A Series of YouTube Videos Detailing the “CRISPR Babies” Experiment (2018), by He Jiankui

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In 2018, He Jiankui uploaded a series of videos to a YouTube channel titled “The He Lab” that detailed one of the first instances of a successful human birth after genome editing had been performed on an embryo using CRISPR-cas9. CRISPR-cas9 is a genome editing tool derived from bacteria that can be used to cut out and replace specific sequences of DNA. He genetically modified embryos at his lab in Shenzhen, China, to make them immune to contracting HIV through indirect perinatal transmission from their father, who was infected with the virus. HIV is a virus that attacks the immune cells of its host and weakens their ability to fight off diseases. At the time of He’s experiment, various treatments already existed at that could prevent the fetuses from contracting HIV without the need for gene surgery. Nonetheless, He’s experiment led to one of the first successful births of fetuses resulting from genetically modified embryos. He kept his experiment secret until he uploaded the videos announcing the birth of the fetuses, born as two twin girls. The experiment discussed in the videos was successful, but many scientists criticized the experiment due to ethical concerns with the way He conducted it.

In his videos, He discusses the technology he used to edit the twins’ genomes when they were embryos, or fertilized eggs that could develop into fetuses. A genome is the set of an organism’s DNA. DNA, or deoxyribose nucleic acid, is a molecule present in all living organisms that contains the genetic instructions for the organism’s development and functioning. Editing a genome therefore changes an organism’s development and functioning. To edit the twin’s genomes, He edited specific genes, or sequences of DNA that encode for a specific trait or characteristic, in his experiment. Scientists can edit the DNA in the cells of an adult human body, which will only affect the adult human. However, if scientists edit the DNA in germline cells, meaning cells such as sperm, eggs, or embryos in their early stage of development, those cells will pass the edited DNA to the next generation of offspring. Because He edited early-stage embryos in his experiment, his edits will not only affect the children who developed from the edited embryos, but also their offspring and future generations.

He used CRISPR-cas9 technology to edit the embryo genomes. Bacteria use CRISPR-cas9, a complex made of a protein molecule called cas9 and RNA, another molecule that carries genetic information, to cut the DNA of viruses invading the bacterial cells to stop the viruses from replicating and infecting the cell. The CRISPR RNA can recognize specific sequences in a viral genome and guide the cas9 protein to that sequence so cas9 can cut that sequence out. In genome editing, scientists create CRISPR RNA that will recognize a specific sequence they want to remove in the genome of the cells of an organism they want to edit. After cas9 removes that sequence, the scientist can provide that cell with a new stretch of DNA to replace it. Scientists can create the new stretch of DNA to encode genes they want the edited cells to express. In 2012, Jennifer Doudna, a researcher at the University of California, Berkeley, in Berkeley, California, and Emmanuelle Charpentier, who at the time was a professor at Umeå University in Umeå, Sweden, first developed CRISPR-cas9 as a method of genome editing, which the won the Nobel Prize in Chemistry for in 2020. Various researchers went on to use CRISPR-cas9 to edit the genomes of many different species, leading to He’s use of the technology to edit human embryo genomes. However, as of 2021, genome editing on early-stage human embryos development is widely considered unethical and is banned in most countries.

He used CRISPR-cas9 to make the embryos in his experiment immune to HIV, which the father of the embryos was infected with. Human Immunodeficiency Virus, or HIV, is a sexually transmitted virus that targets a body’s immune cells, or the cells that fight infection, and weakens the immune system. The most severe stage of HIV infection is called Acquired Immunodeficiency Syndrome, or AIDS. People with AIDS have severely damaged immune systems, and contracting infections often proves lethal because their body has a harder time fighting off other infections. HIV replicates by inserting its own genetic information into the genomes of their host’s immune cells.

HIV is not a genetic disease, meaning that parents do not pass HIV to their children through their DNA. Rather, HIV is a virus that children can get infected with from their parents if they come into contact with the virus. Mothers can pass HIV to their offspring during instances when the offspring comes into contact with the mother’s bodily fluids that carry the virus, such as pregnancy, delivery, or breastfeeding. Direct father-to-child transmission of HIV is very rare, though not impossible. If a father is HIV positive, as in the case with the father in He’s experiment, there is a risk that he can pass HIV to the mother, who will pass it to their children. However, various methods exist that can reduce the chance of HIV-positive parents transmitting HIV to their offspring close to zero. Due to the existence of those methods, many researchers saw He’s intervention to prevent HIV as unnecessary.

He was born in the Hunan Province of China in 1984, making him thirty-four years old at the time of his experiment. He began researching how CRISPR evolved in 2007 for his thesis while pursuing his doctoral degree in biophysics at Rice University in...
In 2012, He moved back to China as part of the Thousand Talents program, an initiative the Chinese government created to bring prominent Chinese researchers and entrepreneurs working abroad back to their home country by offering monetary incentives. After moving back, he opened The He Lab at the Southern University of Science and Technology in Shenzhen, China, otherwise known as SUSTech. He conducted his experiment on human embryos at The He Lab.

On 25 November 2018, five videos were uploaded to a YouTube channel titled “The He Lab.” The videos each lasted under six minutes. Throughout those videos, He and Qin Jinzhou, who studied the prenatal development of embryos and fetuses in He’s lab, announce that they have successfully genetically edited human embryos, a process they call “gene surgery,” and review why and how they conducted it. In the first video titled “Draft Ethical Principles of Therapeutic Assisted Reproductive Technologies,” He argues that gene surgery should be accessible because it can improve children’s quality of life and lists principles that researchers should follow when conducting it. In the second video titled “Designer Baby is an Epithet,” he asserts that a child is not something to be designed and that gene surgery should only be used to protect a child from lethal or debilitating diseases. In the third video titled “Why We Chose HIV and CCR5 First,” He states that they chose to work on HIV because of the abundance of existing research on the virus and the potential to improve a person’s quality of life by preventing HIV. In the fourth video titled “Gene Surgery in Embryos: An Embryologist Explains How It Works,” Qin reviews how researchers perform the gene surgery. In the last video titled “About Lulu and Nana: Twin Girls Born Healthy After Gene Surgery as Single Cell Embryos,” He announces that two twin girls were successfully born from edited embryos. He argues that parents need access to technologies like gene surgery to improve the lives of their future children.

In the first video “Draft Ethical Principles of Therapeutic Assisted Reproductive Technologies,” He defends the use of gene surgery and lists principles that should be followed while performing it. He declares that genome editing should be used to provide mercy for families that need technologies to repair a broken gene, treat [in]fertility, or prevent transmission of a disease to have healthy children. Secondly, the researcher expresses that gene surgery is a risky procedure and should only be used to treat serious diseases. He maintains that it should never be used to change a child’s appearance, strength, or mental capabilities. Next, the scientist notes what he calls the principle of respect for a child’s autonomy. He asserts that a child born from a modified embryo should have equal rights to life, work, and privacy, and are not obligated to their parents or any organization in any way for the gene surgery. Fourth, He clarifies that a person is not defined by their genes, and that a person’s life and achievements result from other factors. Lastly, He declares that everyone deserves freedom from genetic disease, and that wealth should not influence the accessibility of gene surgery.

In the second video titled “Designer Baby is an Epithet,” He argues against calling children “designer babies,” saying that the term is an insult to parents with genetic diseases. He states that most parents do not want to design a perfect child but want to prevent genetic diseases from debilitating their child’s life. The researcher pleads that parents should not have to watch their children suffer from genetic disease. If scientists have the technology to prevent a genetic disease, He argues that it is inhumane for them to not use that technology to protect children. He goes on to contend in the video that The He Lab is on the right side of history and predicts that there will be no question about the morality of the practice in twenty to thirty years. Lastly, He appeals to his audience saying that while there will be many critics of gene surgery, people should keep in mind the families that gene surgery will be able to help.

In the third video “Why We Chose HIV and CCR5 First,” He explains that his lab chose to focus on treating HIV because they believed it would be a relatively safe and beneficial procedure. First, He introduces the CCR5 gene, which codes for the production of the CCR5 co-receptor. Cell co-receptors are molecules present on the surface of cells. Extracellular molecules bind to cell coreceptors to send a signal to the cell. However, when an HIV virus binds to the CCR5 co-receptor, CCR5 allows HIV to enter the cell, where HIV replicates itself and ultimately destroys the cell. If CCR5 is disabled, then HIV will not be able to enter and kill immune cells it targets. In humans, HIV targets CD4 cells, which are responsible for initiating the immune response to fight pathogens that come in contact with the immune system and have CCR5 co-receptors. By reducing the amount of CD4 cells in the body, HIV weakens the immune system’s ability to fight off other pathogens. As a result, when HIV positive people catch diseases, it could be fatal as they have a weakened ability to fight the pathogens that cause those diseases. He aimed to disable the CCR5 gene to prevent the production of the co-receptor that allows HIV to enter and destroy CD4 cells.

He proceeds in the third video to express that the first reason his lab chose to focus on HIV was because protecting against it was a safer option than protecting against other diseases due to how widely the CCR5 gene had been studied. Most humans are born with their CCR5 gene enabled. But, according to He, more than 100 million people have a natural genetic variation that causes them to be born with a disabled CCR5 gene. The researcher asserts that people with a disabled CCR5 gene are protected against HIV without the genetic variation compromising other aspects of their health. He details that decades of researchers had attempted to mimic that genetic variation to disable the CCR5 gene and doing so had been proven safe. Thus, He’s lab aimed to reproduce that genetic variation as well through their gene surgery because they felt secure that it would be a
safe operation. Additionally, the scientist explains that reproducing that genetic variation requires minimal genome editing. Protecting against other diseases such as familial cancer or muscular dystrophy would be more complex and riskier.

He ends the third video by disclosing that his lab’s second reason for choosing to protect against HIV was because they believed that their operation would have real-world medical value. The researcher states that among many countries, HIV is a top cause of death and that no vaccine or cure exists. While there are treatments, He argues that taking pills everyday can have health consequences. Additionally, the researcher contends that people with HIV are discriminated against in many countries. Therefore, He insists that gene surgery to prevent HIV is ethical and can help many families at risk across the world.

In the fourth video titled “Gene Surgery in Embryos: An Embryologist Explains How It Works,” Qin describes how gene surgery works in single-celled embryos as the video displays footage of him working on the embryo. He states that similarly to in vitro fertilization, researchers begin by retrieving eggs from a woman and sperm from a man, and place the eggs on a petri dish. Next, Qin states that the researchers inject sperm into the egg with a very small needle to fertilize the egg. Once the sperm fertilizes the egg, researchers inject CRISPR-cas9 into the embryo cell. The CRISPR RNA is encoded with instructions to recognize the sequence of the CCR5 gene. It guides the cas9 protein to the CCR5 gene, and the protein cuts the gene out. Qin explains that by the time the egg has divided into three or four cells, the gene surgery is complete. It takes anywhere from three to five days for the cell to replicate and divide into multiple cells. During that time, the egg is stored in a petri dish with temperature safe surroundings and kept outside of a woman’s body. After the gene surgery, the embryo is placed back in the woman’s uterus so it can continue developing. Qin asserts that every gene surgery has some risks, like the possibility that the edits may affect other genes around CCR5, so the researchers paid close attention to the genes that surrounded the CCR5 gene during surgery to ensure they were not affected. They can examine the genes through electron microscopes, a microscope with the ability to greatly enlarge an image through the use of electrons to illuminate an image. Qin also states in the fourth video that the lab had conducted three years of preclinical research that found the CCR5 gene surgery to be safe.

In the last video, “About Lulu and Nana: Twin Girls Born Healthy After Gene Surgery as Single-Cell Embryos,” He announces that the gene surgery led to the birth of two infant girls who He refers to as Lulu and Nana, born to parents Grace and Mark. He explains that his lab performed the gene surgery on Grace’s embryos when they were just single cells to disable the CCR5 gene and protect against HIV. Before returning the embryos to Grace’s uterus, the lab researchers checked to ensure the gene surgery went properly through whole-genome sequencing. Researchers use whole-genome sequencing to read the DNA code in the genome. By using that technique, the researchers could ensure that no other genes other than the CCR5 gene had been altered. He declares that the genome sequencing indicated the gene surgery had been safe and successful. After the fertilization and the genome sequencing, they inserted the embryo back into Grace so the cells could grow into fetuses. He assures that Grace’s pregnancy was normal and that they monitored it closely through blood tests and ultrasounds. Around early November 2018, the twin fetuses were born healthy and safe, according to He. After Lulu and Nana were born, researchers sequenced their genomes again to confirm that the gene surgery was successful and that no other genes were affected or harmed.

He goes on to that claim that Lulu and Nana’s births gave Mark’s life a new purpose because Mark never thought that he would be able to have kids due to being infected with HIV. He states that developing countries are highly discriminative towards people like Mark who have HIV, and people with the virus are often denied medical care and fired from their jobs. The researcher claims that Mark and Grace wanted their embryos to undergo gene surgery to protect their children from being exposed to such discrimination. He finishes the video by stating that most parents who seek out gene surgery are not looking to create designer babies, but just want to protect their potential child from suffering from a debilitating disease. As of 2021, there have been no updates on Lulu and Nana’s health.

The videos were posted a couple of days before He was supposed to give a talk at The Second International Summit on Human Genome Editing, a conference held in Hong Kong, China, from 27 November through 29 November of 2018. Various organizations that researched science and medicine organized the summit, including the US National Academy of Science, the US National Academy of Medicine, the Royal Society of the United Kingdom, and the Academy of Sciences of Hong Kong. Greely states that about twenty-four hours before the scheduled conference, on 26 November 2018, He’s story broke out after a reporter found the videos that He had published. According to Henry T. Greely, a professor of law and genetics at Stanford University in Stanford, California, He’s experiment became a central discussion of the conference, and various scientists denounced the secretive and unethical nature of He’s work. He delivered a twenty-minute talk on the experiment on 27 November 2018 and was heavily questioned and criticized on stage afterwards, according to Greely. He had also been scheduled to deliver a second talk at the conference two days later, but cancelled it and left the conference after his first talk.

Greely professes that the news of He’s gene surgery experiment created an uproar within the scientific community as many scientists, including Greely himself, believed that He’s actions were unethical. First of all, many critics condemned the secretive way that He went about conducting the gene surgery. Typically, scientific experiments undergo a rigorous approval process before being conducted. However, He’s home institution SUSTech asserted they had no idea about the experiment while He was conducting it. Four unnamed hospitals that provided the embryos He used also claimed to not have known what He was doing or approved it. Additionally, there was no external ethical oversight of He’s experiment, and according to the Health Commission of China, He also misled the couples in his study about how great the risks to their potential children actually were.
A second reason researchers stood against He is that they saw his experiment as unnecessarily risky. At the time of He’s experiment, many viable [80] options were available to prevent the transmission of HIV from the paternal to maternal carrier, including antiretroviral drugs. If those options were taken advantage of, there would have been a very low risk that Lulu and Nana would have contracted the virus. Due to the existence of such options, critics thought the risks of He’s genetic intervention outweighed the benefits. As scientists are only beginning to develop genome [7] editing technologies, using them could have had many unintended consequences on the embryos that could affect the potential children’s quality of life.

Many academics denounce the idea of performing genome [7] editing on human embryos altogether. Multiple genome [7] editing techniques are being developed to treat human diseases such as cancer, cystic fibrosis [21], or sickle-cell disease in children and adults. However, genome [7] editing on early-stage embryos, or what He calls gene surgery, is considered unethical because it changes the lives of future generations who cannot give their consent to having their genomes modified. Additionally, all future generations would also be at risk of suffering from unintended consequences of genome [7] editing, which could arise in unpredictable ways.

Lastly, many academics such as Francis S. Collins, a physician who researchers genetic diseases, worry that genome [7] editing on germline cells raise issues of equity and justice. Collins suggests that genome [7] editing technology may be limited to those who can afford it, giving only a select few the option to improve their potential offspring’s lives by editing genes [8] that could supposedly improve appearance, mental abilities, or risk of contracting chronic illnesses. Moreover, the Center for Bioethics and Human Dignity raises concerns that genome [7] editing of germline cells is closely tied to eugenics [22] due to its capacity to permanently alter the genomes of future generations. Eugenics is a practice that seeks to supposedly improve the human species through methods such as selective breeding that affect the genetic heritage of a child. Eugenics movements of the past have culminated in atrocities such as forced sterilizations and genocide in the name of improving the human race, most prominently in the Holocaust during World War II. The Center for Bioethics and Human Dignity warns that genome [7] editing of germline cells could easily be used to practice eugenics [22].

As of 2021, most of the scientific community has condemned He’s experiment. Stephanie Malia Fullerton, a Professor of Bioethics and Humanities at the University of Washington School of Medicine in Seattle, Washington, asserts that there had been broad scientific consensus that researchers should not be making permanent genetic changes to the human genome [7] before He’s experiment. Fullerton clarifies that He was not treating a genetic disease so much as preventing the possibility of the embryos contracting a virus, a practice that approached unethical genetic enhancement. She articulates that news of He’s experiment was unexpected and premature to most researchers, and many worried about the wellbeing of Lulu and Nana. Moreover, Doudna, one of the developers of CRISPR-cas9 as a genome [7] editing technology, was quoted saying that she was horrified after hearing about He’s experiment.

Nonetheless, a few ethicists and scientists do support continued research in genome [7] editing for human embryos. George Church [23], a genetic researcher involved in controversial projects such as de-extinction, or the recreation of extinct species, defended He. Church argued that the main complaint other scientists had against He was that he did not follow the usual protocols to get scientific approval, and that He’s overall goal was justified. Additionally, Julian Savulescu, the Director of the Oxford Uehiro Center for Practical Ethics at Oxford University in Oxford, England, and Peter Singer, a professor of bioethics at Princeton University [24] in Princeton, New Jersey, have argued that society has a moral imperative to continue research on genome [7] editing in embryos because of the technology’s potential life-saving capabilities. Despite that, Savulescu still denounced He’s experiment as monstrous after hearing of them.

In late November 2018, around the same time as the international conference, He’s team submitted a paper detailing their experiment and results titled “Birth of twins after genome [7] editing for HIV resistance” to the scientific journal Nature. The paper listed nine contributors, including He as the first author and Deem, He’s former professor at Rice University, as the senior author according to STAT News. However, Nature rejected the paper due to the ethical controversy surrounding the experiment. Then in January 2019, the Health Commission of China published an official investigation in which they found He’s work violated Chinese research rules through practices such as using fake ethical review certificates and misleading his participants. SUSTech fired He a week after the report was released. Finally, in December 2019, a Chinese news agency announced that the Chinese government fined He three million Chinese yuan, or 429,000 US dollars, and sentenced him to three years in prison for illegal medical practice according to the Chinese government. Two other embryologists and one doctor connected to the gene surgery were also fined and imprisoned. Rice University also investigated Deem’s involvement but as of 2021, Deem was never arrested or fined for his connection to He’s experiment.

The videos He uploaded detailed one of the first successful births from a genetically modified human embryo. Even though the gene surgery was known to have been successful, the procedure caused mass controversy in the scientific community. He’s procedure advanced an international conversation on the ethics of editing genomes of germline cells, and motivated countries such as China to implement tighter regulations on scientists and genetic engineers. As of 2021, He’s work is highly criticized, and gene surgery has not publicly been re-attempted.

Sources


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