NEWS IN FOCUS

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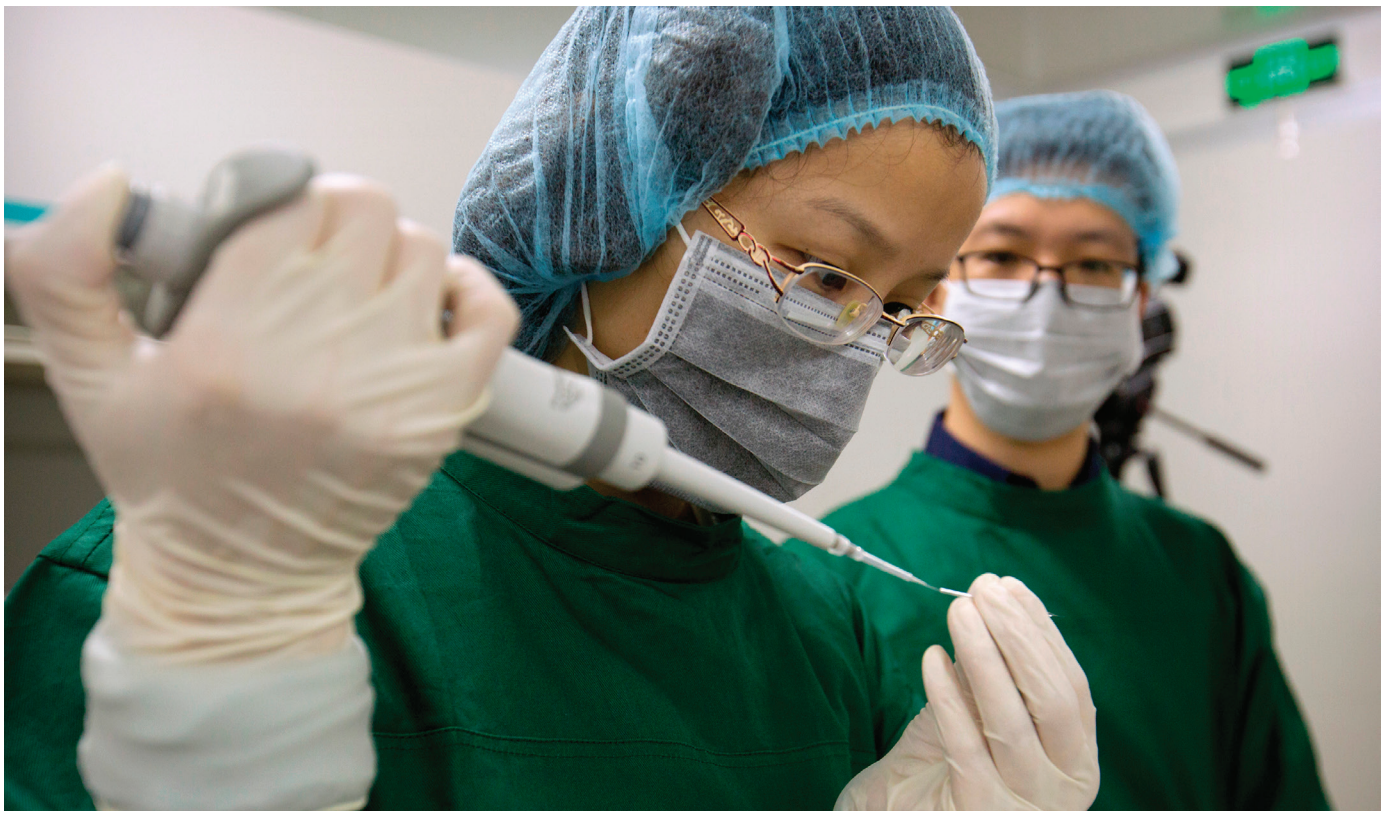


The CRISPR–Cas9 tool was used to genetically modify embryos before implanting them into a woman.

GENE-EDITING

CRISPR-baby scientist fails to satisfy his critics

He Jiankui reveals details of how he edited babies' genomes, but many questions remain.

BY DAVID CYRANOSKI

He Jiankui, a Chinese scientist who claims he helped to produce the first people born with edited genomes — twin baby girls — appeared at a gene-editing summit in Hong Kong to explain his experiment. On 28 November, he delivered his talk amid legal threats and mounting questions about the ethics of his work, which until then he had outlined largely in YouTube videos.

Scientists welcomed the fact that he appeared at all — but his talk left many of them hungry for answers, including whether his claims are accurate.

"There's no reason not to believe him," says Robin Lovell-Badge, a developmental biologist at the Francis Crick Institute in London. "I'm just not completely convinced." An independent body should confirm the test results by thoroughly comparing the parents' and children's genes, say Lovell-Badge and others.

Many scientists faulted He for the seemingly cavalier nature in which he embarked on such a landmark, and potentially risky, project.

"I'm happy he came, but I was really horrified and stunned when he described the process he used," says Jennifer Doudna, a biochemist at the University of California, Berkeley, and a pioneer of the CRISPR–Cas9 gene-editing technique that He used. "It was so inappropriate on so many levels."

Alta Charo, a bioethicist at the University of Wisconsin–Madison and a member of the summit's organizing committee, says: "Having listened to Dr He, I can only conclude ▶

that this was misguided, premature, unnecessary and largely useless."

CCR5, the gene that He edited using CRISPR-Cas9, is the door through which many strains of HIV infect immune cells. Many scientists have criticized He's choice to alter this gene, in part because there are other ways to stop people from contracting HIV. Critics also say that other diseases would make more obvious targets for elimination through editing embryonic genomes. Huntington's disease or Tay–Sachs disease are examples of conditions that, in some circumstances, might be averted only through gene editing, said George Daley, dean of Harvard Medical School in Boston, Massachusetts.

HIV-RESISTANT TWIN

He revealed that one of the genetically modified twins will be resistant to HIV, because the gene edits removed both copies of her *CCR5* gene. The other twin could still be susceptible to infection, because the gene-editing process inadvertently left one of her copies of *CCR5* intact, he said.

He's decision to implant the second embryo drew strong criticism. "Why choose this embryo? It just doesn't make sense scientifically," said geneticist Jin-Soo Kim of Seoul National University. He Jiankui said he had explained the situation to the parents and they decided they wanted to do it anyway. He also made clear that his aim is to prepare the technique for global use: "For millions of families with inherited disease or infectious disease, if we have this technology, we can help them."

He initially worked with eight couples in which the men were HIV-positive and the women HIV-negative, but one couple later dropped out of the study. His team first washed the men's sperm to ensure that HIV was not present. The researchers then injected the sperm, and CRISPR–Cas9 enzymes, into unfertilized eggs from the men's partners. This produced 22 embryos, of which 16 seemed to be viable and to have been edited. Two of the four embryos from one couple contained modifications to *CCR5*, and He says that he implanted these, even though one embryo still had an intact copy of the *CCR5* gene, to produce the twins.

It is not clear what has happened to the other embryos. He said that he has now put the experiments on hold, but that he had already implanted a gene-edited embryo into another woman.

Kim says he's 90% sure that He succeeded in editing the twins' genomes as claimed, in part because He used state-of-the-art sequencing methods before and after implantation to show that the embryos contained no unwanted mutations.

"He has to be given a chance to explain what he did. We cannot have unruly behaviour."

But He's talk leaves a host of questions unanswered, including whether the prospective parents were properly informed of the risks; why He selected *CCR5* modification when there are other, proven methods for HIV prevention; why he chose to do the experiment with couples in which the men have HIV, given that women with HIV have a higher chance of passing the virus on to their children; and whether the risks of knocking out *CCR5* — which could have necessary but still unknown functions — outweighed the benefits.

Nobel-prizewinning biologist David Baltimore, chair of the summit's organizing committee and former president of the California Institute of Technology in Pasadena, called He's experiment "irresponsible". Baltimore also accepted blame on behalf of the scientific community: "There has been a failure of self-regulation."

In response to questions about why the community had not been informed of the experiments before the women were impregnated, He cited presentations he gave last year at meetings at the University of California, Berkeley, and the Cold Spring Harbor Laboratory in New York. But Doudna, who organized the Berkeley meeting, says that He did not present anything showing he was ready to experiment in people.

He also said that he discussed the human experiment with unnamed scientists in the United States. But Matthew Porteus, who researches gene-editing at Stanford University in California, says that's not enough for such an extraordinary experiment. Porteus wants He to post his data to a server such as bioRxiv, so that other scientists can analyse them.

BIG EXPECTATIONS

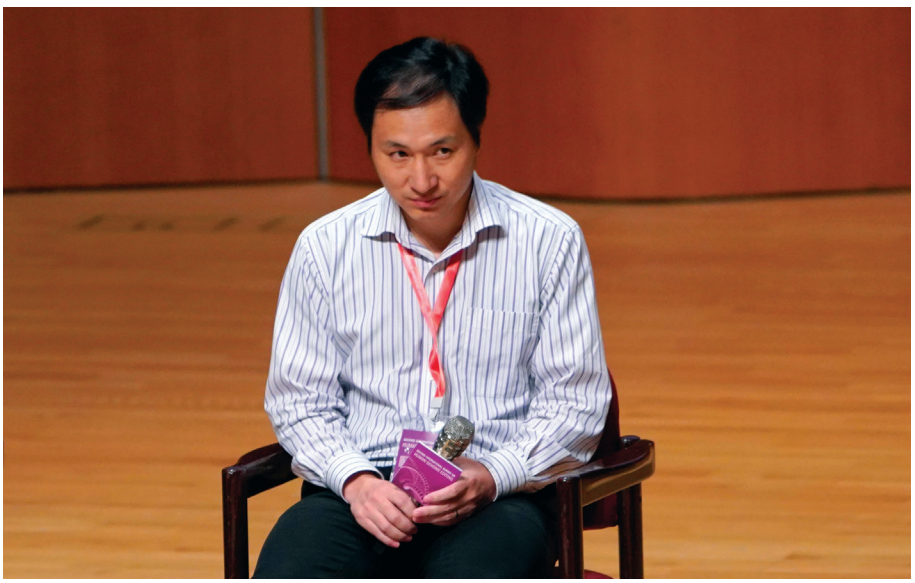
Pressure was mounting on He ahead of the presentation. On 26 November, the Chinese national health commission requested the Guangdong health commission — which is in the same province as He's university — to investigate. The Chinese Academy of Sciences has issued a statement condemning He's work, and the Genetics Society of China and the Chinese Society for Stem Cell Research jointly issued a statement saying that the experiment "violates internationally accepted ethical principles regulating human experimentation and human rights law".

The hospital cited in China's clinical-trial registry as having given ethical approval for He's work posted a press release on 27 November saying it did no such thing. The hospital, itself now under investigation by health authorities, questioned the signatures on the approval form and said that its medical-ethics committee had never held a meeting related to He's research. He has not responded to *Nature*'s requests for comment on these statements and investigations.

On 28 November, Francis Collins, director of the US National Institutes of Health (NIH), said in a statment that "this work represents a deeply disturbing willingness by Dr He and his team to flout international ethical norms".

Fears are growing that He's actions could stall the responsible development of germline gene-editing, the modification of genes that are passed on to future generations. At the summit, Daley urged support for such research: "It's possible that the first instance came forward as a misstep, but that should not lead us to stick our heads in sand and not consider a more responsible pathway to clinical translation."

The pressures facing He were clear ahead of his talk, in particular when Lovell-Badge made a plea uncharacteristic of scientific meetings. "He has to be given a chance to explain what he did," said Lovell-Badge. "We cannot have unruly behaviour." There was also heightened security, with men in dark suits near the stage, and cameras lining the back of the auditorium. Porteus says that He's appearance was a first step, but that He will have to start answering lingering questions soon. "He's already at risk of becoming a pariah." ■



TPG VIA ZUMA

He Jiankui faced tough questions after his talk at the gene-editing summit in Hong Kong.