

STATE OF THE ART AND SCIENCE

Is Editing the Genome for Climate Change Adaptation Ethically Justifiable?

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Abstract

As climate change progresses, we humans might have to inhabit a world for which we are increasingly maladapted. If we were able to identify genes that directly influence our ability to thrive in a changing climate, would it be ethically justifiable to edit the human genome to enhance our ability to adapt to this new environment? Should we use gene editing not only to prevent significant disease but also to enhance our ability to function in the world? Here I suggest a “4-5 framework” for analyzing the justifiability of gene editing that includes these considerations: (1) safety, (2) significance of harm to be averted, (3) succeeding generations, and (4) social consequences.

Introduction

Gene editing is no longer a theoretical possibility. It is a stark reality that raises vexing ethical and regulatory questions for scientists and society. Scientists have successfully edited a human preimplantation embryo to repair a mutation in the *MYBPC3* gene that is associated with hypertrophic cardiomyopathy (HCM) [1]. HCM is a serious disease that is the most common cause of sudden death in otherwise healthy young athletes. Using CRISPR (clustered regularly interspaced short palindromic repeats)/Cas9 (CRISPR-associated nuclease 9) to recognize specific genome sequences, scientists were able to efficiently target cells and activate DNA repair to correct a mutation in the gene that is responsible for approximately 40 percent of all genetic defects causing HCM [1]. CRISPR/Cas9 technology is a powerful editing tool to disrupt any gene. To create gene disruptions, a single guide RNA (sgRNA) directs the Cas9 nuclease to cut through a specific sequence of DNA. (The cell's native DNA repair mechanism typically mends the damage, but it is error prone and insertions and deletions can be introduced that disrupt gene function.) This technique has revolutionized genome editing, allowing for targeted editing of genes and the ability to manipulate many genes at once. While the technology for gene editing has rapidly advanced and continues to improve, scientists are marching ahead without clear guidelines on the use of the technology.

The ability to use gene editing to prevent the development of a life-threatening genetic disease that arises from a single gene mutation raises the possibility of using gene editing for other purposes. While we are likely to achieve a consensus on the ethical

permissibility of using gene editing to prevent life-threatening diseases, there is an urgent need to clarify the boundaries for which the technology should be used and who should decide when it is used. Should we use gene editing not only to prevent significant disease but also to enhance (i.e., modify, with the goal of improving) our ability to function in the world? Should we enhance human beings so they are more resistant to disease? Who has the authority to make these decisions? Should parents be allowed to decide to use gene editing on behalf of their children and future generations? These questions will be explored in considering the potential use of gene editing to enhance humans' adaptability to climate change, and a general framework for making decisions about the use of CRISPR/Cas9 will be presented.

A recent international report on the state of climate change by the American Meteorological Society found that the year 2016 was the earth's warmest year on record. Our sea levels also reached a record high in 2016, and the concentration of carbon dioxide at the earth's surface is the highest it has been in 800,000 years, which is as far back as ice records extend [2]. As climate change progresses, we humans might have to inhabit a world for which we are increasingly maladapted. If we were able to identify genes that directly influence the ability to thrive in a changing climate, would it be ethically justifiable to edit the genome to enhance the ability to adapt to new environmental conditions? As will be discussed in what follows, this question has been affirmatively answered by some agricultural and animal geneticists, with sparse societal deliberation. Answering this question for human beings will surely be next, but given the differences in the potential risk—physical and ethical—of using this new technology in plants, animals, and human beings, we need robust societal deliberation and a systematic framework for deciding when to proceed. Here I suggest a “4-5 framework” for analyzing whether to proceed with human gene editing. To determine when gene editing is ethically justified, we need to consider: (1) safety, (2) significance of harm to be averted, (3) succeeding generations, and (4) social consequences.

Precedents for Editing the Human Genome

We have already begun to see the benefits of gene editing. Genome editing of crops provides opportunities to increase productivity by introducing traits such as disease resistance, drought tolerance, and nutrient-use efficiency. CRISPR/Cas9 has been used to improve climate-related agronomic traits, such as pathogen resistance in crops, and to create new varieties that are high yielding with high nutritional value [3]. Gene editing has produced pigs that are resistant to porcine reproductive and respiratory syndrome, one of the most significant diseases in this animal [4]. In addition to preventing disease, however, the technique is being used to introduce desirable genetic variations into livestock such as dairy cows without horns (relieving them of the pain associated with routine dehorning to prevent injuries) [5] or super dogs with double the normal muscle mass who are stronger runners and can be used for hunting or military applications [6]. Our experience with gene editing in plants and animals not only to prevent disease but

also to enhance traits might persuade some that the technology would be safe in human beings and that it is ethically justified to use gene editing to both prevent disease in and enhance human beings.

Engineering the human genome for purposes of human enhancement, however, is ethically contentious. The ease with which the technology can be employed and its use in human embryos has stirred wide debate and concern that it will be used to create designer babies [7]. While genome editing has the potential to obliterate serious life-limiting diseases, it can also potentially be used to improve human characteristics such as intelligence and appearance. Whether such power is used to shape humanity for good or bad, what impact gene editing to enhance humanity will have on our understanding of what is normal, and whether we will create a segment of society that is genetically superior are open questions that should give us pause.

The 4-S Framework

The potential use of gene editing to enhance our ability to thrive in a changing climate requires consideration of what I refer to as the 4-S framework for analyzing whether to proceed with gene editing: (1) safety, (2) significance of harm to be averted, (3) succeeding generations, and (4) social consequences.

Safety. The safety of gene editing is a foundational factor in the assessment of whether to proceed with CRISPR/Cas9 in human beings. The challenge is that the technique's safety ultimately needs to be assessed through evaluation of the resulting product, not the process itself. While CRISPR/Cas9 is elegant in its simplicity, efficiency, and high specificity, there is the risk of off-target cleavage in gene edits. Preliminary studies suggest that the incidence of off-target mutations is low [8], but further research is needed to characterize this risk and ensure that the benefits of gene editing outweigh the consequences of off-target mutations. Even if the incidence of off-target mutations is very low, it will be difficult to predict all of the salient consequences of editing the human genome. For example, a gene may be associated with a serious illness but also confer some advantages in terms of preventing disease. Gene editing may therefore result in our trading one known disease for another unknown disease. Establishing the safety of gene editing in animals is a first step toward greater confidence that the benefits are likely to outweigh the risks of the technique in human beings. Much animal research has the goal of providing insights that are useful for understanding human biology and the response of human beings to particular interventions. While cross-species translation has limitations, it can also provide us with valuable information on the technical possibilities and potential complications of interventions [9].

Significance of harm. The significance of the harm to be averted by gene editing should help guide our assessment of the technique's risks and benefits. Rarely is an intervention completely safe, so our threshold for embracing a novel technique is dependent on

whether the potential benefits outweigh the risks. To make this assessment with regard to enhancing our ability to adapt to new environmental conditions, we would need to understand the consequences of being maladapted to a changing climate. If the health effects of climate change are significant in terms of morbidity and mortality and cannot be adequately addressed through other medical and public health interventions, then we should have a lower threshold for using gene editing than we would to ameliorate a mild illness. The significance of medical need should guide our decision making.

A recent UN report highlights the rising [impact of climate change](#) on human health [10]. The effects of climate change will be increasingly prevalent, and we are likely to see direct effects on health resulting from heat-related mortality and increased disease transmission, particularly from the spread of infectious diseases that are sensitive to climate. We will also see indirect effects of climate change resulting from its impact on food production, which might cause malnutrition and the inability of people to work in extreme weather conditions. Efforts are underway to explore mechanisms for adapting to climate change [11]. We should embark on interventions that are effective but pose the lowest risk to humanity. Given the uncertain consequences of gene editing to improve our ability to thrive in a changing climate, it is prudent to pursue this option only when the consequences of not intervening with gene editing are significant and after other options have been tried and failed.

Some might argue that using gene editing to improve our ability to adapt to climate change is a form of [enhancement](#) and, like any genetic enhancement, is therefore ethically unjustified [12]. Underlying this argument are concerns about eugenics, playing God, a slippery slope toward designer babies, opposition to the desire for genetic perfectionism, and an extreme emphasis on individual autonomy. Enhancement per se, however, is not ethically unjustified. In fact, in some cases it is not only ethically permissible, but morally required. For example, vaccines are enhancements that our society has mandated. What matters is why we are trying to enhance a person, who is deciding to proceed with enhancement (i.e., the government, the individual who would be the subject of enhancement, or another person, such as a parent on behalf of a child), and what are the associated risks. Caffeine, braces, LASIK eye surgery, as well as vaccines, are all forms of "enhancement" that in some cases can have effects on a cellular level and that most of our society has accepted as ethically permissible. Claiming that gene editing to improve our ability to adapt to climate change is a form of enhancement and therefore ethically unjustified is not a compelling argument. While it might not be medically necessary right now to edit the human genome to improve our ability to thrive in a changing climate (and we should refrain from proceeding until it is medically necessary), there may be a pressing need to do so for some segment of our population in future decades. It would therefore make more sense for us to consider whether gene editing is intended to significantly improve human health or not and

whether the benefits outweigh the risks overall, as opposed to whether it is considered “enhancement.”

Succeeding generations. We are on the threshold of overcoming the safety concerns raised by gene editing, and there are surely clinical situations in which the benefits would outweigh the uncertain risks. Nevertheless, many may have a lingering apprehension about the use of gene editing. Underlying this uneasiness is, I think, a worry about the unknown consequences not only for the individual subject of gene editing but also for succeeding generations. The distinction between editing the human germline (the effects of which are passed onto future generations) and editing somatic cells (the effects of which are limited to individual patients and not inherited by their offspring) is important. Because the former has implications for succeeding generations is not sufficient reason to claim that under no circumstances would editing the human germline be permissible. Why should we not want to alleviate the burden of life-threatening illnesses in future generations? In some cases, the severity of an illness may justify eradicating it from future generations. For example, there are likely women who carry a mutation associated with Huntington’s disease who would, reasonably, embrace opportunities to safely prevent their future generations from having the mutation. Tampering with our genes is complex, and we might not be aware of advantages conferred by a gene that we are cleaving. As a safeguard, human germline editing should be first explored in animal models and used only when there is no other way to prevent a devastating genetic disease in the offspring.

Social consequences. In addition to considering safety, significance of medical need, and succeeding generations, we should also consider the social consequences of gene editing. As we begin to employ a new technology that confers benefits to individuals, we need to be mindful of how we can ensure a just distribution of this resource. Concerns for fairness necessitate that gene editing is available not only to those who have the ability to pay but also to all of those who are in need and would benefit from the intervention. If genes that directly influence our ability to thrive in a changing climate could be identified and edited, we would want to ensure that those individuals—including children—and communities who are most susceptible to the harmful consequences of climate change have access to this intervention.

Conclusion

Gene editing has unprecedented potential to improve human health. CRISPR/Cas9 has a specificity and simplicity that opens up wide possibilities. If we are unable to prevent serious negative health consequences of climate change through environmental and public health measures, gene editing could have a role in helping human beings adapt to new environmental conditions. Any decision to proceed should apply the 4-S framework. The outcome of gene editing must on balance be safe; the technique should only be used when there is significant medical need; the impact on succeeding generations should be

considered; and concerns about a fair distribution of benefits should be addressed. By applying this framework and developing a national and international regulatory oversight process for gene editing, we will be able to realize the potential of this disruptive innovation for improving human health.

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