The Biological and Ethical Repercussions of Using Gene-Editing Technology to Alter the Human Germline

In December of 2019 Chinese researcher He Jiankui made an exciting yet troubling announcement: he claimed to have edited the genes of a pair of twin girls in order to prevent them from developing the Human Immunodeficiency Viruses (HIV) infection, an attempt which has not yet proven to be successful.[1] Although at first this experiment may appear beneficial, it caused a cascade of criticism from scientists all over the world due to its negative implications. The main question lingering from Dr. He's experiment is whether scientists should use gene-editing technology, like CRISPR-Cas9, to edit the inherited human germline (sex cells used to pass genes to the next generation). Though using this technology could result in positive health benefits as shown in Dr. He's experiment, allegedly, because the technology's abilities advanced much more rapidly than conversations surrounding the ethics of this technology and so little is known about the effects of editing the human germline, it would be reckless to use CRISPR-Cas9 to begin editing human germlines.

In order to understand the ethical implications of gene editing, understanding how scientists are able to accomplish this feat is crucial. Scientists use CRISPR-Cas9, a biological tool, to add, remove, or edit specific genes in an organism's genome. CRISPR stands for Clustered Regularly Interspaced Short Palindromic Repeats, while Cas9 is a nuclease, a DNA-cutting enzyme. Scientists attach Cas9 to a guide RNA molecule, which forms a Cas9-RNA complex. The guide RNA is the same sequence as the target DNA sequence in the gene of the organism. The Cas9 enzyme recognizes the PAM site (NGG) on the target gene, then separates the two strands of DNA. If the guide RNA is exactly the same as the 20 base pair sequence towards the 5' end of the DNA from the PAM site, Cas9 reshapes and slices through the target sequence through both DNA strands, always three nucleotides upstream from the PAM

site.[2] Cutting the gene inactivates it, allowing scientists to try and figure out what phenotype that gene coded for by comparing the genetically edited organism with one in which the gene is intact.

There are many valid potential beneficial results from using this powerful technology. Editing genes in the germline could prevent the person, and more significantly their offspring, from developing serious diseases like Huntington's disease (a progressive brain disorder). These single gene or single nucleotide mutated gene diseases are potentially preventable through gene editing, therefore also preventing future generations from suffering. In addition to the germline, if scientists research the effects of gene-editing technology on embryos now, the information would be indispensable in the future should scientists want to use the technology for reproductive purposes.[3] Because of the positive effects that germline editing can impose, a portion of the scientific community has concluded that scientists should unequivocally use CRISPR-Cas9 to edit the human germline.

Despite these potential benefits, currently, the scientific and ethical concerns surrounding this technology outweigh its positives. In most cases of single-gene diseases, gene editing is unnecessary and costly. For example, editing the germline could prevent an embryo from having Huntington's disease in the future. However, a cheaper and safer way to accomplish this exists. Alternatively, scientists can use *in vitro* fertilization, followed by preimplantation genetic analysis of the embryos, then only transferring the embryos without the problematic gene. Another significant concern of germline editing is the likelihood of off-target effects. Off-target effects occur when Cas9 slices the DNA in an unintended location, causing unpredictable and likely damaging effects to other genes. These effects have the potential to continue in future generations, resulting in long-term, potentially harmful changes in the genome.

Besides the biological concerns, the potential of this technology warrants additional social and ethical considerations. One of these concerns is that the future generations produced by a person with an edited germline could not consent to their genes also being edited and turned into something other than a naturally-occurring genome. Additionally, the price tag on this procedure severely limits accessibility technology. Only the wealthy could afford it so only they could benefit from this possibly life-saving treatment, which raises an issue of equity. Finally, a more futuristic concern remains: would this technology push science back towards eugenics? Should scientists be allowed to alter traits unnecessarily once they know the genes responsible?[4] Some would say no, but currently not enough regulations exist regarding the possibilities of this technology to restructure society in a trait-based manner. As of now, scientists do not possess total control over the gene-editing process and society has not set a standard on the ethics involved in this process, so editing the germline possesses significant risks to the patient's offspring and should not be conducted until ethical rules are in place.

In summary, though gene-editing technology can result in health benefits, scientists should not use it to edit the human germline until it is reliable and internationally agreed-upon standards are in place for when using this technology is acceptable. Regrettably, as of now these stipulations have not been met, but hopefully will be in the near future. While editing a single nucleotide mutation will likely prevent a patient from experiencing a disease, editing that nucleotide in the germline could cause unforeseen health concerns in the patient's offspring. Until more research is conducted, scientists should not attempt to tamper with the genes of future generations of humans.

1. Wee, S.-L. (2019, December 30). Chinese scientist who genetically edited babies gets 3 years in prison. *The New York Times*. https://www.nytimes.com/2019/12/30/business/china-scientist-genetic-baby-prison.html
2. *CRISPR*. (n.d.). Retrieved August 6, 2021, from https://media.hhmi.org/biointeractive/click/CRISPR/
3. Experts debate: Are we playing with fire when we edit human genes? (2015, November 17). STAT. https://www.statnews.com/2015/11/17/gene-editing-embryo-crispr/
4. Experts debate: Are we playing with fire when we edit human genes? (2015, November 17). STAT. https://www.statnews.com/2015/11/17/gene-editing-embryo-crispr/

Article summary:

As technology in genetics advances rapidly, ethical questions surrounding these advancements arise slower, creating powerful technology that is used without discussing proper usage and application. In her article, Roma Kale ‘23 explores the ethical and biological consequences of using gene-editing technology like CRISPR-Cas9 to edit the human germline.