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Ethics in Gene Editing: A Narrative Literature Review

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A B S T R A C T

Gene editing is the process of making precise, intentional changes to the DNA sequence of an organism, including humans, animals, and plants. However, there are always ethical questions to address, especially when the manipulation involves the human genome. This literature review aimed to describe the ethics of gene editing and its application. There is currently an urgent need to actively pursue those conversations as commercial gene sequencing and editing technologies have become more accessible and affordable. Gene editing has enormous potential both as a research tool and a therapeutic intervention. While other types of gene editing are relatively uncontroversial, gene editing has been strongly resisted. In conclusion, gene editing research can be conducted safely in ways that carry manageable and reasonable risks.

1. Introduction

Gene editing is the process of making precise, intentional changes to the DNA sequence of an organism, including humans, animals, and plants.[1] This is usually done using techniques such as CRISPR-Cas9, which involves cutting the DNA at specific locations and then using the cell's own repair mechanisms to introduce desired changes to the genome.[2,3] Gene editing has the potential to be used in a wide range of applications, including in medical research, agriculture, and the development of new therapies for genetic diseases. However, it also raises ethical and safety concerns, particularly when it comes to using gene editing techniques in human embryos or germ cells, which could have permanent and heritable effects on future generations.[4,5]

There are several ethical concerns surrounding gene editing, particularly when it comes to editing the genomes of humans or other organisms that could have significant implications for future generations. Some of the most significant ethical concerns include safety, consent, equity, stigma, and long-term consequences related to gene editing. Gene editing techniques can have unintended and potentially harmful consequences, including off-target effects and other genetic abnormalities that could lead to health problems or other unintended consequences. The use of gene editing techniques in humans raises complex issues around informed consent, particularly in cases where gene editing is being done for non-therapeutic purposes.[6]

Gene editing could potentially exacerbate existing social and economic inequalities, as those who can afford to access these technologies could gain significant advantages over those who cannot. Gene editing could be used to reinforce negative social

stigmas around certain conditions or traits, leading to discrimination against affected individuals or groups. However, the potential long-term consequences of gene editing on future generations are not well understood, raising significant concerns about the potential risks and unintended consequences of these technologies.[2,5] This literature review aimed to describe the ethics of gene editing and its application.

Gene editing and selection

Genetic selection happens in nature, and natural selection is the mechanism that drives Darwinian evolution. Humans have also been practicing artificial selection for thousands of years, selecting phenotypic traits when breeding plants and animals. New technologies have been developed over the last 53 years that allow the selection of an embryo based on various criteria such as sex, ploidy, and polymorphisms. Fluorescence in situ hybridization (FISH) was the first cytogenetic technique to be used for preimplantation genetic testing (PGT). Fluorochrome-labeled site-specific probes were hybridized to sample DNA, revealing aneuploidy and translocations.[6,7]

A number of other cytogenetic techniques for comprehensive chromosome screening (CCS) have been developed. They are digital PCR which can detect CNV, aneuploidy, mutations, and rare sequences; quantitative real-time PCR (qPCR), in which a preamplification step prior to real-time PCR allows for rapid detection of aneuploidy in all 24 chromosomes; single nucleotide polymorphism (SNP) array which can detect imbalanced translocation, aneuploidy, and monogenic disease; and next-generation sequencing (NGS), the high-through-put, massively parallel DNA sequencing technologies that allow for significantly quicker and cheaper sequencing than the Sanger method and make it possible to screen for everything from SNPs to aneuploidy.[8]

Ethics of gene editing

Next, the main aspects that have caused greater controversy in scientific, technological, legal, or philosophical forums about the existence of a human genetic identity and the free initiative to modify that identity. This framework does not include other types of human improvement that science puts forward–physiological, cognitive or moral improvement through external elements such as drugs, surgery, or somatic genes–even if the focus remains similar: the happiness and well-being of individuals. The fundamental difference of these tendencies with genetic enhancement in germline lies in a concept previously mentioned: the autonomy of the individual. The recipients of the genetic enhancement have not chosen to be better, something that is required for any other pharmacological, neuronal, or surgical improvement, which usually includes free, informed consent. Therefore, we focus on specific areas in which genetic improvement affects the fundamental rights (including future identity, dignity, and a good lifetime) of individuals who are especially vulnerable and without autonomy, such as embryos or a newborn.[9]

Some arguments against gene editing dispute the authority of current individuals to make decisions on behalf of future generations. In outlining their decisions to continue not to fund gene editing research, the NIH pointed to the ethical issues presented by altering the germline in a way that affects the next generation without their consent. This argument is pursued less directly in the Nature commentary, which refers to the difficulty in obtaining informed consent when calling for a moratorium on gene editing.[10]

It is not made clear in either piece why the consent of future generations should be seen as vital for decisions involving gene editing but not for other major decisions with long-term effects. The central question with gene editing, as with all interventions that create risks for individuals who cannot consent, is not whether the individuals who would be exposed to the risks would consent to them, but whether they will also (expectably) enjoy benefits that outweigh the risks.

Suppose first that our pursuit of gene editing will affect what future people come into existence. Thus,

the individuals who will bear the risks of gene editing will also exist only because it is pursued. These individuals will enjoy existential benefit from the pursuit of gene editing. In rare cases, individuals may also suffer harms from gene editing that outweigh these benefits in the sense that we have a stronger reason to avoid the harms than to produce the benefits. This would most plausibly be so if gene editing causes severe side effects to make an individual's life not worth living. But provided, gene editing is sensibly regulated so as to mitigate risks. Such cases will be extremely rare. It thus seems reasonable to expect that the existential benefits will collectively outweigh the risks.

However, many will enjoy concrete person-affecting health benefits in the form of reduced (risk of) disease. It seems nearly universally accepted that we can benefit people by reducing rates of disease. Moreover, it is again plausible that if gene editing is sensibly regulated, these benefits will outweigh the risks. One common concern about gene editing is that it will be used as a tool of human enhancement and not merely to prevent disease. Gene editing has a much greater capacity to be used as a means of enhancement than conventional selection methods. This is because it can target a large number of genes simultaneously and could be used to insert genes that would not occur naturally. While genetic selection allows selection within the normal human range, gene editing would allow the enhancement of human capacities to supranormal levels.

Many believe that if gene editing were used as a tool of human enhancement, it could cause widespread social harm. There are several different ways to understand the term 'enhancement', which are often only imprecisely communicated by opponents of enhancement. No commonly offered definitions describe something clearly morally problematic. Further difficulties arise when considering how biological enhancement can be differentiated from non-biological enhancements, which are nearly universally celebrated. However, suppose for the sake of argument that biological enhancement is universally problematic. It is doubtful that this would count decisively against permitting and funding the therapeutic use of gene editing or the continuation of gene editing research.[11,12]

Many medical technologies currently being used or developed for the treatment of disease could also be used as enhancements. Many of those who are against the use of these technologies for enhancement purposes are still in favour of pursuing their development and therapeutic uses. Some will argue that the stakes are much higher with gene editing than with these other technologies. Furthermore, some are sceptical that regulations could prevent gene editing from being used as an enhancement. It concedes that if the use of gene editing to enhance traits poses a very significant moral risk, and regulations cannot limit gene editing therapeutic uses, then there may be a reason not to develop gene editing as a clinical tool.

2. Conclusion

Gene editing research can be conducted safely in ways that carry manageable and reasonable risks. This of course, would be moot if the development of gene editing carried no benefits. Also, there is a significant medical case for pursuing gene editing to combat single gene disorders and polygenic disorders and, importantly, a research case for pursuing this technology to better understand the genesis of disease.

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