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A Constructivist Critique of Gene Editing

Macaulay-Adeyelure, Olawunmi

Abstract

Gene editing is a technique in modern day medicine used in the treatment of genetic diseases. Such diseases are effects of defective or malfunctioning genes. Genes are the genetic material which bears hereditary details of any living organism. In genetic editing, attempts are made to correct these defects by altering the anomaly in the gene. This technique is however fraught with inherent risks such as, unwanted immune system reaction, infections and even possibility of tumors growth. These risks aside gene therapy has proved to be a viable treatment either for management or effective treatment of genetic diseases due to the extent of research and understanding of the nature of genes. Most uses has been in treatment of some forms of cancer. Why does this technique generate so much fear and concern? What are the moral issues in gene editing? Can this technology be put into safe and effective use? This paper discusses the moral issues surrounding the technology of genetic therapy as it affects social, economic and heredity the paper attempts finding a viable road map to understanding and accepting this technique with hopes of scaling down the mistrust which trails this technology. This paper employs the Rawlsian idea of constructivism which advocates for the search for reasonable grounds of resolving social and ethical problems, bearing in mind that this resolutions are solely based on the thesis that the truths in a society are constructed and not given. This allows the conclusion that this technology can be harnessed to its full potential with strict and proper guidelines.

Keywords: *gene, gene editing, genetic therapy, heredity, constructivism*

Introduction

Healthcare and the treatment of diseases have continued to take centre stage among major concerns of clinicians, doctors and scientist for centuries. It is a well-known fact that most diseases are easier managed when they are not as a result of genetic disorders. Most genetic diseases are not easy to treat as they involve the very structure and working of the constituents of living cells that make up living organisms. A breakthrough in genetics that led

to the splitting and recombination of the DNA afforded scientist to look into the possibility of treating genetic diseases. The duo of Herbert Boyer and Stanley Cohen in 1973, perfected the technique of the splitting and recombining of genes, in the wake of this discovery was an outcry of ethical concerns involving the procedure and use of the technique

In this paper, we shall be looking at gene editing its processes and uses and the moral issues surrounding its use and application. Why do we have ethical concerns raised? How best can we proffer solutions to these ethical concerns?

Gene editing is a process of manipulating and controlling the DNA of living organisms. By dividing and recombining the DNA, researchers on genetic engineering believed they could find a way of curing specific resistant genetic diseases. At first glance gene therapy appears to be a simple and direct solutions to diseases that are genetically caused. When a gene is malformed or malfunctioning and appears to be the source of a disease, it appears to be a direct solution for medical researchers who possess the knowledge and technique to cure or restructure such defective genes, to put this knowledge into good use to correct the anomaly by removing the defective material and replace it so as to guarantee the elimination of disease. Such innovative technique most certainly should be a welcomed idea, this is however not the case. On the contrary this procedure is considered as human experimentation, on the basis that, the interactions between genetic components run into many millions and gene therapy does not prepare the scientists with all possible effects of such interventions. The concerns are that the outcomes can not be predicted or anticipated, these concerns though valid should not be the basis for a total rejection of this technique because genetic diseases are so delicate in that it affords those with genetic diseases a better and more permanent solution.

Sandel elaborates that approximately 1% of all malignancy is caused by single gene inheritance and between 5% and 10% of common cancers such as breast, colon and ovary have a strong genetic component. By the age of 25, 5% of the population will have a disorder in which genetic factors play an important role. Taking into account the genetic contribution to cancer and cardiovascular diseases, such as coronary artery exclusion and hypertension, over 50% of the older adult population had a genetically determined medical problem (Sandel, 2003.6).

The breakthroughs in genetics presents us with promises and problems. The fact that normally incurable diseases have a shot at getting cured on one hand, is a promise that cannot be taken lightly however, the envisaged problem however is the possible indiscriminate use of this technique for purposes outside the medical one, an example of such instances is the possible use for enhancements and eugenics. Non therapeutic purposes like sex, height, athleticism, mental capacities can be altered or engineered, the creation of deadly viruses which can be used for biowarfare, restructuring of genetic codes and history and the cloning

of super humans Such applications definitely have nothing to do with medical emergencies.

We must however put into consideration that majority of genetic disease have proved to be resistant to conventional treatments as a result of this any treatment that holds the promise of successfully modifying the genetic code with the view of repairing or recoding the gene to function properly thereby eliminating disease, is a worthwhile venture. This promise that gene editing holds, forces the urgency to find resolutions and mid-grounds.

Gene editing is a technique that typically involves the singling out of identified genes or some part of the chromosal constituents from a particular gene and subsequently transferring it into a different cell with a differentiated genomic background. This process allows for overcoming the barriers which usually limit illegitimate cross breeding in other words jumping the specie barrier of breeding, which accounts for only members of a species being crossed with each other where as it is ordinarily impossible with individuals of another species. The only instance where this can naturally occur is when we have inter-specie hybrids, but hybrids essentially occur between closely-related species.

The Science of Gene editing?

There are three different sites for editing nucleases

- ZFN; Zink finger nucleases
- TALENs: Transcription activator like effects or nucleases.
- CRISPR – Cas 9; clustered regular interspaced short palindromic repeats.

The CRISPr – Cas 9 is instrumental in reversing harmful genetic mutation in the human genome. The Cas9 guarantees a site specific DNA break that is subsequently repaired by the receiving host, it also serves as a competent and reliable tool in germ line engineering.

Genome editing methods is predominantly based on protein recognition of specific DNA sequences.

Gene editing technologies can be used to make changes that are of very high accuracy and frequency this appears to strung the research interest in developing safe and effective therapies that can offer options beyond the replacements of an entire gene.

In the field of biomedicine, genome editing can be used for three general and broad purposes.

- Research
- Somatic interventions; in body this affects only the patient
- Germline intervention; in the gene (DNA) affects not only patient but generations after.

Most basic research on human cells uses somatic cells—nonreproductive cell types such as in liver, lung and heart cells. We still find some using germline cells

i.e. reproductive cells, with some involving early stage human embryonic cells and some using cells from female eggs and male sperms. This later example brings about serious ethical and regulatory considerations regarding the collection and the purpose for such collections, even where it is found that no actual pregnancy and transmission of changes to other generation is involved.

The United States and majority of countries that have a well-rounded regulatory system proposes that clinical applications of this technique must undergo a supervised research phase before the onward use of patients. While this paper is not a scientific paper it is important to have a clear idea of the techniques involved in gene therapy so has to understand the specific areas of concerns. The next section takes care of that.

Repairing the DNA

The abnormality of mutations in the DNA if left unrepaired could have some grave consequences for the affected person and subsequently the offspring's such person will eventually have. The stability of DNA is largely dependent on the continuous repair by a number of different mechanisms, which involves removal of damaged nucleotides by an exonuclease, resynthesis of the missing nucleotides and the gap in the DNA molecule being filled by the enzyme (Emerys 2001: 27).

Gene mapping:

The identification of the defective gene responsible for a single gene disorder to ensure an immediate clinical diagnostic application is quite central if therapeutic interventions is being considered. The physical mapping of a gene is an essential step that must be taken first for identification and probable cloning. Researchers do these via a process known as gene mapping. The procedure of gene mapping solves the problem of not knowing where to return the recombined gene, which earlier procedures lacked

Gene mapping are of two main types. The technique of assigning a gene or DNA fragment to specific chromosomes or a particular region of a chromosome also known as low resolution mapping. The second technique involves a finer level of analysis which provides detailed mapping information also known as high resolution DNA mapping. This allows the identification of neonatal transmission of transmission of genetic disease and the particular genes involved.

The Ethical Debate on (Gene Editing) Genetic Therapy

The concerns around gene therapy as mentioned earlier are centered on two fundamental issues. The first relates to patient/ practitioner relations of ensuring informed consent on the part of patients who wish to participate in gene therapy or clinical trials. Decision affecting adult patients and parents of affected children desperate to find solutions to genetic diseases who might choose to participate in gene therapy research particularly if their disease is otherwise incurable. This apparent desperation might cause the temptation to disregard the possible

hazards and risks. Moreover, because of the complexity of most genomes, we cannot predict the effects of such manipulations (Koepsell, 2007, 7).

The second aspect of gene therapy which generates concerns is the possibility that it could be used for eugenic purposes. Consequently the British Joint Committee on genomics in medicine gave a recommendation that genetic modification that could affect the germline should be discouraged. Consequently, by limiting gene therapy to non reproductive cells it basically should not be possible for newly modified genes to be transmitted to future generations. The committee also recommended that somatic cell gene therapy should only be used when treating serious diseases and not to alter human characteristics such as mental capacities or athleticism.

The potential benefits of gene therapy are enormous and if we put aside the disappointments that marred its initial successful applications, with recorded cases of deaths. Succesess however have been recorded in recent times, gene editing has proved instrumental in the treatments of cancer, sickle cell disease, restoring eyesight and the regeneration of new skin. We would find however, that discussions on the ethics of somatic and germline therapy will continue to take front burner as it is a very central theme when discussing the very nature of humans. Again there is no doubt that each new discovery in gene therapy would definitely be accompanied with new challenges and these challenges would raise new difficulties for which there are no easy solutions.

We can begin by focusing on views ranging from uncertainty and safety and move our discourse to cover other frontiers : Gene therapy involves a lot of uncertainties we must attempt to bring to the barest minimum these uncertainties relates more to safety concerns, this safety concerns emanates from the question of what if untargeted genes are altered? What if gene editing is not completely done? Or as Krimsky presents the worrying thesis of the French researcher Jean Dausset that the Genome project could open doors to severe "nazi like" atrocities (Krimsky 2015, 242). This question of uncertainty has however elicited several responses. Krimsky quotes Lee Silver as saying that all of the reasons people have given against gene therapy are either irrational or religious-based for nature's way of procreation is fraught with uncertainties and if indeed we have the way and means to regularize them, why not? It will be our best gift for posterity. For unedited genes are catastrophes happening now (op. cit).

On another pedestal is the dilemma that the medical profession faces. Futuristically, if we continue to explore the present frontiers of genetic editing, and it does come out positively, among the challenges it does portend is the question- do we need doctors anymore at that point? What does the future hold for medics and other health related professionals? In continuing we toy with the financial, emotional and other substantive aspects of these set of individuals in society. Perhaps we might end up being unfair in our quest. This suggestion can easily be waved aside on the grounds that we cannot encourage an unhealthy population because of the economics of medical practitioners.

There is also a possibility that a total loss of empathy will be doled out to people who still suffer from one sickness or disease that can be genetically altered. These sorts of ailments could be termed as low-class sicknesses and if this becomes the case, personal, group or government efforts toward social provision and care for these sorts of persons might be reduced (Fukuyama 16)

However Kotze argues that this argument has no substance for this divide still exists in present society as the wealthy have access to better medical procedures and care than the poor. However as it may, I agree with him on the latter part of his argument for it must be stated that the human characteristics of empathy is not lost yet as may be the case if a more unbreakable gulf is created with the GE technology (Kotz 2015, 72).

In another light, Gavaghan summarily asserts that what would be unfair about genetic therapy is not that some people would end up having undue advantage for even in the natural sense these situations exist, people inherit genetic traits that gives them an edge over others unlike situations where both parents are genetically mediocre. He argues that his problem with the germline innovation, is that some people would be able to afford genetic procedures that stack the odds overwhelmingly in their favour with perhaps no gaps for imperfection and that it is man's own effort and decision that compounds the situation (Gavaghan 2007:182).

Also bearing in mind that many common diseases are polygenic, that is a host of genes have to be mutated in order to avoid certain disabilities, ailments and diseases and that the relationship or binary flow and interaction between genes and how they relate substantially to themselves and the environment is not also so straight forwardly established. This raises another fundamental problem.

Another line of argument lies in what I term the undue advantage claim. In this hypothetical situation, we are not just only looking at the prospects of giving birth to children with silver spoons and golden genes in their chromosomes. If parents so wish they may succumb to procuring procedures that guarantees perfection, promoting and demanding all manner of accomplishments from their children (Sandel 2007:6). As Krimsky points out that the main battle is not between editing somatic cells and germline cells but where to draw the line between disease prevention and enhancement (Krimsky 2015:243).

Constructivism and Genetic Therapy

Constructivism in ethics holds the thesis that normative truths are not fixed by generally accepted facts rather are objective and independent consensual reason and judgement. Normative constructivism is the view that the moral principles we ought to accept are the ones that the society agree to or endorse after a process of rational deliberation[Stanford encyclopaedia of philosophy 2021] going by this we find that there are no moral principles devoid of rational agreement. In applying this to genetic engineering it is very important that papers like this are written to help form the basis for agreements on the moral status of gene editing.

If we can agree that this technique is an answer to a problem that otherwise had no solution we can accord to it a constructivist moral status of right. Constructivism can be traced to Immanuel Kant, who made attempts to understand the nature of moral and normative truths and asserted that we are moral agents not because of our desires and interest but rather because of our agency of reason, what makes a moral norm binding is on our reliance on reason and obligation.

In the first place genetic diseases does not align with the constitutive requirement in constructivism, this requirement upholds the thesis that as clearly highlighted by Korsgaard;

> According to the constitution requirement, conforming to the standards that apply to an object, at least to some extent, is what constitutes the object as the kind of object that it is. This is not to say that things cannot violate the constitutive standards that apply to them, and still be the kinds of things they are. But there is a limit—if the object falls too far below the standard, the object ceases to exemplify the kind [Korsgaard 2005 p.5]

Genetic diseases violates human constitutive requirement as evident in most cases it limits the normal functioning of the human species, gene editing allows for the repair of the DNA for sufferers to live to their maximum potential.

Korsgaard's variant of constructivism gives premium to the value on humanity; humanity being the capacity for rationality. She believes that we possess the power to attribute value on our actions by employing reason when making choices. Effectively the value placed on any object is directly dependent on the rational capacity of the assessors. {Korsgaard 2005}

Rawlsian constructivism engages the process of reflective equilibrium as the mechanics of societal reasoning about contemporaneous issues in order to find generally acceptable solutions. Brandstedt et al aptly captures the core thesis of Rawlsian constructivism thus:

> The motivating idea of Rawlsian constructivism is that normative ideals have a practical function: they guide agents in situations in which there is disagreement or uncertainty about which actions to take towards a successful solution of that predicament. The point of formulating and justifying normative ideals is given by the practical-social function: it is to evaluate and seek to improve solutions to action problems. On this basis, Rawlsian constructivism puts forward two related methodological ideas that inform the process of justification: (1) that one should not expect a unison solution to all problems, but rather be pluralistic; and (2) that proposed solutions must be evaluated on a relatively concrete level of description at which real-life agents can relate to them and understand how they connect to problems they face. [Brandsedt et al 2020] When societal problems are evaluated it is quite necessary to consider only the normative judgement relevant to the problem being evaluated. This process is a continual one and needs to be continually updated, by so doing we arm ourselves with better understanding of the issues being discussed and hopefully reduce the points of variance. It is with this at the

back of our minds that we take a more critical look at the ethical issues surrounding gene editing in the next section

Gene Editing, Justice and the Future

Ethical issues arise in all branches of human endeavour medicine inclusive, but what we find as particularly contentious in gene editing is because of its potential powers, in changing genetic information through recombinant DNA techniques. How does this technique affect the individual, the family, the society and the human species? It needs to be reiterated that gene editing can easily be confused with eugenics, which can be defined as the science of "improving" a species through breeding or aligning particular genetic traits. The focus of gene editing is towards curing by improving genetic details or particular genetic traits. This is differentiated from the objective of eugenics philosophies which were promoted in Nazi Germany and any idea of creating a racially superior class.

Concerns bordering on the marginalization of those not afforded the opportunity to alter their genes have also been raised, we need to emphasize that naturally differences already exist and most importantly there should not be much of an issue when defective genes are involved, how does repairing a defective gene bearing cancer lead to creating a class of super humans or the marginalization of those carrying healthy genes? The real fear actually is to use this therapy for non-therapeutic purposes on such occasions can such misuse be controlled?

Aristotle believed that justice in the society involves giving each their due, so presumably giving genetic treatments to those with genetic diseases encourages social justice and not necessarily inequality.

Medical and psychological studies involving clinical trials are serious issues as history is replete of serious infringements on the treatment of humans in the name of medical science. We need however for there to be a balance between the welfare of people who novel therapies might be the only course of action towards the restoration of good or manageable health, not forgetting that these treatments create useful and valuable data for better results.

The truth is, no matter how we choose to test new medical techniques on non human subjects, if the final purpose is to treat diseases in humans it means the first recipient of such treatments would be exposed to the possibility of something going wrong, but we know that we learn from failures especially in empirical procedures.

It is somewhat clear that we fall into a serious problem of indeterminacy when we try to extrapolate justice as it is in our present familiar settings to another setting which is largely built on conjectures that is not in its remotest sense connected to any recognizable social setting. We talk about a hypothetical setting where knowledge is higher, and for now we possess a vague idea of how such perfection will grow, it is therefore out of place to decide and impose limits on the future, for if in our present situation we are indeterminate about many

things as the future we also lack the theoretical and moral tools for making accurate judgments about how one can make excellent judgment. Fredrick Nietzsche opined quite rightly that morality should not be treated as an absolute as it is dynamic and dependent on the general disposition of the society, and its present reality.

It is clear that some benefits and risk discussed in this work are fairly factual and can be supported with a fair degree of certainty. However science being inductive, and as Wesley Salmon puts it, "ampiliative" a host of others remain uncertain, mere hypothesis (just as the buildup of science is) and in dire, sincere need for further investigation. gene editing and clinical trials would continue to engage social debates and the likes in order to access these limitless probabilities of better health care. Its configuration is one which corresponds with the Khunian conception of paradigm shift. The utility of science as a tool to save humanity and harness all its untapped resources must continue. Conclusively, I borrow from Rousseau that man's innate desire for self- improvement and the quest for perfection must continue although not unchecked.

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