ought implies can” — if a person is morally obligated to do something, they therefore must have the ability to do it. The new study flips that.

“I think this study is making the ‘can’ part look like it may happen sooner and thus puts the ‘ought’ question (or really questions) more front and center,” Cohen said.

CRISPR had been shown in previous studies, including by Egli’s lab, to be a dangerous tool for editing embryos. CRISPR cuts both strands of DNA, and the repair process often leads to chromosomal abnormalities. This provided an easy out for scientists as they continued to debate the safety, ethics and risks of editing the genes of embryos — the technology was simply too clumsy for this application. Base editing only nicks one strand of DNA, and the new studies both show it avoids the major DNA errors that made CRISPR unsafe.

Meanwhile, the idea of “optimizing” reproduction has caught fire among fertility companies funded by tech investors, which sell services to help couples doing IVF select embryos with genes that make them more likely to have lower disease risk, higher IQ or other traits.

Kian Sadeghi, chief executive of Nucleus Genomics, said in an interview that gene editing of embryos could be one of the future tools in a “genetic optimization stack” for IVF.

Sadeghi sees gene editing as part of a continuum of tools to help prospective parents who want to avoid heritable diseases. Already, the company allows customers to choose embryos that don’t carry genetic risks for serious disease, he noted. But some couples don’t have unaffected embryos to choose from — and might opt for gene editing.

Nucleus plans to support some of the future research in Egli’s laboratory. Cohen said that given the limits on federal funding for research on human embryos, scientists doing this work must turn to alternate sources. But he argued that it was important to draw a line between “optimization” and avoiding serious diseases.

“Which disorders are so debilitating and life-shortening that heritable gene editing might be appropriate, at least as initial targets, and who decides?” Cohen asked. “When, if ever, would it be appropriate to move from that small number of targets to other diseases? Would enhancement uses ever be appropriate?”

Egli said he did not agree with all the statements Nucleus has made about gene editing. “What matters is what’s going to be done in the project ... we want to fix mutations,” Egli said.

It’s hard for any scientific paper to land in this uneasy terrain without polarizing scientists and bioethicists, who have often very different opinions about the technology’s potential. Separating the tool as it is applied in one experiment from broader potential applications is difficult.

Fyodor Urnov, director of research and development at the Innovative Genomics Institute at the University of California at Berkeley, called the Nature paper “scientifically stellar,” but raised concern about how its results will be used.

“The authors do an exemplary job clearly pointing out how far away we are from using human embryo editing for reproductive purposes,” Urnov said in an email. “Despite their best efforts it is certain that the ‘better babies via embryo editing’ crowd will use this work to supercharge their unethical and misguided work.”

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