Genome Therapy and Ethical Implications with CRISPR-Cas9

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***Abstract*— CRISPR-Cas9 is a precision gene-editing tool deriving from a natural defense mechanism in bacteria. Unlike previous viral methods that were often imprecise or difficult to engineer, CRISPR acts as a pair of "molecular scissors" guided by RNA to target and modify specific DNA sequences with unprecedented accuracy. This technology has transitioned gene therapy from a theoretical possibility to a clinical reality, offering potential cures for previously untreatable genetic disorders such as sickle cell anemia, cystic fibrosis, and certain types of muscular dystrophy. However, its ease of use and efficiency have put society into a large ethical debate. The difference between treating existing patients (somatic editing) and altering embryos or reproductive cells (germline editing) raises questions about babies made by design and long-term evolutionary consequences. These also add questions of informed consent and the social equity of access to biotechnology. Analyzing CRISPR Cas9 applications through moral frameworks such as utilitarianism and duty ethics allows for the exploration of the ethical dilemma in the systems behind its implementation. Off-target effects are cause for ethical concern of the use of CRISPR technology, while the use of germline editing presents ethical evaluations of possible eugenics. Beyond personal cures, CRISPR is vital to modern medicine because it allows for the rapid development of cures for potential patients and for the possible expansion of bioengineering in other fields. For gene editing to be ethically viable, scientific advancement must strictly follow regulations that prioritize patient safety and ensure that life-altering treatments are accessible to all economic classes..**

Keywords—CRISPR-Cas9, somatic editing, germline, ethics, social equity, patient safety

I. Introduction

CRISPR-Cas9, or Clustered Regularly Interspaced Short Palindromic Repeats CRISPR Associated Protein 9, has revolutionized precise DNA editing. It has demonstrated much success, as it had been used to treat a liver disease deemed incurable. CRISPR-Ca9's ability to target and modify DNA, highlights its potential to cure several genetic diseases such as anemia, cystic fibrosis, and certain cancers [1]. Beyond cures, this technology is also essential for designing in vitro experimental conditions using cell cultures to model and mimic different diseases, as well as recreating organ and tissue cultures to study a variety of different diseases and its effects on different parts of the body [2]. CRISPR-Cas9 is also used to edit the genetic make up for different crops, giving them the ability to survive harsher conditions thereby improving global food security [3]. Despite its promising ability, the rapid advancement of CRISPR-Cas9 has sparked significant ethical debate. Because the technology is relatively new, it lacks well developed policies and legislation for testing, evaluating, and long-term oversight, which leaves it vulnerable to unregulated and unethical use such as the potential for designer babies and eugenics. Additionally, critics argue that although not all CRISPR-Cas9 applications are unethical, practices such as germline editing, which is the process of editing DNA, interfere with autonomy and consent. Further concerns like the creation of biological weapons and the unpredictable effects on different ecosystems further compound its moral implications [4],[5]. Alternative therapies such as RNA-target therapeutics and allogeneic stem-cell transplantation have emerged which utilize natural donor cells. These therapies are beneficial because they use cells that contain native gene expression, so they behave predictably in the body. However, these cures rely on the donor cells to manage the symptoms. By genetically modifying the cells using CRISPR-Cas9, cells are permanently corrected, which allows for a permanent solution instead of relying on donors and having to get continuous procedures, which is expensive and often painful. CRISPR-Cas9 remains a powerful tool, but its lack of regulation, limited long term research, and the potential for increased eugenics and widen disparities in marginalized communities, underscore the need for caution. To ensure that CRISPR-Cas9 is used ethically and for its intended purpose, it is essential to establish regulatory frameworks that define clear policies on gene editing, ensure informed consent, and set form ethical boundaries [6].

II. Problem and Importance

CRISPR-Cas9 is an important and rapidly advancing technology with the potential to treat conditions once considered incurable, such as mitochondrial and sickle cell diseases. Additionally, CRISPR-Cas9 offers new approaches and less invasive procedures for treating deadly illnesses including cardiovascular disease, HIV, and muscular dystrophy [5]. In addition to treating existing disease, CRISPR-Cas9 can target

DNA in the embryo, preventing certain conditions from developing and ultimately improving quality of life. CRISPR-Cas9 has shown great potential to change the lives of many people with a variety of illnesses, however, it still is continuing to be developed. CRISPR-Cas9 has been shown to modify the wrong gene sequences, leading to genetic mosaicism which can have significant health consequences [6],[7]. Besides the basic safety concerns, CRISPR-Cas9 is also ethically criticized often through a deontological lens. Deontology judges actions by principle instead of consequences, highlighting that everyone has a right to autonomy [8]. As a result, they believe that no action that takes away a person's autonomy is moral, even if it might improve their quality of life. This criticism is often voiced when it comes to germline editing or editing embryos that cannot consent to genetic changes that may have adverse effects and will affect future generations who likewise cannot consent. Another major concern is eugenics. CRISPR-Cas9 has the ability to alter genetic and physical traits, which allows for the possibility to use CRISPR-Cas9 as an enhancement tool, which although some argue, that these are positive changes, making people faster, stronger, or giving them more desirable traits, when done on babies and embryos, also take away their autonomy. Being able to genetically modify traits, combined with its high cost, could allow wealthier populations disproportionate access to desired traits, a problem worsened by the underrepresentation of minority populations in genomic research [4]. Because this technology is still new, there is still little regulation to govern its use [2]. Although CRISPR-Cas9 is revolutionary and offers the possibility of curing disease, making people live longer with surgery, radiation, or other invasive procedures, its accuracy, potential side effects, and lack of regulation continue to raise important questions about its ethical use [9].

III. Stakeholders and Public Policies

The current and future applications of CRISPR Cas9 genetic editing involve a broad range of stakeholders. Patients who receive this treatment are directly affected and the primary stakeholders. There are currently patients who are undergoing gene therapy through somatic gene editing, which can be applied in vivo or ex vivo. This has been successful in numerous cases in respect to Duchenne muscular dystrophy, HIV, and other diseases. However, there is still cause for concern with gene drift, off-target mutations, and unknown side effects [10]. Furthermore, long-term side effects have yet to be thoroughly studied and characterized. Many individuals are living with gene mutations or illnesses that significantly impact their ability to live. Depending on their particular case, options for treatment may be extremely limited, making CRISPR-based gene therapy a necessity[11]. Another layer of complexity arises from the implications of germline editing versus somatic gene editing since future generations would also be affected if gene editing is done within the germline. The DNA of every person born from the gametes of the individual whose germline was edited will also be changed. Since future progeny has not consented to these genetic edits, this brings into the discussion the ethics of consent.

Additional key stakeholders are the public, scientists, and the future of science overall. All of these systems must operate under the established legal frameworks. However, a critical regulatory issue is the current lack of explicit legislation on genetic editing research of human embryos in the United States [12]. Germline editing is prohibited from receiving federal funding through the FDA, and there are some states with further restrictions [13]. Policy and regulations surrounding genetic editing vary by country and typically reflect the "norms" of that country. One example of this is with researcher He Jiankui who was found guilty of violating an ethics law in the People's Republic of China for performing germline editing embryos that were brought to pregnancy and birth [14]. While it is difficult for countries to develop laws and regulations regarding genetic editing due to the increasing developments and testing, multiple world organizations have established and published their stance.

IV. Ethical Evaluation of CRISPR-Cas9

The ethical evaluation of CRISPR-Cas9 hinges significantly on the distinction between somatic and germline editing. Somatic editing involves modifying non-reproductive cells to treat existing patients, a practice that enjoys broad ethical consensus because the changes are limited to the individual and cannot be inherited [9]. From a Utilitarian perspective, which seeks to maximize the amount of good done for the greatest number of people, somatic editing is widely supported. Because it modifies non-reproductive cells to treat existing patients, the utility is high, it alleviates individual suffering without risking the well-being of the wider population. In contrast, germline editing alters embryos, sperm, or eggs and introduces permanent genetic changes that are passed down to future generations [9]. This raises a deontological concern with this framework being centered on duty and universal rules, regarding the lack of consent from those yet to be born and the potential irreversible alterations to the human gene pool, leading many international bodies to call for a moratorium on germline clinical applications.

Beyond the philosophical divide, safety and biological risks present immediate practical hurdles that challenge the virtue ethics of science. Current CRISPR technology, while revolutionary, lacks the absolute precision required to ensure consistently accurate genomic repairs. One major concern is "off-target effects", where the Cas9 enzyme cuts DNA at unintended locations, potentially causing mutations that lead to cancer, other cellular dysfunctions, genome fragmentation, or instability [6]. Furthermore, the use of CRISPR in gene drives designed to spread specific traits through wild populations carries significant ecological risks. These genetic interventions could inadvertently disrupt entire ecosystems or lead to the accidental extinction of non-target species highlighting a need for rigorous containment and global oversight.[6]

Finally, the technology forces a difficult confrontation with the ethics of human enhancement and eugenics. Utilitarianism might theoretically argue that smarter or stronger humans could benefit society, virtue ethics warn that such pursuits may stem from vanity rather than a pursuit of the "good life". While there is general support for "therapy" correcting debilitating genetic diseases the line becomes blurred when considering "enhancement", or using CRISPR to augment traits like intelligence, height, or physical performance [9]. This shift risks reviving eugenic ideologies, where society may begin to view certain genetic profiles as "superior" or "inferior". The use

of germline editing is closely linked to the risk of eugenics, the international breeding of the human species to select specific traits. This poses a major social concern regarding the potential for genetic inequality and the creation of a superior class based on access to enhancement technologies. [9] This shift risks reviving eugenic ideologies, creating a deontological conflict regarding justice and fairness. If such enhancements become available only to the wealthy, it could make biological inequality into the human experience, creating a genetic divide that exacerbates existing social and economic injustices. By turning genetic profiles into commodities, we risk exacerbating existing social and economic injustices, transforming a medical tool into a mechanism for permanent social stratification.

V. Alternatives to Gene Therapy

While gene therapy has rapidly advanced and is increasingly being introduced to the public, it still faces significant hurdles that include high upfront costs, the risk of unpredictable mutations, and complex ethical challenges [4], [9]. Because of these drawbacks, the medical community continues to rely on and develop several alternatives to gene therapy that do not involve permanently altering a patient's DNA. One established alternative is Enzyme and Protein Replacement Therapy (ERT). This treatment involves the delivery of synthetic proteins that a patient's body cannot produce naturally. ERT has become the standard for conditions like Lysosomal Storage Disorders and other metabolic diseases [15]. Because it only replaces the missing protein rather than modifying the underlying genetic code, it completely avoids the ethical controversies surrounding CRISPR. However, it typically requires lifelong, repeated infusions.

Another promising approach is RNA Targeted Therapeutics. Instead of cutting the DNA itself, this method uses Antisense Oligonucleotides (ASOs) or small interfering RNA to intercept and modify RNA before it translates into a defective protein [16]. This method has been highly successful in treating severe neuromuscular diseases such as Spinal Muscular Atrophy and Duchenne Muscular Dystrophy. RNA therapies offer a practical middle ground which is to precisely target genetic expressions but are temporary, meaning any adverse off-target effects are not permanently coded into the patient's genome. For Small Molecule Pharmacotherapy, a different route is offered by using chemical drugs designed to physically bind and fix the shape of defective proteins. A prime example of this is the use of CFTR modulators for treating Cystic Fibrosis. Rather than trying to rewrite the mutated gene that causes the disease, these small molecules help the resulting defective protein function correctly within the body [5].

Lastly, Allogenic Stem Cell Transplantation remains a critical option to certain genetic disorders. This procedure involves wiping out a patient's defective bone marrow and replacing it with healthy, genetically normal cells from a donor. It has a proven track record for treating Severe Combined Immunodeficiency, sickle cell, and various blood disorders. While it carries its own significant medical risks, it relies on natural donor cells rather than lab-engineered genetic modifications

VI. Recommendations

CRISPR-Cas9 is no doubt a revolutionary therapy. To keep CRISPR accessible, ethical, and affordable it is advised to focus on somatic cell editing for clinical applications and restrict germinline editing as these are often cause for ethical and safety concerns. Additionally, by improving CRISPR precision to reduce off target effects, allows for less chance of medical complications, as well as taking information from long term studies to learn from potential side effects and make CRISPR-Cas9 safer. There has also been concern around consent and patient autonomy, it is important for researchers and doctors to provide a clear and comprehensive risk and disclose all information especially regarding uncertainties and long term effects. For more at-risk and vulnerable populations, additional protections should be given to ensure that they know what CRISPR-Cas9 is and its possible effects. It is also important that everyone who needs this technology has access to it, and not only wealthy populations. Insurance companies need to be informed and also should include these gene therapies in their coverage. To help fund CRISPR-Cas9, there should also be public funding available so that all populations have access to these therapies. Addressing the ethical criticism CRISPR-Cas9 citing the issue of eugenics and using gene therapies as enhancement, it is important for scientists to come to a consensus and make clear distinctions between what is therapy and what is enhancement, and for legislation to prohibit non-therapeutic genetic enhancements. Overall, to make CRISPR-Cas9 as safe as possible it is crucial for the public to be well educated on different gene editing technologies so everyone is able to make informed decisions about their health. There is also a responsibility for scientists, ethicists, and policy makers to facilitate debate amongst one another to continue to discuss how CRISPR-Cas9 can be made safer, more ethical, affordable, and more accessible to everyone.

Acknowledgment

Dr Garrick Louis – Systems Engineering Department at University of Virginia
Dr. Nare – Electrical and Computing Engineering Department at Hampton University

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