Faraday Papers

Ethical Issues in Human Genetic Engineering

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Summary

The ability to edit DNA offers the possibility of curing genetic diseases and preventing their transmission to future generations. This seems like an exciting prospect, but raises questions about what is natural, what it means to be human, and how we respond to those who have disabilities. Is this a form of embryo healing, remembering that healing, restoration and caring for the disadvantaged have always been a part of Christian action? Is it part of the God-given arsenal of techniques for alleviating human suffering or is it 'playing God' or the 'slippery slope' to human enhancement and the generation of 'designer babies'?

Introduction

The CRISPR-Cas technology for genome modification, for which its discoverers received the Nobel Prize for Chemistry in 2020,[1] has been described as a scientific discovery with an impact on society that 'is likely to be so immense that even an abundance of superlatives may not do it full justice'.[2] This versatile technology provides a means for precisely modifying (editing) an organism's DNA to correct errors and optimise or enhance genetic functions. CRISPR-Cas9 is simple to use, easily adapted and cheap, and is being used in many laboratories as a research tool for studying cellular function. It has already been used for altering plant and animal DNA, in which it raises many of the ethical questions about genetic modification that have been posed for several decades.[3] However, unlike GM it need not involve the addition of DNA from another organism, but can be used to 'optimise' the combination of genes that are naturally found within a particular species. This paper will focus on its potential for modifying human DNA to correct inherited genetic conditions or to generate offspring that are endowed with the best combination of genes ('designer babies').

Several thousand heritable genetic conditions are known which originate from small changes in DNA sequence, that are sometimes only one letter variations within the three billion letters in the human genome. Examples include sickle cell disease, thalassaemia, cystic fibrosis and haemophilia. Replacing these 'defective' genes with the functional version seems like an appealing method for treating disease and alleviating suffering. It is being tested for treating children or adults (somatic cell editing), though this is a very inefficient process as there are several trillion cells in a fully formed human body, each of which will contain the same DNA error that needs to be corrected. Nonetheless, in some instances, correcting the error in a few cells is sufficient to overcome the symptoms of the disease, especially for specialised cell types such as diseases of the blood.[4] A spectacular example of its success is in personalized cancer treatment which uses the CAR-T method to remove a patient's blood, modify the DNA and return the edited cells to the patient, with some remarkable examples of remission.[5] Its use for treating individuals is not without some ethical questions, which are similar to those posed by other forms of gene therapy, in which the correct version of the gene is directly introduced, often within a harmless virus. These include questions

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1 The Nobel Prize in Chemistry 2020 https://www.nobelprize.org/prizes/chemistry/2020/press-release/;
Jennifer Doudna and Samuel Sternberg, (2018) *A Crack in Creation: The New Power to Control Evolution,* Vintage Books

2 Parrington, J., (2000) *Redesigning Life* Oxford University Press

3 Bryant, J., (2007) Faraday Paper No 7: *Ethical Issues in Genetic Modification*

4 CRISPR Clinical Trials: A 2022 Update https://www.newswise.com/articles/crispr-clinical-trials-a-2022-update

5 'Designer cells' reverse one-year-old's cancer https://www.bbc.co.uk/news/health-34731498

of risk and patient safety, distinguishing between therapy and enhancement, and ensuring that there is fair access to treatment. However, far more serious issues arise from the potential to modify human embryos or germ cells, to produce offspring in which all the cells in the developing organism will be modified/corrected, with effects that persist into subsequent generations. The ethical issues raised were quickly realised by the scientific and ethical communities across the world, who proposed a moratorium on its use for generating embryos that could lead to pregnancies.[6] Early laboratory experiments demonstrating successful gene correction were therefore only performed with embryos that were non-viable.[7] There was then widespread condemnation when, in November 2018, Dr Jiankui He from the Southern University of Science and Technology in Shenzhen, China, announced the birth of two girls that had been modified as embryos, permanently disabling their CCR5 gene, thereby making them resistant to HIV infection. The widespread criticisms of this experiment centred around aspects of risk, that the modification was unnecessary, that it did not meet a medical need, and that there had not been proper informed parental consent or compliance with the local ethical procedures. These and other ethical issues will be considered in this paper, adding questions of what it means to be human, and asking whether we are 'playing God' and venturing into areas where humans should not go.

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Risk

The most common concern from within the scientific community is one of risk. Although the CRISPR technique is remarkably accurate, there is always the possibility that it will also randomly alter other sections of DNA, producing undesirable off-target effects. Laboratory studies have given different answers to the extent of these 'off-target' effects, some of which are not inconsiderable. There may also be other unintended genetic consequences, as genes do not work in isolation, but function in complex genetic networks to produce diverse physiological effects; pulling the net in one place could have unintended consequences on other interacting genes. However, the technology is continually improving. If we come to the point where the risks are no greater than those involved in natural conception, then would that put an end to all criticisms? Is risk the only factor that poses ethical dilemmas?

Determinism and DNA

Despite its fundamental importance for life, DNA is not a blueprint. It contains the information needed to produce proteins and to regulate their production, but genes function as parts of complex systems. They do very little by themselves, and traits emerge from the interactions between genes and developmental and environmental factors.[8] There is no simple deterministic relationship between genes and physiology and other factors play important roles that affect when and where each gene is active. The emerging area of epigenetics shows that many external factors affect which genes are switched on or off. We should therefore be careful to avoid genetic determinism, which sees genes as pulling all the strings in our lives. Genes are very important, and technical and moral questions surrounding genome editing need to be discussed carefully. Yet we are much more than the sum of our genes, and it takes much more than genes to make a human person.

Is it necessary?

Of course, people who are opposed to all forms of embryo manipulation, including in vitro fertilisation (IVF), will inevitably be against genome editing. Any modified embryos will need to be screened by pre-implantation genetic testing (PGT) at the 8-cell stage, to determine which ones have been successfully modified. This process will inevitably involve decisions on what to do with embryos that have been incorrectly modified or for which modification has been unsuccessful. PGT is already practised using IVF to test for embryos with some known genetic risks, and there are very few single gene diseases for which healthy embryos, lacking the faulty gene, cannot already be screened and selected by PGT. There might be a few rare scenarios in which there are no unaffected embryos, if one parent is homozygous for a faulty gene for a dominant disease, or if both parents are homozygous for a recessive genetic disease. As Francis Collins has written 'Advances in technology have given us an elegant new way of carrying out genome editing, but the strong arguments against engaging in this activity remain. These include the serious and unquantifiable safety issues, ethical issues presented by altering the germline in a way that affects the next generation without their consent and a current lack of compelling medical applications'.[9]

Ethical Issues

Putting aside the question of embryo research itself, and the issues of risk, what are the other ethical issues that are raised by genome editing of embryos? If done legitimately, would it be ethically permissible to use it to correct a devastating

6 Lanphier, E. et al., (2015) Don't edit the human germ line. *Nature* 519, 410-411;
Lander, E et al., (2019) Adopt a moratorium on heritable genome editing *Nature* 567, 165;
CEC Bioethics Thematic Reference Group, (2019) Moral and Ethical Issues in Human Genome Editing: A Statement of the CEC Bioethics Thematic Reference Group.

7 Liang, P. et al., (2015) 'CRISPR-Cas9-mediated gene editing in human tripronuclear zygotes', *Protein Cell,* 6: 363–72;
Ma, H et al., (2017) 'Correction of a pathogenic gene mutation in human embryos', *Nature,* 548: 413–19.

8 Alexander D.R., (2020) *Are We Slaves to Our Genes?* Cambridge University Press.

9 'Statement on NIH funding of research using gene-editing technologies in human embryos', https://www.nih.gov/about-nih/who-we-are/nih-director/statements/statement-nih-funding-research-using-gene-editing-technologies-human-embryos

genetic disease? Opinions are divided among Christians (of all theological persuasions).[10] Is this a form of embryo healing, remembering that healing, restoration and caring for the disadvantaged have always been a part of Christian action? Is it part of the God-given arsenal of techniques for alleviating human suffering? We have become familiar with organ transplants; is this merely a DNA transplant? Many think that it is not the same, but we need to be cautious about giving a negative response too quickly, conscious of Jesus' question to those who rigidly adhered to the letter of the law: "Is it lawful to do good or to do harm on the Sabbath, to save life or to kill?" (Mark 3:4)

Genome editing of embryos raises questions as to what conditions should be treated in this way: what is normal and what would be an enhancement of natural abilities? Would it be ethically permissible to modify the genome of an embryo:

- that will otherwise die? This would then be a means of giving life.
- that will survive, but with an unpleasant condition that may shorten life expectancy or alter quality of life, such as cystic fibrosis or sickle cell disease?
- that will be born healthy, but with an underlying disease that will develop much later in life (such as Huntington's, Alzheimer's, or risks of some forms of breast cancer).
- for cosmetic reasons, such as eye colour or height?

Most people would argue against the latter, but where should we draw the line in this sliding scale?

Human Dignity

It has been argued that modification of our genome would be an affront to our dignity, since the possession of a human genome is an essential human characteristic. The UNESCO declaration on the human genome states: 'The human genome underlies the fundamental unity of all members of the human family, as well as the recognition of their inherent dignity and diversity. In a symbolic sense, it is the heritage of humanity'.[11] Is the human genome therefore 'sacred' and untouchable? However, such ideas of preserving humanity's genetic heritage assume that there is such a thing as the human genome. Every person's genome is unique and is subtly different from anyone else's, varying at about one position in every thousand of the three billion letters of the human genome. Genetic variation is an example of our individual human uniqueness, and new genetic differences arise randomly in every generation. A child inherits a new, random combination of the parents' genes, as well as natural mutations at a rate of about 30 random changes per generation.

Disability

We also need to ask what this type of modification says to people who are genetically disabled? To quote Tom Shakespeare, a spokesperson for disabled rights, who has achondroplasia, "People with disabilities are, in my view, unlikely to be queuing up for genetic modification: their priority is to combat discrimination and prejudice."[12] He goes on, "To 'fix' a genetic variation that causes a rare disease may seem an obvious act of beneficence. But such intervention assumes that there is agreement about the boundary between normal variation and disability. Contrary to the prevailing assumption, most people with disabilities report a quality of life that is equivalent to that of non-disabled people, and the voices of people living with illness and impairment need to be heard". This is a rightfully influential perspective, though does not address those many tragic genetic diseases that lead to early childhood death, for which arguments in favour of gene editing seem more compelling.

Will genome modifications, especially genetic enhancements, reinforce an ableist mentality, which assumes that independence and physical functioning should be maximized?

What is natural?

But if we now focus on those genetic mutations that do not prevent development to teenage years and beyond, what then is normal, what is a disability, and what is enhanced ability? Is there a difference between a disability and an illness? There are many natural differences in physical abilities (such as muscle type and physical stature) which produce perfectly healthy people who are not in any way disabled. My limited athletic ability may sometimes be a frustration, but it is not a disability! Will genome modifications, especially genetic enhancements, reinforce an ableist mentality, which assumes that independence and physical functioning should be maximized?

For example, what about those who are born deaf? Some may argue that deafness isn't a disability, it's a way of life, with a different culture. In one instance, a deaf couple undergoing IVF asked for embryo selection for a deaf child.[13] The law refused permission for this selection. But what seems like disease and weakness to some can include significant strengths and opportunities for others. Through his thorn in the flesh, the apostle Paul learned that God's 'power is made perfect in weakness' (2 Corinthians 12:9). Nonetheless, Christians should not accept disease too lightly, with a misplaced fatalism that sees everything as God's will. On the other hand, an over-blown enthusiasm for genome editing runs the risk of avoiding the question of how society includes people whose impairment will not simply be edited away. Are we effectively saying to them, 'I wish that you hadn't been born'?

Some people argue that altering genes should be left to God or 'nature', and that natural processes are more reliable

10 Stammers, T., (2017), The Ethics of Gene Editing *Rendle Short Lecture* https://www.cmf.org.uk/resources/publications/content/?context=article&id=26706
Peters, T., (2017) Should CRISPR scientists play God? *Religions* 8, 61.

11 UNESCO's 1997 Universal Declaration on the Human Genome and Human Rights, https://en.unesco.org/themes/ethics-science-and-technology/human-genome-and-human-rights

12 Shakespeare, T., (2015) 'Gene editing: Heed disability views', *Nature*, 527 : 446.

13 'Is it wrong to select a deaf embryo?' http://news.bbc.co.uk/1/hi/health/7287508.stm

than any attempts at human editing. However, therapeutic genome editing would not necessarily introduce any new DNA sequence information into the human genome, but merely return a mutant form to what is found in the rest of the population. Many enhancements would not produce new gene variants but merely redistribute the existing naturally occurring variations. An edited individual would be provided with the version of a gene that is naturally present in other people with the desired attribute. This would only generate a new combination of genes that occur naturally in other people. Editing an embryo's genome to restore the healthy version of (say) the gene that, when mutated, causes cystic fibrosis, does not introduce any new variants into the human gene pool. This is healing, not enhancement.

Many people think negatively about enhancements because they perceive them as unnatural and wrong, as they attempt to improve on God's good creation. However, life today is already 'unnatural' compared to what it was like two thousand, five hundred or even one hundred years ago. Moreover, the biblical declaration that creation is 'good' does not imply perfection, or even any moral quality, but simply that it is fit for purpose. This does not mean that nature is idyllic or must remain as it is. Indeed, humans are told that there is work to be done and they are instructed to 'subdue the earth' (Gen. 1:28), to look after God's good creation. Nature as we find it is not sacrosanct, and human interventions are not out of bounds merely because they change something that has been arranged differently in God's creation. Of course, not every human intervention in nature is good, and many may turn out to be harmful. Yet we are not 'playing God' simply by modifying genes.

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Social pressures

There is a danger that non-therapeutic genetic enhancements might be used to reinforce social norms, pushing those who are less able, or who are less productive or who are perceived to be unattractive, to the margins of society. Would people with minor, unusual characteristics find themselves labelled as ill rather than different if genetic enhancement became the norm? Where does regular variation and diversity end and debilitating disease begin? Consider the genetic condition achondroplasia, which results in stunted growth. This does not necessarily cause pain or limit life. Should we not regard this as one variation within the diversity of human body shapes? It is therefore possible that gene-editing technologies may lead to further discrimination and social exclusion. We should be careful to ensure that these do not reinforce social prejudices. This is already seen in the use of cosmetic surgery, where technologies that were developed to deal with disfigurements as the result of accident or injury, are now used to reinforce what are perceived to be beautiful bodies with unnecessary nose-jobs, breast enhancements or reductions in unwanted cellulite. The true moral test of a society is not how pretty or clever it is, but how it treats its most vulnerable citizens. Any genetic medical progress should therefore go hand-in-hand with renewed public commitment to support people with chronic diseases or disabilities.

Social and economic pressures might also encourage people to consider therapeutic embryo editing. A disabled child might be dependent on social care and so become a drain on economic resources, though most people would agree that there is more to human life than an economic balance sheet. However, it is not such a great a leap from 'you can have a genetically improved baby' to suggest that it would be irresponsible to have a disabled child and therefore that 'you must have a genetically improved baby'.

Designer babies

Even if we decide that therapeutic genome editing is permissible in some circumstances – for healing rather than enhancement - many people fear that this is the start of the 'slippery slope' to human enhancement for non-therapeutic reasons and for producing designer babies. Here we are still largely dealing with science fiction, though we should prepare for this in advance as today's science fiction quickly becomes tomorrow's science fact. In this dystopian future, parents might have potential offspring gene-edited for characteristics such as intelligence, athletic prowess, or musical ability. However, each of these attributes is the combination of hundreds of genes working together. We should also remember that while our genetic endowment may enable or limit our capacities, it alone doesn't define who we are. DNA doesn't control everything about us, and we are much more than the sum of our genes. In terms of intelligence, access to a good education has a much greater impact than any single gene modification.

In many ways life isn't fair! Some people are born with a combination of genes that gives them increased potential for athletic prowess or musical ability or intelligence. Would it be possible to 'level the playing field', not by introducing new genes, but by 'shuffling the pack' so that a child receives the best combination of naturally occurring genes? In this way parents might be able to choose what characteristics should be optimised for their offspring. However, as Francis Collins observed, 'The application of germline manipulation could change our view of the value of human life. If genomes are being altered to suit parents' preferences, children become more like commodities than precious gifts.'[14] Germline enhancements could fundamentally change the child-parent relationship. If an embryo's genome is altered to suit parents' preferences, then the child becomes more like a product than being welcomed as an unknown precious gift. In most situations, children are loved by their parents regardless of their genetic makeup. With genetically enhanced offspring, there is a risk that children could become more like products that have been ordered at will. The parent-child relationship

14 'A debate: Should we edit the human germline?' https://www.statnews.com/2015/11/30/gene-editing-crispr-germline/

will also be compromised if the design does not turn out as expected or if the child later questions their parents' choices.

People commonly accept their children as 'gifts' and they treasure them irrespective of their health, abilities or beauty. While some people view the gift as coming from a divine giver, others still use this as a helpful metaphor. Children are respected and cherished as gifts from God. It is an uncomfortable fact that many aspects of human life are gifts, not achievements.

Others have compared the understanding of children as 'gifts' with the distinction between 'begetting' and 'making'. Christian creeds describe God the Son as 'begotten not made', emphasizing the close relationship with God the Father. In this way 'begetting' describes a personal, non-manipulative relationship between parent and child, in contrast to technological procedures that could be described as 'making', and that can reduce children to products of our clever creating. The natural process of 'begetting' retains an element of mystery, whereas by gene editing, parents extend their own ambitions into the next generation and so compromise the open relationship with the child.

Even if only a small percentage of parents modify their children's DNA, to enhance their physical or mental capabilities, this could result in a form of genetic one-upmanship, in which others feel obliged to keep up with the latest genetic fashion. Genetic enhancement to Life 2.0 may then become inferior as soon as Life 3.0 becomes available, and children born with today's enhancements may be outdone by children born with later more powerful enhancements. Ethicist Arthur Caplan commented that "renegade scientists and totalitarian loonies are not the folks most likely to abuse genetic engineering… You and I are, not because we are bad but because we want to do good…The most likely way for eugenics to enter into our lives is through the front door as nervous parents – awash in advertising, marketing and hype – struggle to ensure that their little bundle of joy is not left behind".[15] More fundamentally we need to ask whether the promised greater capacities will lead to a better life? The pursuit of enhancements is based on the assumption that greater physical or mental capacity will make a better life. However, the consumer mentality of 'more is better' is simplistic and in many cases turns out to be inadequate or wrong. Faster, brighter and stronger does not necessarily mean better.

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Autonomy and Diversity

Questions of autonomy and consent have been raised concerning embryo editing, as the embryo itself, and the child that will develop later, will have played no part in the genetic decisions that affect their later life. These decisions will have been taken by the parents. However, parents already act as decision makers for their children (both before and after birth). Healthy fetal development is influenced by the mother's choice of diet and the parents continue to make many other choices on behalf of the child for many years after birth. Moreover, an athletic enhancement does not by itself turn the child into an athlete; this will be determined by the child's decisions of what, if any, sports to pursue and how often to train. No genetic fix will bypass the hard work of training that will still be necessary to achieve greater fitness. An athletic enhancement, if such a thing is ever possible, would increase the potential for fitness, but would not make it inevitable. So, personal choice will still belong to the child, albeit under the influence of the parents' expectations.

Human diversity is what it takes to make a society. To use the apostle Paul's analogy of the body, we cannot all be hands or feet, but we are all equally valued by God. The biblical Scriptures value our bodies so much that they are described as the 'temple of the Holy Spirit' (1Cor. 6:19). Here, the body is not only valued for its mundane functions, but through our bodies we worship and praise God. Indeed, Christians see the ultimate affirmation of the human physical form in the incarnation, in which God himself took on human flesh; the God of the genome took on DNA. In a celebrity culture that gives greater worth to high achievers, we should emphasise that all human persons have equal worth and dignity, regardless of what they can or cannot do. Most people acknowledge the free, unmerited nature of some aspects of life and see these as a gift. We speak of an athlete's or a musician's natural talents as their 'gift'. The excellence of a brilliant musician or of an athlete depends on their inherited natural talents and gifts, which they still need to nurture and develop.

Behaviour

There is undeniable evidence that genes can influence our behaviour, by modifying levels of hormones or neurotransmitters that affect aggression, sociability or risk-taking. A few authors have therefore proposed a 'Genetic Virtue Project', which would use genetic engineering to improve our moral characters.[16] This is in the realm of science fiction, but they suggest that it might be possible to use biotechnology to promote virtue, and thus to improve our behaviour. Christians would surely argue that we choose to behave morally, within the limitations of our natural characters and traits, rather than being constrained to do so. Loving God and our neighbour is a matter of personal resolve – we are not moral automatons, but choose to obey God.

15 Caplan, A., (2001) What should the rules be? *Time Magazine* 22 Jan.

16 Walker, M., (2009) 'Enhancing genetic virtue: A project for twenty-first century humanity', *Politics and the Life Sciences* 28: 27–47.

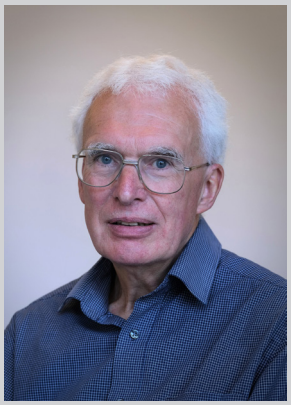
Fairness

Genome modification will be expensive and will therefore only be available for a small number of wealthy people, who will be able to buy enhancements for their children. This technology is unlikely to benefit the poor and needy, but will instead put more power into the hands of the rich with the divergence of humans into the genetically enhanced *GenRich* and unenhanced *naturals*.[17] Altering genes may therefore exaggerate social inequalities and lead to the emergence of a genetic underclass. There is considerable truth in C. S. Lewis's words, written long before gene editing could have been envisaged: 'Man's power over Nature turns out to be a power exercised by some men over other men with Nature as its instrument'.[18]

What is a human?

The issues of genome modification raise the question of what it means to be human and whether this is diminished by alterations in DNA sequence. A fundamental Christian principle is that we are made in the image of God, and any changes should not corrupt that delegated value and status bestowed by God on humankind. In this context, we need to think carefully about what the image of God means. It clearly does not refer to our physical bodies, for God is not flesh and blood like us and it therefore cannot represent any inherent property of our genomes. Being made in the image of God is something that is gifted to all humans, rich or poor, strong or weak, healthy or disabled. In the past most Christian thinking about the image of God focused more on human capacities such as rational thought and moral responsibility, but now is more often considered in terms of our mandate to act as God's representatives and our responsibility to care for creation. The command to 'subdue the earth' arguably includes work to cure disease and alleviate suffering, and the application of science is one of the ways in which we fulfil that calling. As we explore new technologies, we should act as God's collaborators, being careful not to misuse that power or to desire to be God. The Christian doctrine of sin should make us cautious of the dangers of hubris and arrogance.

We may hope and pray that embryonic germ-line gene editing will not happen, but if it does, we will need to resolve how to treat genetically modified people. They are not freaks or museum pieces. They too will be made in the image of God, with all the usual human responsibilities, privileges and relationships. They will be fallen people, like you and me, in need of salvation in Christ.



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17 Silver, L., (1999) *Remaking Eden: Cloning, Genetic Engineering and the Future of Humankind?* Phoenix Giant

18 Lewis, C.S., (1943), *The Abolition of Man* (New York: Harper One, 2001), 55.

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