Gene Editing and its Ethics: Prenatal and Postnatal Approaches

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The genome lies at the most basic level of human biology and heredity. Made up of DNA, the genome codes for all of the proteins in the human body, each with their own function, ranging from determining hair color to carrying oxygen throughout the body. One gene codes for one protein, and each gene has two alleles (versions of the gene), one from each parent. The double-helix structure of DNA, first discovered by J. D. Watson and F.H.C. Crick in 1953, has a sugar-phosphate backbone and complementary sequences of nitrogenous bases, which, when transcribed into mRNA and arranged in groups of three (codons) during translation will produce different proteins depending on the codon. Now, a little over 70 years later, scientists are able to modify the human genome both before and after birth. However, embryonic gene modification calls for great ethical debate within the scientific community, while gene modification in adults is a more painful process. Both methods have their pros and cons, but either way, gene editing will allow for more permanent solutions to previously incurable issues. Still, only future research can tell how the treatments will change.

In the past, genetics relied on mutations that arose spontaneously in studied populations. However, in the mid-twentieth century, Hermann J. Muller and Charlotte Auerbach determined that radiation or chemical treatment have the ability to increase the rate of spontaneous mutations. By the 1970s and 1980s, scientists had begun to induce certain insertions in model

organisms. These relied on homologous recombination: a type of genetic recombination where two almost identical DNA molecules will exchange genetic information, swapping which molecule carries a certain sequence to target certain genes. However, this process, while a major development, was relatively inefficient. Modern genome editing technologies resolve this issue by making a DNA double strand break (DSB) in a certain target location. The tools used to do this have roots in research on DNA damage repair, since the human body uses a similar process in meiosis. Genetic recombination during meiosis relies on intentional DSBs, and experimentation with similar nucleases paved the way for the modern gene editing tools. In current gene modification technology, targeted DSBs are made by a nuclease at a specific site, relying on internal DSB repair proteins to fix the break. This allows for incorrect sequences to be easily removed; however, insertion of new sequences is more difficult. By altering the levels of homologous and non-homologous products, this insertion has been moderately successful, but this is heavily dependent on the specific sequence of the DNA (Carroll 2017). As this technology has improved, the debate surrounding where to go next has centered around the ethics of gene editing, especially in embryos.

The legitimacy of genetic modification has been contested from multiple standpoints, especially in terms of whether genes *should* be modified in embryos and in children. Until 2015, the human could only be edited in somatic cells (cells that are not a part of the germline, and thus, do not reproduce), meaning that any alterations would not be heritable. However, recent debates in terms of human genome editing ask whether the benefits—possible improvement of the general condition of the human race for future generations—outweigh the risks—a “threat to

human dignity" and a slide into eugenics. By treating certain disorders, such as sickle cell anemia or Type 1 diabetes in the germline, one could prevent carriers or affected individuals from passing the disorder to any of their children, which would certainly improve the quality of life for future generations of their family. However, the definition of "improvement" to quality of life can have many different meanings, and some fear that making these decisions when an embryo is unable to give consent would be ethically wrong (Segers & Mertes, 2020). Additionally, this consent issue extends to children, who may not be able to give informed consent to participate in clinical trials, especially because little regulation has been passed in terms of genetic modification (Pepper et.al., 2018). Finally, many ethics arguments surrounding this type of genetic engineering call attention to whether humans should be "playing God" with their bodies or with the bodies of their children. From a theological standpoint, some religions believe that a higher power shaped humanity, and thus, humans do not have the right to alter their body in this way, especially in embryos (Joseph et.al., 2022). Due to many of these ethical debates, research has begun to turn to how these disorders can be addressed in adults without modifying embryos because editing the genome of an adult is less ethically dubious than editing the genome of an embryo which lacks the ability to consent.

Medically, research is turning towards treatment for adults, both in somatic and germline cells. In terms of somatic cell gene modification, many gene therapies are currently arising where some of a person's stem cells may be removed for modification while the rest are removed from the system. Thus, when these cells are reinjected, this person will only produce the cells with the modified gene, allowing for permanent treatment of the disorder. This is how a new treatment for

sickle cell anemia works: by using the CRISPR-Cas9—a system using a guide RNA and an endonuclease at specific sites—to edit the genome to include the functioning sequence. Many other research programs direct their attention toward lysosomal storage diseases using adeno-associated virus (AAV) vector therapy, which relies on gene editing in the liver. In terms of germline modification, certain labs have begun looking into possible editing reagents for in vitro fertilization (IVF), which could eliminate certain diseases from the gene pool, although this type of modification is likely still quite far off and would require great consideration of the ethical implications (Carrol, 2017). Regardless, both of these types of treatments seem to have a lot in store for the future of medicine and the future of bioethics.

Works Cited

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