**Salon 49: The CRISPR Baby Controversy**

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**What happened?**

News story: <https://www.youtube.com/watch?v=b0HvLaXOhEY> (0:00-0:50)

In November 2018, Dr. He Jiankui announced the first human babies born with germline gene editing using CRISPR/Cas9. The babies’ parents were recruited through an AIDS advocacy group; the father is HIV positive while the mother is uninfected. After conducting in vitro fertilization of the mother’s eggs with the father’s sperm, He used a CRISPR-based editing method to try to edit a mutation (CCR5 Δ32) into the embryos’ genomes that conferred resistance to HIV. He confirmed the successful mutation by sequencing the embryos’ genomes after CRISPR editing; some cells now carried mutations in CCR5 (not exactly Δ32), while others did not. No off-target mutations were found. The babies, Lulu and Nana, were born with no complications sometime around late October 2018.

He’s research and actions have been met with widespread criticism from the scientific community and beyond for myriad reasons. It is unclear if He acquired informed consent from the parents. Furthermore, the research was largely conducted in secrecy. He first announced his work in a video posted to Youtube, bringing concerns about unreviewed communication of science. Since then, the Chinese government has suspended He’s research; He is being held under surveillance and potentially awaits consequences.

What is CRISPR-Cas9?

CRISPR (clustered regularly interspaced short palindromic repeats) are specific DNA sequences that constitute part of the immune system of bacteria and archaea. DNA from viruses that have previously infected the cell is integrated into these CRISPR elements, which can then recognize and destroy future viruses with similar DNA code. The CRISPR array transcribes RNA sequences that guide the enzyme Cas9 (CRISPR-associated protein 9) to a specific site in the genome, via a perfect 20 base pair match. At this site (determined by the guide RNA sequence), CRISPR-Cas9 “cuts” strands of DNA that are complementary to the guide RNA, and thus, the part of the CRISPR array that was transcribed. An engineered version of this system allows for the simple redesign of the sequence CRISPR-Cas9 detects; users can easily and inexpensively design new CRISPR-Cas9 guide RNAs to cut any specific sequence of DNA. Think of CRISPR-Cas9 as highly specific DNA “scissors”.

Based on He’s actions it can be inferred that resistance to HIV should be viewed as a benefit that merited his non-traditional and secretive actions. The research raises questions about what are and who should have access to from the potential benefits and burden of human germline editing. These questions are implicitly driven by morals or values; this is where ethics can guide critical analysis of the variety of (potentially conflicting) answers people may have.

Ethics:

*Distributive Justice:* Set of principles to identify the morally preferable distribution of benefits and/or burdens. Considerations can include components or assets such as income, wealth, opportunities, jobs, welfare, or utility, who the recipients of these distributions are such as individuals, groups, classes, or society, and how the distributions should be made such as equality, optimization/maximization, group or individual characteristics, or through free transactions.

<https://plato.stanford.edu/entries/justice-distributive/#Scope>

*Egalitarian:* Principle that every person should have equal levels of material, services, benefits, and/or burdens. Justified through the argument that people are morally equal and that this should be represented in the distribution of benefits and/or burdens.

<https://plato.stanford.edu/entries/egalitarianism/>

*Rawlsian Difference Principle:* This can be conceived as equal respect for persons and is focused on inequality or unequal distributions only that improve or raise the level of society’s least advantaged. Not focused on strict equality but instead is focused on absolute position of the least well off rather than the relative position.

<https://plato.stanford.edu/entries/rawls/#TwoPriJusFai>

*Utilitarian:* Principle that aims to maximize the overall welfare, which can be considered, utility, happiness or preference fulfillment, and is not necessarily dependent on if the majority is the recipient of that welfare.

<https://plato.stanford.edu/entries/utilitarianism-history/>

*Libertarian:* Principle that prioritizes individual autonomy or decision making as the indication of how benefits and/or burdens should be distributed.

<https://plato.stanford.edu/entries/libertarianism/>

Gene therapy and debates of its ethics before CRISPR baby:

**“Three parent babies”**: women who struggle conceiving donate eggs for in vitro fertilization. The DNA from the fertilized eggs are extracted and implanted in eggs from a second woman, from which the DNA has been removed. The second egg, with the DNA from the first fertilization, are then implanted back into the first woman. NPR story: <https://www.npr.org/sections/health-shots/2018/06/06/616334508/her-son-is-one-of-the-few-children-to-have-3-parents>

**Jesse Gelsinger**: enrolled in a trial to treat an inheritable genetic liver disease by delivering a functional copy of the mutated gene via viral vector. Jesse died from complications with the treatment during the trial. Investigators failed to disclose serious complications in other patients.

<https://www.nytimes.com/1999/11/28/magazine/the-biotech-death-of-jesse-gelsinger.html>

On the other hand...

**Biohackers**

<https://www.geneticsandsociety.org/internal-content/designer-babies-crispr-genetic-engineering> (25:30-27:00)

**Discussion questions:**

1. In human embryos, what traits would you edit out or edit in? How and why? Is HIV resistance one of them?

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| --- | --- |
| **Okay to edit** | **Not okay to edit** |
| Eye color? | Intelligence? |
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1. Imagine CRISPR gene editing technology was made available to everyone at no cost, with 100% efficacy and no side effects. Has your set of editable or uneditable traits changed? Why?

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| **Okay to edit** | **Not okay to edit** |
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1. Now consider the same question, but conditional upon access to safe germline gene editing being extremely expensive. Any changes?

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| **Okay to edit** | **Not okay to edit** |
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1. CCR5 Δ32 confers resistance to HIV. However, CCR5 deficiency also increases susceptibility to West Nile Virus. How should we balance trade-offs, known or unknown, of the genes we choose to edit?
2. Similarly: CCR5 mutations have been shown in some research to increase memory potential and stroke recovery time in mice. How do you consider unintended “enhancing” effects of edited phenotypes?

**Further reading**

Initial publicity of CRISPR babies:

<https://www.technologyreview.com/s/612458/exclusive-chinese-scientists-are-creating-crispr-babies/>

Are scientists capable of self-governance?

<https://www.statnews.com/2019/01/28/scientists-reactions-crispr-babies-ethics-self-governance/>

Initial call to arms:

<http://science.sciencemag.org/content/362/6420/1215>

Moratorium called for CRISPR germline editing in humans: <https://www.nature.com/articles/d41586-019-00726-5>

DIY CRISPR editing:

<http://www.the-odin.com/humans-animals/>

Biohacks:

<https://www.selfdecode.com/>