# Editing Nature's Code: CRISPR Gene Editing and Jewish Ethics

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Before embarking on a discussion of the ethics of CRISPR, we will clarify how the process works on a technical level. CRISPR [1] technology has been called a "molecular scissors" for its ability to locate a specific DNA sequence and slice the DNA at that site. With CRISPR, researchers have figured out how to repurpose the bacterial immune system into a gene editing tool that has a wide range of applications in science and medicine. How does it work? Bacteria have developed a system to protect themselves against infections by viruses–phages–that infect them that involves "slicing" the phage genome. When first infected by a phage, bacteria store a portion of the phage genome in their own DNA, demarcated with CRISPR array spacer sequences [2]. They then create corresponding CRISPR RNAs [3,2]. Upon phage reinfection, this RNA matches up with the phage DNA, a process that drives a type of bacterial enzyme–an endonuclease, termed Cas9, [4]–to slice the phage DNA, thereby destroying the phage [2]. By synthetically changing the spacer sequence into any other RNA sequence, researchers can use this tool to target and slice almost any DNA sequence [2]. This technique has greater ease of use than previous gene-engineering techniques and therefore serves as a great benefit to the research process [2]. Using these bacterial defense system components to edit genes in the lab, researchers even can target multiple genes simultaneously, which enables them to study diseases whose cause stems from multiple genes [2].

Researchers have classified six types of CRISPR systems. The most commonly studied and used is type II-A from the bacterium *Streptococcus pyogenes* [2]. More research is needed to understand how the endonuclease Cas9 so accurately targets its DNA target and avoids errors [2]. Further research also needs to examine how eukaryotic chromatin–the structure by which DNA arranges itself–impacts Cas9 binding and activity [2]. Likewise, more studies need to determine how DNA unwinding impacts Cas9 activity [2]. A better understanding of how CRISPR/Cas 9 works will further enhance future scientific research, which in turn will lead to better therapeutics and healthcare outcomes.

One recent example of CRISPR lab research involved researchers who genetically modified hamsters to study social behavior. Since vasopressin, a hormone produced by the brain, plays a role in sociability, researchers knocked out the gene for the vasopressin receptor and looked at the effect on social behavior [5]. The hamsters as a result became more sociable, though researchers had expected the opposite [5]. With the greater ease of genetic modification afforded by CRISPR, researchers can more readily find new discoveries such as this one.

*Ethical Questions*

Gene editing raises many ethical questions. This paper will focus on those questions that relate to when and how to use gene editing, namely which types of traits should undergo editing and which might be better left alone. This paper will focus on a few of those questions. While editing out diseases would obviously present a positive outcome, what about the question of "designer babies," as the technique could also edit traits such as eye and hair color? As another question, about more of a gray area, what about editing for traits such as skills or neurotypicality? On the one hand, these traits do not present a medical necessity but on the other hand they present changes more beneficial than simple cosmetic traits. There are additional questions that arise that are beyond the scope of this paper. These include the fact that editing the human

genome could create errors (including those caused by binding to similar off-target sites) [6] and potentially other mutations [7]. There is also concern that those mistakes might pass down permanently [8]. In the future, as the technology evolves, more questions will emerge.

Although CRISPR emerged recently, the question of "designer babies" has remained an ongoing question ever since preimplantation genetic diagnosis (PGD) was introduced in 1990, [9] as PGD allows parents to select embryos with certain traits and was intended to prevent disease, but the PGD process also enables the selection of preferred traits such as hair or eye color. Like PGD, in addition to preventing widespread disease, CRISPR gene-editing technology could also open the door to editing the genome for any number of preferred traits, which raises the same ethical dilemma as does PGD, namely the ethics of selecting certain traits over others.

One additional concern is that of editing genes to manipulate intelligence. According to Daley *et al* in a New England Journal of Medicine editorial, editing for traits such as intelligence remains an unlikely occurrence and therefore only a theoretical concern [10]. "In the long run, our greatest protection against inappropriate genome editing may be the implausibility of influencing traits such as intelligence, which emerge from complex interactions among multiple genes and environmental factors. Our ignorance regarding such complexity may ultimately save us from the hazards of humanity's hubris" [10]. Public opinion thus far seems to agree with this perspective: "Opinion polls show that most people are okay with using it [CRISPR] to wipe out disease mutations. But only about 20% think using it for 'enhancement'—specifically, trying to increase the intelligence of offspring—is a good idea. Luckily for scientists, they don't have to tell us whether they think increasing intelligence is good or bad. It's not possible, they say, so don't worry about it" [11]. The limitations of CRISPR alleviate the need to make difficult decisions about intelligence.

*Jewish Primary Sources*

Although clearly no early Rabbinic sources mention gene editing, it might be possible to extrapolate from the early sources by considering a parallel case that can provide guidance on our modern technology. Modern Jewish sources, discussed below, address the topic, but I would like to add mention of a primary source that could bear weight on the issue. A source in the Babylonian Talmud addresses an issue relevant to CRISPR, that of intervening in the development of an embryo. When the Mishna (Berachot 54a) discourages vain prayer, namely praying for something already determined, and includes mention of praying for the gender of an unborn child, the gemara there (Berachot 60a) limits this prohibition to after forty days of gestation, the point at which the rabbis believed the gender of a child to become determined.

> Mishna: "**And one who cries out over the past** in an attempt to change that which has already occurred, **it is a vain prayer**. For example, **one whose wife was pregnant and he says: May it be** God's will that my wife will give birth to a male child, **it is a vain prayer**" [12]. Gemara: "**From the third day until the fortieth, one should pray that it will be male. From the fortieth day until three months, one should pray that it will not be deformed, in the shape of a flat fish**" [13].

The Shulchan Aruch (Orach Chayim 230) echoes this ruling–one can pray for the gender of the child prior to forty days. For an in-depth discussion of how Chazal view determination of the gender of an embryo, see Niddah 30b and Poltorak, "On the Embryological Foresight of the Talmud" [14]. The gemara in Brachot also suggests that from the fortieth day until three months, one should pray that the fetus does not become deformed. Perhaps here we see a precedent for altering the outcome of an unborn child through CRISPR rather than through prayer.

Traditional sources might also provide a philosophical perspective on our modern technology. For example, Taanit 2a states:

> **Rabbi Yoḥanan said**: There are **three keys** maintained **in the hand of the Holy One, Blessed be He, which were not transmitted to an intermediary**, i.e., God tends to these matters Himself. **And they are: The key of rain, the key of birthing, and the key of the resurrection of the dead** [15].

This list leaves out the outcome of the child–how the child will turn out–which suggests that humans as intermediaries can intervene.

*Modern Jewish Responses*

Now that we have considered traditional sources that pertain to CRISPR, how have modern sources evaluated the issue? As current Jewish thinkers have addressed other medical ethical issues in the past, they likewise seek to address the ethical concerns raised by CRISPR, looking toward traditional Jewish texts for guidance. In the past, Jewish ethicists have addressed similar issues such as assisted reproduction technology and PGD. Likewise, Jewish ethics now face the challenge of discerning how an ancient tradition might view the modern technology of CRISPR, with all of its implications. Several Jewish ethicists, scientists, and physicians have written on the topic. Again, the question remains in its infancy.

On the question of "playing G-d," which arises in a religious context, Drs. Loike and Kadish suggest that "[w]e propose that a Divine directive is for human society to embrace science by actively supporting the research of natural law and *applying it wisely* (emphasis added)" [16]. The imperative to "apply it wisely" suggests that society must establish careful guidelines before embarking on CRISPR use but that the technology itself does not go against any Divine imperative. Cohen points to a medieval source on the idea of interfering with nature, a comment by the Meiri [17] on the topic of sorcery, who implies that Judaism presents no prohibition against manipulating nature, only against doing so using sorcery [18].

Regarding the superficial traits question, Drs. Loike and Kalish ask: "The ethical concerns regarding these biotechnologies are many. Will society limit their use to curing disease, or will also people begin to use technology for non-medical purposes?" From a practical perspective, Loike and Kadish maintain that Judaism would support therapeutic uses for the CRISPR technology but for the most part would not endorse the practice of "designer babies":

> The general rule in Judaism is that gene editing for non-medical applications is ethically wrong and should not be routinely acceptable. In the case of gene-editing a human embryo, we believe it is moral and ethical to genetically edit not only an embryo carrying lethal genes (*e.g.* Tay–Sachs) but also in cases where

the child would be born and burdened with serious health issues (*e.g.* cystic fibrosis) [16].

It remains unclear whether the language of "routinely acceptable" hypothetically could open the door for a case-by-case basis scenario. Cohen argues that the decision on whether to choose characteristics of a child is a moral one and, using traditional sources, posits that we face a *halachic* imperative to use our moral judgment [18].

Rabbi Dr. Tendler pointed out two concerns, the concern that errors will persist perpetually and the concern for genetic enhancement [19]. "Despite these concerns, *halakhah* would favor continued research with its potential to cure genetic diseases, even if a modicum of risk exists" [19]. Further, Rabbi Dr. Tendler maintained that creating changes in the child does not go against Judaism, which considers children as blank slates and gives parents the right to educate/shape them [19]. He left as a question, "Parents can now demand babies who will be seven feet tall or who will have perfect pitch. Can gene-editing designer babies lead to eugenics?" [19]. Again, how the technology develops remains as of yet undetermined and will impact the outcome of these questions.

In an article written shortly after the inception of CRISPR, Dr. Loike and Rabbi Dr. Tendler discuss editing genes for behavior–which falls in the gray area of not quite disease but not quite superficial–and point out how that question might end up changing over time. "We therefore propose that *Halakha* would prohibit, at this point in time, the utilization of gene editing to alter behavioral characteristics because of their unknown, far-reaching consequences on the personality of the individual. As science gains further knowledge regarding these issues, the *halakhic* prohibition may be revisited in the future" [20]. Glick, in contrast, argues in favor of enhancement, given completely ideal conditions (technical, socio-economic, etc.), currently relegated to the realm of the hypothetical [21, 22].

Dr. Milner and Rabbi Cherlow invoke an issue that is raised regarding genetic testing and is relevant to CRISPR as well, the concept of *tamim tihiye im Hashem elokecha*—"you should be complete with G-d" [23] (Deuteronomy 18:13) [24]. According to this logic, one should not interfere with the future but rather leave it as G-d created it. Since PGD and CRISPR involve preventing disease before it occurs, the *halachic* issue does not relate to healing as much as to preventing a future danger [25]. However, Rav Moshe Feinstein compared the genetic testing process to "opening one's eyes" and seeing, namely that genetic testing serves as an extension of our ability to see [24]. Analogously, one can view the process as comparable to moving out of the way of an oncoming truck [25]. Dr. Loike and Rabbi Tendler additionally recognize use of PGD even to avoid carrying genetic risk for common diseases such as Alzheimer's and diabetes [26].

*Halachic Analogy*

The concept of plastic surgery can serve as an analogy for gene editing in Jewish law, in that both involve risk and both involve changes to the natural order of things. Rabbi Chaim Jachter has written an article that summarizes the four main *halachic* positions on plastic surgery from four leading Rabbis and from this summary, one can see that *halachic* approaches to plastic surgery vary. Rav Moshe, based on Rambam and inferred from other sources, allowed one to wound oneself for one's benefit [27]. Rabbi Jachter comments that he is unsure whether Rav Moshe meant this ruling to apply in the

specific situation asked of him from someone in great need or whether Rav Moshe Feinstein extends this ruling to general situations for anyone who wants plastic surgery [27]. Rabbi Breich on the topic of risk maintains that one may take something considered a tolerable risk by society, such as driving a car or flying on a plane and maintains that in our times this premise also applies to surgery [27]. Rabbi Waldenberg, in contrast, presents a blanket ruling against plastic surgery, while Dayan Wiesz remains unsure [27]. Rabbi Jachter offers a philosophical approach, one also relevant to CRISPR: "One could argue that perhaps plastic surgery does not insult the work of the 'Craftsman' because He also revealed to mankind the knowledge and ability to perform cosmetic surgery" [27]. Furthermore, "Cosmetic surgery might be viewed as part of our role as 'junior partners' with Hashem in the ongoing creation of the world (see Shabbat 10a and Ramban to Bereshit 1:28)" [27]. From this perspective, we have received the knowledge and tools to use CRISPR but must use it responsibly.

*Conclusion*

The above sources point to the fact that while traditional religious sources offer some guidance toward how halacha might view CRISPR, the CRISPR technology itself remains too new to reach a full conclusion. As the technology evolves, time will tell how ethicists and halachicists will respond accordingly. A Jewish aphorism states that upon meeting a new person, we judge them in the manner of *k'vodo v'chashdo*, both with honor and with suspicion. This aphorism seems apt for how we could approach a new technology such as CRISPR–with some suspicion as to its potential pitfalls but also with honor for the vast potential that it offers.

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