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RESEARCH ARTICLE

A case for the moral duty of specific human germline genetic engineering

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Abstract
Germline gene editing (GGE) is a controversial procedure, prohibited by most intergovernmental and scientific bodies and is not currently medically utilized. However, given circumstances where GGE would be essential for human survival, it is possible that GGE could be ideal, ethical and even necessary. One such possible instance of this circumstance could be long-term presence of humans on other planets. In our paper, we point out that there is a strong case for genetically modifying humans, including through GGE, for a future settlement in space directed at preserving human (and other) species. To avoid unnecessarily suffering and death from such difficult missions and environments, GGE enhancements should be considered, although only if shown to be safe, well-regulated and efficacious. We also examine and detail how major ethical frameworks can be shown to support, rather than prohibit, such procedures.

Contents

One key purpose for long-term space missions is to enable a human presence on other planets and to increase the chance of Earth's life to survive – for both human and non-human species alike. We omit here other types of justifications and motivations for space missions that are focused on the shorter term and are more commercial, political and/or scientific in nature. For the purposes of this paper, we focus exclusively on this one type of mission, assuming that it is an inevitable requirement of human survival and the culmination of our technological development. Yet, one of the many complexities of this plan is assuming that life, which specifically evolved under Earth's conditions, will be able to not only live, but even thrive in completely new and hostile conditions that it has previously never encountered.

Fortunately, modern tools in genetics enable us to identify and address molecular limitations that may otherwise act as barriers to live, adapt and prosper in different environments, including means to repair or modify genes and even to deploy adaptive lessons from extremophiles. For currently known planets amenable for human exploration, including Mars, survival may require the application of genetic engineering to pre-select for evolutionary traits specific to these new environments. While somatic cell gene editing (SGE) is already being widely deployed for a range of hematological diseases (Frangoul *et al*., 2021) and cancer therapies, (MacKay *et al*., 2020) the easy access to large clinical infrastructures and resources needed for continual somatic editing will not likely be available for long-term human missions, or may be limited. Thus, germline gene editing (GGE) may need to be considered as an option to decrease both mission and long-term risks so humans can become a stable, multiplanetary species. Such GGE usage would enable more tractable survival for each additional generations at a location with either scarce physical and medical recourses (including lack of SGE), with the same, or better, safety profile as the previous generation. Despite the current ethical controversy surrounding GGE (van Dijke *et al*., 2021) and embryo selection (Rutherford, 2021) we argue that GGE in the context of spaceflight, primarily multigenerational missions in locations with scarce resources, high physical risks, or the inability to conduct SGE, may be our moral obligation.

One such use case of this genetic pre-planning for future worlds would be similar to 'speeding up' evolution, such that a genotype, or at least a phenotype, which may be selected for over multiple generations in a given location could instead be actualized within a specific individual before they arrive at the destination. This would enable survival without the need to lose multiple generations of time through natural selection. Ethically, creating these modifications may actually be required of us one day, just as using genetic tools for conservation and cloning of species can be the only means of their survival. As a special case study, researching how extremophiles have acquired molecular adaptations to their hostile environments could elucidate adaptations that could be applied to other organisms. Specifically, the protein Dsup, found in the extremotolerant tardigrades, shields their genome from harmful radiation, effectively making them radiotolerant. It has further been shown that simply expressing this protein within human cells can improve their resistance to radiation, (Hashimoto *et al*., 2016; Westover *et al*., 2020) one of the main hazards of spaceflight.

Since harsh environments may create situations of lethal risk, it may be required to genetically modify a human's genome to improve their chance of survival or enable any survival which underscores the framework of a genetic duty. This decision is thus a duty-based bioethical concept that is originated from having knowledge *that* you should do something, or *that* something will occur, while also knowing *how* to address or prevent it. Further, having knowledge that something should be done while also knowing how you can address it, is the source of the principle of accountability. Having knowledge comes with many responsibilities, and responsibilities then lead to duties. Given that we know that *all* of Earth's life will eventually go extinct if it only stays on Earth, due to the finite life of the sun and its eventually charring of the Earth in a few billion years, we have a responsibility and duty to act on this knowledge. Fortunately, we are beginning to know *how* we can improve the survival of life in these new environments. It is therefore our duty to solve for what genetic or other modifications may be needed to improve survival, how to implement them, when and for which planets.

Virtually all major ethical normative systems support the concept of human genetic modification to improve the chance of survival, derived from knowing *that* and knowing *how*. This is justified by the aforementioned deontological ethics, one of the most important concepts in normative ethics, which points to duties such as the duty to protect and preserve life or, more broadly, to care for life as a categorical imperative. In the least, it points to the duty to avoid killing. There is a well-known debate in bioethics about the difference (or lack thereof) between killing and allowing to die (action versus omission). (McGee, 2015) If we assume that knowledge comes with duties and responsibilities, then a person is at least partially responsible for the results which come from their failure to act in accordance with their knowledge, whether that result is the death of an individual or even the future extinction of a species or all of life.

Another major group of theories of normative ethics are consequence-maximizing ethical approaches, which also support the possible usage of GGE, as it is consistent with both beneficence

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and non-maleficence principles (insofar as the effects of genetic modification do not reduce the quality of life of the modified generations). However, the difference in the quality of life within this concept needs to be assessed by comparing the expected or probable quality of life of the genetically modified generation compared to what they would experience without modification. Of course, these considerations must be accounted for, as best as possible, before any type of therapy, including both SGE and GGE, is used. Further, defining the quality of one's life is highly personal. Some may see death, with the quality of life equal to zero ($q = 0$, where q is quality of life), as a better option than continued pain and medication side-effects (their self-proclaimed quality of life being negative till the day they die); while others with the same condition, and same medication side-effects, may think of death as the quality of life equal to negative infinity ($q = -\infty$), and any life – regardless of the amount of suffering – would therefore have a greater quality of life than death, itself. Further, how does suffering of an individual, or even a single generation, extrapolate to the ethical continuation of further life – which has the potential to thrive, love and exist with a positive quality of life after the suffering of the previous generation? (Kovic, 2021) This question, by its very nature, requires an inter-generational framework for resolution. Namely, the first non-existent generation, which does not get the chance to live, could also never experience or even imagine their quality of life (cf. the critique of the 'interest in existing argument'). (Cohen, 1996) However, with adequate knowledge, studying the pleiotropic effects of potential modifications, the gradual inclusion of additional alterations and importantly retaining the ability to always revert a change – ie, *in vivo* genetic engineering to change an alteration back to wild-type, we can guarantee both an adequate quality of life, which should be superior to the generation's quality of life without genetic engineering, and meet the criteria of intergenerational justice for future people.

Finally, the third major normative concept in ethics, virtue ethics, also justifies the possibility of GGE. According to virtue ethics, the criterion for the morality of an act is how a person that is considered to be virtuous would behave. What would a virtuous person do, if they poses the capability to improve the lives of a generation and their future generations, or even guarantee the survival of an endangered species? Would they use this knowledge and ability to save the survival of the species, or would they oppose the application of such knowledge? First, we can imagine a situation in which the person recommending genetic modification is himself subjected to it and thus acquires a greater moral right to recommend and apply it. The application of such knowledge, such that we minimize risk and maximize utility, is important. Just as no medication is given to the general public before gradual, and then extensive, clinical trials, so too would such genetic modifications be tested in a step-wise, and multi-generational, setting. Further, any genetic modification should have the ability to be reversible, such that the given loci could be switched back to wild type or alternative allele, or in the least engineering the gametes themselves, essentially reverting back to previous 'versions' of genomic builds. The modification, and its advantages, would likely also define who, if anyone, may be required to have them. As an example, if a modification only helps cosmetically the individual, and poses neither a risk nor benefit to others, perhaps it should not be required for a mission. However, if having a specific genetic modification decreases risk to others in the society or ship – similar to choosing to be vaccinated to reach herd immunity– then it may be a requirement to join the mission. The decision to refrain from acting to save a life, or even simply improve someone's quality of life, would not be considered to be a virtuous action, nor is it the action of a person worthy of being called virtuous.

Given the above evidence, major normative ethics appealing to duty, consequence or virtue should support human genetic modification for human survival. In our example, we discuss the application of the concept of genetic duty to a specific case, the survival of the human species during space settlement. This is a situation in which the goal of genetic modification is to stay alive and prepare in new extremes – assuming this is the only, or at least the best, alternative – and the effect of the modification will be to increase the quality of life for the modified generations relative to their quality of life if un-modified. However, this does not mean that these ethical systems must support the concept of genetic duty for more trivial purposes, whether on Earth or in relation to space exploration. It may be that the concept of genetic duty is a type of bioethical specification applicable only to a specific type of scenario, such as requiring germline editing for dangerous missions to settle new worlds and decrease the chance of extinction, but it might not be applicable to force alterations for missions of pleasure or leisure.

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Despite the fact that a mission focused on the survival of the species provides the strongest ethical justification for GGE, it would be paradoxical to expose non-genetically modified astronauts to health problems or even death simply because the mission's main objective is not to decrease the chance of extinction. Further, it is difficult to estimate the extent to which a given mission, even if there is no scientific motive, may contribute to preparing humanity for space exploration. Thus, we emphasize that there are strong reasons to recognize the bioethics of future long-term space missions as potentially exclusivist. As such, it may be seen similarly to military ethics, which treats autonomy and the concept of informed consent in a more limited way (Erler and Müller, 2021), serves specific purposes and operates in a special context. Nevertheless, an outright ban on genetic modification, even germline, is not the correct option, and should instead be handled in a case-by-case, or even mission-by-mission, bioethical manner.

Finally, it is useful to refer to the distinction between therapies and modifications for the sake of modifications (so-called human enhancements), devoid of therapeutic rational. This distinction has its advantages in classifying the reason for the genetic intervention, but it also introduces potential limitations that can impede progress when used to define what should and should not be allowed on new planets or space environments. As an example, the classification of 'enhancement' may lead to a situation in which the absence of an existing disease precludes the use of the genetic modification, even when it does not harm the modified individual (such as SGE to increase muscle strength and performance for competitive sports or military purposes). Instead of trying to relate a modification to a specific disease, the definition of which may change over time, it is more useful for us to talk about liberating ourselves from self-imposed limitations, opening greater genomic liberty. Further, there is no reason for us to treat our genetic landscape as some kind of magical, unmovable barrier – evolution has not, and neither should we, especially if our survival (and all of life's survival) depends upon it.

The concept of genetic duty, deontogenics (Mason, 2021), also justifies the moral legitimacy of human genetic modification for the survival of not only the human species, but all of Earth's life. This moral imperative is further reinforced by the fact that humans are the only (known) species aware of (1) the inevitable end of our planet (either by the death of the Sun, meteors or life itself), and (2) capable of prolonging the existence of life by travelling to additional locations beyond Earth.

Despite our position expressing utility of GGE for future space exploration, we would like to point out how the GGE application policy may vary according to different types of missions. We point to such missions as interplanetary space travel, a planet or moon with altered gravity, and even farther travel. In the last two sections, we will also address criticisms of the GGE concept, as well as space exploration, formulated from the perspective of feminist philosophy, as well as from the point of view of conservative bioethics.

Interplanetary space travel

The most obvious and proximal location for interplanetary travel is Mars. A flight to Mars lasting 6–7 months will take place in microgravity and lead to increased exposure to cosmic radiation. The mere fact of being in microgravity conditions for several months is not a new challenge for humans, as both astronauts and cosmonauts have been continuously in the International Space Station (>1 year) for longer than the anticipated flight to Mars. Rather, a greater challenge will be to protect against exposure to cosmic radiation and stress on the body, which is stronger in interplanetary space. Modifications that can reduce stress and other potential mental and behavioural risks may also be recommended.

Assuming that GGE can affect these functions and increase our adaptation to the aforementioned risk factors, the difficulties identified are rather logistical and political in nature. After all, a decision would have to be made as to which future individuals, not yet born, would undergo GGE in order to take part in interplanetary travel a few decades later, after reaching adulthood and receiving appropriate training. But for such a selection to be possible, it would have to be made decades before the first interplanetary flight, for which it will be determined that GGE of its future participants is necessary. Such a space policy requires synchronization of the candidate selection programme with work on space medicine using GGE, as well as with advances in space technology. Thus, if we assume that the first humans will be able to take a flight to Mars in, for example, thirty years, it would be appropriate to select candidates for this flight now, making a decision together with the parents of future humans to subject them to appropriate germline modifications. However, this is impossible for several reasons. First, the use of GGE is unacceptable today. Second, there are no mechanisms, either legal or ethical, that allow for this type of selection of future humans. Also, inter-generational tracking of clinical dynamics is rare and not yet broadly established, save for rare examples like the Farmingham heart study and the Cornell Aerospace Medicine Biobank (CAMbank). (Overbey *et al*., 2024) Therefore, the use of GGEs for interplanetary travel may be a solution that will be introduced only after such missions are in place. It will also require significant changes in the conditions of our life on Earth, perhaps also significant changes in policy and ethics to justify selecting candidates among yet unborn humans.

A planet or moon with altered gravity

If we stay with the Mars example, allowing or even recommending GGE will struggle with the same problems that will arise when applying GGE for interplanetary travel. However, the subject of discussion and controversy will no longer be the protection of the crew during the flight itself, but also the justification and desirability of a mission to another planet. If the GGE requires the selection of future humans who do not exist at the time of selection, a strong justification will be required for the postulate of determining the lives of future humans in such a way that they will be forced to leave Earth – for a certain period of time, or perhaps forever. Leaving aside the controversial nature of such an idea, a rethink will be required of our philosophy of space exploration with regard to what goals and expectations we have for space exploration and exploitation. It will also be important to consider whether a particular type of GGE will cause the type of changes that would make it impossible for a participant in a future mission to Mars to readapt to Earth conditions. What space policy will be for future humans selected for a GGE is also important. Will they be forced to take part in such a mission, or will they be left with a choice? In this context, reversible genetic alterations would ensure the greatest degree of cellular, physical and planetary liberty.

Interstellar travel

In light of the logistical, political and ethical controversies outlined above, the type of space mission least devoid of these problems is interstellar travel. The idea of such voyages presupposes a multi-generational stay on a spacecraft, which justifies the use of all possible types of GGE designed to adapt future humans to such specific conditions. It seems reasonable to assume that the conditions of life on Earth will force those with such capabilities to take advantage of interstellar travel. Thus, a special justification will become the desire to save at least part of the human species, given the current trajectory of the sun's demise, or a more urgent one that may emerge (e.g. climate catastrophere or asteroid collision). An additional argument in favour of the use of GGE will also be the desire to minimize evolutionary changes that could lead to the evolution of significant differences between the population of such a multi-generational spacecraft and the population remaining on Earth. GGE may therefore be a mechanism that will offset evolutionary changes. What is not clear, however, is whether humans remaining on Earth should care about stopping the evolutionary changes of participants in such interstellar travel.

Feminist critique of GGE and space exploration

The perspective we have presented corresponds to the traditional way of thinking about human beings and bioethical problems, which is abstract in nature. This is because such paradigms do not normally pay attention to the dynamics shaped by gender, race, ethnicity or degree of disability. Therefore, it is worth paying attention to the perspective inherent in feminism, which exposes and criticizes inequalities in power structures. With regard to the selection of future candidates of space missions to require GGE, the question arises about the selection criteria for such candidates. Will they be privileged or rather vulnerable and exploited? With regard to the purpose and justification for a space mission requiring a GGE, feminism raises the question of the legitimacy of such a mission and who will get the benefits from it. An analogous problem arises with regard to GGE for interstellar travel. While in the previous two cases, it is not clear whether participation in an interplanetary flight and a mission to another planet or moon always means a change for the better for their participants, it seems that interstellar flights will always mean a change for the better. The risk in selecting future humans, therefore, will not be the possibility of exploitation and sending them on dangerous missions, but the exclusion of those who do not have the necessary power and privileged position. An example of the potential risk of exploitation could be the situation of workers in the space sector, such as space mining. As Erika Nesvold notes, workers in space will be vulnerable to exploitation in a special way, due to the difficulty or impossibility of migrating, escaping, returning to Earth. (Nesvold, 2023) GGE can therefore be a specific tool for the exploitation of future workers, and should be safeguarded against, along with the medical risk, to ensure ideal utilization of these technologies for human spaceflight and survival.

It is difficult to ignore the feminist critique of capitalism inherent in Marxist and socialist feminism in particular. Drawing attention to the dangers of exploiting both people and the environment, as well as the pursuit of continuous capital accumulation, is a significant contribution to feminist reflection and can be taken into account. (Federici, 2003; Fraser, 2022) However, it is worth noting a few points that remain debatable. First, even if feminism is right about the fact that the GGE will function as a tool for the exploitation of workers from the space, then anything that serves to prepare us for the labour market should have the same status. In a sense, everything, including the entire education system, is subject to this as long as we are workers for wages. In this light, the feminist argument from the critique of the risk of exploitation does not expose anything new or unique inherent only in the GGE but is a total critique of the functioning of capitalism. Besides, not only capitalism, because the idea of applying GGE can also be considered outside the framework of capitalism. Moreover, applications of GGE would not necessarily be less exploitative in a socialistic or communist framework, since their use may be driven more by the political dynamics of the time rather than long-term ethical frameworks.

Secondly, it is worth emphasizing that it is still unclear what purpose long-term space missions will have to which GGE could be applied. Commercial purposes may be just one of many other goals, to accompany the scientific purpose. The commercial perspective should not be ignored, since Earth science pursues both goals in parallel, the commercial one precisely and the purely scientific one, aimed at learning the truth and explaining space-related phenomena.

Third and finally, we take the position that the human presence in space is something desirable in a global and universal sense, with many positive consequences that today may not even be perceived or realized. GGE may be necessary for safe and effective human life in space. The indirect effect of our long-term presence in space will be the establishment of permanent settlements to expand, protect and understand life itself. Thus, any action for our presence in space, including genetic modification, should be seen as another essential element in the path of ensuring our ability to live in space.

Bioconservative criticism of the GGE

The bioconservative critique of GGE is based upon a reticence for deploying new technologies to life or ecosystems. The criticism has and continues to apply to new inventions both non-biomedical, such as the Internet, and biomedical. In the latter case, organ transplants or assisted reproductive technologies have been, and sometimes still are, criticized. Since we have subjected the arguments opposing the GGE of bioconservative bioethics to criticism many times elsewhere, (Mason, 2021; Szocik, 2023a, 2023b) we will limit ourselves to demonstrating the issues of the main objections raised by bioconservatives.

One of the arguments against GGE is the argument from so-called human nature, which opposes deliberate interference in changing it, as well as pointing to the need to care for its integrity. 'Human nature' is merely a metaphysical concept, suggesting essentialist thinking about human beings. However, it is difficult to see what would be included in such a 'human nature' and how it would remain unchanged, and is also not supported by current understandings of genetics or organisms, all of which continuously adapt to selective pressures. We therefore reject this metaphysical concept. On the other

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hand, having in mind a set of certain characteristics that can be considered characteristic of human beings, we point out that we are subject to constant change on the path of both biological and cultural evolution.

Another argument is to point to the threat to an open future and the autonomy of the future individual, who would be deprived of these opportunities if subjected to GGE. The very idea of an open future is paradoxical if one pays attention to the number of factors determining us, affecting our development. Environmental influence, socialization especially, is fundamental. In this context, the GGE does not seem to significantly limit the open future of a modified individual, and it could even enable more possibilities. Nor is it clear what the future of the individual would have been without being subjected to GGE. Above all, however, in favour of rejecting this argument is the fact that GGE will be applied only for morally legitimate purposes, motivated by the protection of health and life. In this context, it is difficult to consider the application of GGE as an action that will worsen the status of the individual and 'close' her future.

The argument from the open future, on the other hand, could take on particular significance in the context of space settlement if GGE were applied on Earth with the idea of allowing modified individuals to participate in long-term space missions. If we imagine that there are types of GGE that are either attractive or required for participation in long-term space missions, but would make it impossible or difficult for such an entity to remain on Earth, then the argument from the open future would take on special significance. This is because it would imply a situation in which an entity, subjected to a GGE modification on Earth, is in a sense forced to leave Earth in the future due to the 'closure' of its future caused by the GGE. However, this is a peculiar situation, the moral status of which is unequivocally negative, and is actually more of a legal problem than a moral one. However, it is possible to reverse this argument from an open future and point to a scenario in which an individual's failure to undergo a GGE on Earth leads to the 'closure' of her future in space, or inability to visit other planets, and thus would be a loss of liberty. This would occur in a situation where an individual would like to participate in long-term space missions where a GGE is required, but due to her parents' pursuit of the argument from the open future, she was not subjected to a GGE.

The arguments of bioconservative bioethics against GGE tend to be metaphysical and ontological in nature and ignore many other deterministic factors, focusing instead on the potentially bad effects of GGE. In our view, metaphysical and ontological criticisms of GGE are not justified and cause unnecessary opposition to GGE by associating GGE with something morally wrong, an attack or threat to 'human nature', or even something that is not worthy of human beings. Critical arguments should be purely medical and focus on safety and risk. The bioconservative critique is part of a broader trend of opposition to new technologies, especially biomedical ones, resulting in delays in the application of life-saving or life-enhancing solutions. It is worth noting that the actual arguments against the use of GGE are of a practical, technical and logistical nature rather than a moral one.

Of a more practical nature are feminist arguments, which suggest that the use of GGE may reinforce the marginalization and exclusion of groups already marked by marginalization and stigma, particularly women, as well as LGBTIQA people, or people with disabilities. There is no doubt that marginalization and, on the other hand, the risk of stigmatization and exploitation of these groups can happen when GGE is applied. Already on Earth today, prenatal testing, *in vitro* fertilization, and embryo selection target people with disabilities and lead to their *de facto* negative selection through the fact that these characteristics are eliminated even at the embryonic stage. We agree that according to the logic of GGE, disabilities, but also any other traits defined as negative or undesirable, can be subject to selection and elimination. However, it does not appear that the space environment magnifies the problematic nature of this phenomenon to a greater extent than its problematic nature on Earth. We believe that perhaps GGE for space missions would gain additional justification from environmental considerations in space, where the need to adapt humans to harsh conditions not found on Earth would justify the need for GGE. Such a necessity may be lacking in many cases where GGE is discussed only in relation to the Earth context.

Conclusions

The purpose of our paper is to show that we have a moral obligation to develop research and work on the actual application of GGE for humans. We propose to limit the application of GGE to the context of our future in space, the end goal of which will be our permanent presence. With such a long-term goal in mind, we should use our knowledge and science to develop GGE so that it is safe and effective. Science is never neutral. (Lekka-Kowalik, 2010) Therefore, we should consciously direct research and scientific activities towards its positive applications for humanity. We do not resolve whether our arguments are applicable only to the cosmic environment and do not carry over to an exclusively terrestrial context. We stand in a position that rejects moral exceptionalism, which assumes that different moral rules may apply in different environments. Nevertheless, given the controversial nature of the GGE, we show that future space exploration provides special justification and reinforcement for the GGE even if the GGE is itself uncontroversial (except for feminist arguments, which, however, apply to many other procedures, which does not make the GGE the only procedure that leads to discrimination and marginalization of certain groups), and the objections of bioconservative bioethics are misplaced and merely metaphysical in nature.

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