**Review article:**

Ethico-legal aspects of CRISPR Cas-9 genome editing: A balanced approach

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**Abstract:**

Notably, reproductive technology and its applications in human subject are not only debatable ethically but also religiously, where objections are raised by the contemporary scholars and specialists of the field on CRISPR Cas-9 due to its potential application for the genome editing. This does however generated a dialogue both in religion and modern ethico-legal world regime. Some contemporary bioethicists are of the view that this technology is one of those issues which have the most complex ethical concerns, fearing that this technology could transforms with the expectations and ambitions about human control over the biological world. Consequently, this is an area of anxiety not only for the bioethicists but also for the theologians. Thus it needs proper investigation, as it is not solely a scientific innovation, but in fact an ethical, legal and biomedical issue.

**Keywords:** Crisp; Bioethics; Germ line modification; Genome editing and Islam.

**Introduction**

Nowadays CRISPR Cas-9 is considered a very recent genome editing technologies. Initially genome editing technique was discovered in early 1960s and till around 2005 it was utilized by the scientists. Thus germ-line editing has been the subject of debate since 1980s and until around April 2015 when for the first time Chinese scientists used CRISPR based ‘Cas-9’ technology to modify human embryos. Although modification in DNA and editing in its sequence is well established method, used in plants, fish; zebra-fish, animals (including birds, reptiles and mammals) like, monkeys, rabbits, mice, pigs, and even in living human cells. But due biotechnological advancement and its effective usage in the human reproductive cells including modification/alteration is an area of tension not only for the bioethicists but also for the theologians. Thus it needs proper research, as it is not merely a tool and technique, but purely an ethical, legal and biomedical issue. Remarkably, CRISPR’s potential application for genome editing generated a dialogue both in religion and modern world legal regime. Bioethicists consider this technology could transforms with the expectations and ambitions about human control over the biological world. Although genome editing could one day offer an alternative approach for prevention of innate diseases. Consequently, we may presume that it could be a very useful technology, as it may not only cure heritable diseases but also force to prevent it from being passed on to next generation.

**Genome editing**

Genome editing has emerged as an important field of therapeutic development for curing hematopoietic diseases. Through it specialists modify various types of blood cells, including hematopoietic stem cells (HSCs) to cure hematopoietic diseases, like bone marrow and etc. Scientists are very keen to assure that this technology can modify accurately and can alter the DNA sequence safely. Genome editing and the transfer of genes from one organism to another are known as genetic manipulation/modification/editing. It may also be termed as genetic technology/DNA technology. Although this technology is not newer as is generally supposed to be, because a lot has been done earlier.

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through it. However, advancements are made in the field of biotechnology, and hence, certain features of the genome editing set a new ideas apart from the earlier traditional and scientific methods. That is why CRISPR made it possible to transform/edit a gene in minimum time25,26,27. Thus “CRISPR is far better than older techniques for gene splicing and editing”28. Despite of its advantages, some ethical questions are involved in genome editing, as some consider it immoral on the grounds that “all forms of genetic engineering/editing is unnatural as an interference which go against the nature”29. Commenting on the said argument ‘Qaiser Shahzad’ holds that “in one sense all human activities that produce changes not occurring naturally will amount to interference with nature, thus all medial activities from the prescription of eye glasses to the repair/replacement of a damaged hearts would then be unnatural. Likewise, there may be some activities that can be contrary to nature, although there are other human activities in the field of biotechnology (like human reproductive cloning and other forms of artificial insemination) which do not prove anything unnatural”30.

Generally, the religious and theological response to the morality of genetic modification is outright rejection on the grounds that it gives to human overmuch power on animals, which is a form of slavery and thus it is unnatural. Similarly, some clerics accepting it with a view of its effective benefits, while others due to fear and unfair usage of the genetic technology urge it with certain caveats31.

Germ-line editing
Scientifically, germ-line editing mainly mean; modification in the reproductive/sex cells. Due to effective modification in human embryos it has some grave ethical objections. Although some researchers divided it into two; first: intentional germ-line editing, and secondly: unintentional or unintended germ-line editing32 viewing that “unintended modification of germ cells in the course of an in vivo gene-editing therapy are not different from the therapeutic approaches that would used for gene addition”, while “intentional germ-line editing: this does however has some serious ethical concern due to the direct intentional alteration of the germ-line”33,34,35. Thus it can effect to eliminate pathogenic mutations through childbearing introduce the modified genomes into the human gene pool along with other ethical considerations including the goal of the intervention: disease curative or ‘genetic enhancement’ and whether the manipulation will re-create that what is naturally found in human genetics or it adversely affect and will create what is not normally found in human genomic location”36.

Arguably, gene-editing/manipulation can ethically and morally be justified on the ground; that in case of pre-conception gender selection (PGS), Islam does respect the rights of persons to make choices in their personal life37,38. Although it might not adversely affect the rights of others, thus, couples/parents are allowed to make choices and left the matter to the nature. Where in case any kind of failure in technology, the parents will not mistreat the resultant offspring39. However some others apposed it on the grounds of gender discrimination, and consequential psychological harms40. Perhaps, this view (of gender discrimination) can be overruled on the ground that it depends on the availability and easy access of technology to all members of the society, as it requires resources. Questionably, whether an ordinary member of a society can be able to avail such facility? Resultantly no and never, hence the question of gender discrimination in all forms is out rightly rejected in this regard.

Ethical concerns and resulting issues
Recently, the Nuffield Council on Bioethics issued an ethical review on genome editing. It their view genome; “generally refers to the entire sequence of DNA of an organism, which includes genes, the sequences of DNA with specific functions that are involved in the production of the proteins needed to carry out many biological roles”. It also includes “realms of DNA that promote or restrain gene activity that do not appear to have an effect on protein production or its function”41. Several members of the said Council considered its potential usage for possible advances in various fields, like food production, industry, public health and health care. While some of them fear because of its effective application in human embryos, and viewing that legislation is needed before it becomes a proper technique to alter gene at embryonic stage42.

The main idea behind CRISPR is to reduce harm and to enhance benefit for the human beings, in order to improve their living standards43. Debatably, alteration/modification of human DNA having ethical concerns, and it is all about the targeted organism and the risk of ‘off-target’ editing44,45 in the DNA sequences (which may not supposed to be changed due to its efficacy, where recent research contended quality with no detected off-target effects)46. The traditionalists are of the view that man cannot go beyond their limits, and thus they consider human intervention amounts to opening the doors
of abomination. Hence, for them regenerative innovations like CRISPR and others were sums to crossing the limits what is dictated by the nature. Thus insertion and alteration in human DNA will be disregarded ethically, morally, legally and religiously, even if it has been used for curing the fatal diseases in artificial ways, because we are not allowed to go beyond the conventional treatments. Although treatment and curing itself is allowed in any religion and in Islam in case of necessity/need, one can go beyond the limits of that what is prohibited by the Allah almighty. Then, why they/traditionalists forget the case of necessity; where humans are allowed to take prohibited food stuff and can get treatment and curing itself is allowed in any religion.

One of the most recent application of CRISPR Cas-9 which faces a lot of controversy, because of reproductive cell modification, although non-reproductive cells can be edited by any means, just because that somatic cells forming the human body cells which includes all cells except germ/sex cells. Thus the ethical concerns regarding the germ-line editing is the center of debate due to its effective application in the germ cell, as it can affect the newer generation, since the genetic substance are being passed from one generation to the next generation through the sex cells. Consequently, editing in germ-line and its practice in clinics is considered illegal, in UK and in many other countries of the world. Conversely CRISPR Cas-9 technology is being used for somatic cells editing, and very much useful without any controversy, but editing in sex cells sparked debates. However, the human fertilization and embryology authority (HFEA) in the UK has given permission to ‘Kathy Niakan’ to perform in-vitro research using clustered associated protein-9/Cas-9 for genome editing/manipulation in human embryos.

Due to an assessment CRISPR/Cas-9 germ-line editing technology divulge that some of the concerns already rose in 1980s because of ethical implications. But those speculative fears are outmoded, in the context of medical advancement, where more serious issues are emerged. That is why, if CRISPR/ Cas-9 is applied safely in near future, issues of injustice and accessibility might arise due to costly therapies, and thus it can cause fear and an increase in the ethical objections on the development of eugenics.

CRISPR Cas-9, Religious perspective

Notably, scientists considering that CRISPR minimizing unprecedented harms and ameliorate living standards. Moreover it is only to cure fatal diseases. However the usage of CRISPR base technology as a research technique [to know about the pathogenesis and its growth by treatment], keeping in-view the guidelines of National Institutes of Health (NIH) may possibly render it as permissible. Thus Scientists/specialists while conducting these kinds of sensitive innovations are bound to abide by the precautionary measures.

Islam; view point

Arguably, before going into details of CRISPR based germ-line editing, it is quite necessary to note here that in 2002 American National Bioethics Advisory Commission (NBAC) on stem cell research, invited ‘Dr. Abdulaziz Sachedina’ for Islamic view point on embryonic stem cell research, he maintained that “embryonic stem cells research made possible by biomedical intervention in the early stages of life is regarded in Islam as an act of faith in the ultimate will of God as the Giver of all life, as long as such an intervention is undertaken with the purpose of improving human health”. So improvement in human health is prerequisite to preserve a life, and protection of life is one of the basic objectives of Shariah. (Islamic view point will be dealt separately in part-2, for more details see: CRISPR Cas-9 and Islam: A religious perspective).

Judaism; view point

The Jewish law permits innovative research and advancement in human reproductive cells. In this regard ‘Rabbi Eliot N. Dorff’ expresses his opinion that “Jewish law permits both autopsies and organ procuring for the benefit of living with necessary conditions, hence embryonic stem cells research even in sperm and in egg is permissible for the therapeutic purpose”. Generally, the Jewish leaders are encouraging and supporting all the possible assisted techniques for conception. Hence, newer technologies like CRISPR are justified as per Jewish law.

Equally the utilization of medical treatments for the infertile couples is also permitted, hoping that it will bring auxiliary livings for Jewish families. For this purpose many ‘Rabbis’ allowed to practice surrogacy and other artificial methods. Thus curing infertility by any means, especially surrogacy is permitted provided that the gestational carrier must be of the Jewish community, because in Jewish law system effects is given to wombs and not to the gamete i.e. sex cells.
Christianity; view point
In Christianity, Father ‘Kavin Wildes’ took this position that “research should minimize the risk of harm to the subject, and hence any research involving human stem cells will harm the embryos”. While Father ‘Meilander’ urges for the embryonic stem cells research “only for fatal diseases, like bone marrow, placenta and umbilical cord”73. Whereas ‘Roman Catholic Church’ maintained that, usage of regenerative technologies such as IVF and etc for procreation and to manipulate newer generation, runs counter with the intentions of God. As these procedures defy natural order in which God fashioned the humanity76, 77. Although many ‘Catholics’ argued against the stance of ‘Roman Catholic Church’, arguing that even in case of reproductive treatments, God’s influence cannot be dispelled throughout the innovative procedures. Hence, resultantly the things will remain as it was in original. Therefore, no one can seize God’s-Will, rather success of reproductive procedures entails his intervention through these procedures78, 79. That is why the catholic’s physicians believed that “they were the vessels through which God’s-Will was acting, and in fact it was God who would ultimately decide whether such reproductive process would be successful. Thus the power to create life, through assisted technologies, lies with and under the God’s control”. Although ‘Protestant’ leaders have divergent opinion, as some considers all forms of assisted reproductive technologies are elusive, whereas others advocates its usage with certain caveats80, 81. Notably, in 1984 the ‘Church of England’ through its official statement affirmed assisted reproductive technologies and asserted for its usages for human subject82.

Conclusion
Consequent upon the facts if CRISPR technology is used to enhance human capabilities and their living conditions in an appropriate manner, then retaliation of harms and acquiring of benefits can be justified in any religion. Resultantly, any change will be considered as preordained, as alteration cannot change the God’s-Will. Various verses of the holy Quran are evident that God is the sole/ultimate controller of all things83 Same is the case in Christen theology, viewing that no one can seize God’s-Will, rather success of the reproductive technologies entails of His intervention84, 85. Further to note that Jews also supporting assisted techniques with a view that it might bring supportive lives for their community86.

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day enable scientists to create genetically modified humans]. http://www.geneticsandsociety.org/article.php?id=9124


16 Baohui Chen. op. cit. note 10.


20 Elliot Hosman. op. cit. note 13.


26 YG: yourgenome. What is genome editing?. http://www.yourgenome.org/facts/what-is-genome-editing

27 Liang P. op. cit. note 1.


30 Qaiser Shahzad. Biomedical Ethics: Philosophical and Islamic Perspectives pp. 185–186 (IRI, IIU, Islamabad, Pakistan, 2009).

31 Michael J. Reiss and Roger Straughan. op. cit. note 29, pp 85–89.


36 Donald B. Kohn. op. cit. note 32.

37 “The story of ‘Noah’ is referred in many places in the holy Quran. Where in chapter no. 71, verse no. 12, p. 1738, ‘Noah’ saying to his people about the blessings of God, “For your Lord; He will give you increase in Sons”. Thus in the meaning of this verse “increase in male offspring” is considered one of the blessings of Allah almighty. For the reason, gender selection is also legitimized in this sense in Islamic law”.

38 In other place where ‘Zakariyyah’ prayed to the God secretly for giving an heir due to public need. Indeed Allah almighty answered his prayer and give him a son named ‘Yahya’, although his wife ‘Mary’ was barren. Therefore, the male progeny is considered to be one of the highest blessings of Allah. See: Al Quran, chapter no. 19, verses no. 2–5, pp. 847–848; along with chapter no. 3, verse no. 38–49, pp. 151–152. (Hence, keeping in view the above story–in case of infertility or any disorder in the reproductive cells, couples are allowed to adopt biomedical technology to meet their wishes/desires. And it because that curing infertility or gender selection through artificial methods at time were unavailable, otherwise thy people might have would adopted, since Islam does recognizes the desires of couple. The holy Quran in chapter no. 25, verse no. 74, p. 1035 stated: “Our Lord, grant unto us wives and offspring who will be the comfort of our eyes”.

39 Ethics Committee of the American Society for Reproductive Medicine, Preconception Gender Selection for Non-Medical Reasons, Fertility and Sterility, 2001;75(5):861–864.

40 Ethics Committee of the American Society for Reproductive Medicine, Sex Selection and Pre-Implantation Genetic Diagnose, Fertility and Sterility, 1999;72(4):595–598.


42 Nuffield Council. op. cit. note 41.


44 PHYS/ORG. op. cit. note 19.


46 YG: yourgenome. op. cit. note 25.

47 The doors of evil; Islamic scholars consider reproductive techniques as zina, viewing that these techniques are runs counter to the intention of God. Thus they present verse no. 32, chapter no. 17 of the holy Quran: “Nor come night to adultery: for it is a shameful deed and an evil, opening the road (to other evils)” to strengthen their view point. But the said verse is reveled for zina. Thus these newer technologies does not come under the
rubric of this verse, nor it come under the definition of zina. Therefore embryonic stem cells research and other methods like CRISPR, if used to cure lethal diseases to overcome prospective disorder in human gene to enhance human capabilities will be rendered as permissible.


The HFEA of UK “permitted human genome editing for research, but so for its practice is banned in the clinics”. While Argentina “banned reproductive cloning, but research applications of human genome editing are not clearly regulated”. US; do not allow the “usage of federal funds to modify human embryos, but there are no outright genome editing bans, and for clinical development it may require prior approval from the concerned authorities”. Although other countries like Japan, China, India and Ireland have unenforceable guidelines that “restrict genome editing in human embryos”. While Germany “imposed strict laws on the use of human embryos in assisted reproduction, and they also limited research concerning human embryos, and in case of violation it could result in criminal charges”.


Anderson WF. *op. cit.* note 50.


Martina Baumann. *op. cit.* note 60.


Martina Baumann. *op. cit.* note 60.


Testimony before NBAC. *op. cit.* note 69, C. 1–5.


Testimony before NBAC. *op. cit.* note 69, E. 3.


Roberts EF. *op. cit.* note 77.


Abdullah Yusuf Ali. *Al Quran English Translation and Commentary* chapter no. 30, verse no. 30, (Dawah Academy, IIU, Islamabad, Pakistan, 2004). See also, chapter no. 6, verse no. 102, p. 362. See, chapter no. 54, verse no. 49, p. 1583. See also chapter no. 28, verse no. 68, pp. 1115–1116. See, chapter no. 16, verse no. 8, p. 728. See also, chapter no. 39, verse no. 62, p. 1360. See, chapter no. 13, verse no. 16, p. 672.

Roberts EF. *op. cit.* note 77.

Benagiano, G. *op. cit.* note 79.

SM Kahn. *op. cit.* note 74.