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Review Article

The Evolving Role of Genome Editing: A Societal Perspective

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Abstract

Genome editing technologies, particularly CRISPR-Cas, have revolutionized biomedical research and offer transformative potential in various fields. This review provides an in-depth exploration of the historical context, current applications, and societal implications of genome editing. The introduction of CRISPR-Cas in 2012 represented a major leap forward, simplifying and improving the accuracy of gene editing compared to older tools such as zinc-finger nucleases and transcription activator-like effector nucleases. This simplicity has hastened the uptake of genome editing technologies in both research and clinical environments, allowing researchers to delve deeper into gene function and disease mechanisms. CRISPR-Cas holds promise for treating genetic disorders like cystic fibrosis and sickle cell anemia, potentially providing more effective and less invasive therapies than conventional approaches. Despite the promise of genome editing in biomedical research and therapy, ethical, legal, and social considerations abound. The ability to edit the human germline raises ethical questions about the potential for designer babies and genetic enhancement. Ensuring equitable access to these technologies and preventing unintended consequences are paramount. Strong regulatory frameworks and policies are necessary to guide the safe, efficient, and ethical application of genome editing technologies. Global collaboration and ongoing dialogue among scientists, policymakers, and the public are essential for addressing these challenges. Societal perspectives play a crucial role in shaping policies and regulations to ensure that genome editing is used responsibly and ethically. In agriculture, genome editing offers solutions to challenges posed by climate change and microbial pathogens.

Gene editing in crops can improve resilience to environmental stressors and enhance nutritional value, contributing to food security and sustainability. Ethical considerations around genome editing, particularly in human germline editing for biomedical enhancement, raise complex issues. Dialogue and consensus building are essential to navigate these challenges and ensure that genome editing is used for the benefit of society as a whole. Taken together, genome editing holds immense promise for addressing global health and agricultural challenges. However, its responsible implementation requires careful consideration of ethical, legal, and societal implications, underscoring the need for collaborative governance frame works to guide its ethical and equitable application.

Introduction

Genome editing technologies, once nascent in the 1990s, have recently surged in popularity, largely due to the introduction of CRISPR-Cas tools in 2012 [1,2]. This technology has been transformative, with profound implications for both science and society [3,4]. Its simplicity compared to earlier tools like zinc-finger nucleases (ZFNs) and transcription activator-like effector nucleases (TALENs) has led to its rapid adoption and consideration for a variety of uses [5,6]. The precision of CRISPR-Cas in modifying genes has revolutionized biomedical research, accelerating our understanding of gene function and disease mechanisms [7,8]. This innovation offers promising ways to treat genetic diseases like cystic fibrosis and sickle cell anemia, potentially with greater effectiveness, and fewer side effects than traditional treatments [9,10]. While genome editing holds promise as a transformative therapy for patients, it is still in its early stages. These advancements also bring up ethical, legal and social considerations [11,12]. Concerns include the ethics of editing the human germline, ensuring fair access to these technologies, and preventing unintended consequences [13]. The fast development of genome editing highlights the necessity for strong regulatory frame works

and policies to guarantee its safe, efficient and ethical application [14]. Meeting these challenges necessitates global collaboration and continuous conversation among scientists, policy makers and the public [15,16]. As a result, the legal and ethical frameworks surrounding genome editing have yet to be comprehensively addressed and will become more critical as the technology progresses towards more controversial areas such as germline modification [17-19]. By approaching these issues from a societal viewpoint, we can navigate the intricacies of genome editing to guarantee that its advantages are ethically and fairly realized, ultimately shaping a more sustainable and equitable future [20].

Examining the changing role of genome editing through a societal lens is critical for several reasons. First, technologies like CRISPR-Cas9 have the potential to transform fields such as medicine, agriculture and biotechnology, offering new possibilities for treating genetic diseases, improving crop yields and developing novel biofuels, among other applications [21-23]. Understanding the societal impacts of these technologies is crucial for ensuring their responsible development and utilization. Second, genome editing raises ethical, legal and social implications(ELSI) that need to be addressed [24,25]. These concerns encompass the precise delivery to target cells, the effectiveness and accuracy of the editing process and the various methods of making DNA alterations, all of which pose significant bioethical challenges [26,27]. Nevertheless, the importance of genome editing technologies in medicine remains undeniable, despite the potential for unintended consequences such as off-target effects, and the ethical issues related to editing the human germline [28,29]. By considering these issues from a societal standpoint, we can shape policy and regulatory frameworks to guide the responsible advancement and application of genome editing [13-15].

Lastly, societal perspectives can help uncover and address public attitudes, values and preferences regarding genome editing [30]. Public engagement and dialogue are essential for building trust and ensuring that the benefits and risks of these technologies are well-understood and balanced appropriately [31]. Overall, exploring the evolving role of genome editing from a societal perspective is essential for fostering responsible innovation, addressing ELSI concerns and ensuring that these technologies benefit society as a whole [24,25]. Following this brief introduction, the remainder of the review will delve into the historical context of genome editing, its current applications and the societal impact of genome editing, along with a detailed examination of the regulatory landscape. These topics will be discussed in separate sections as the article progresses towards its conclusion.

From sequencing to editing: The evolution of genome technology

Our understanding of the human genome has undergone a profound evolution since the landmark sequencing efforts of 2003 [32]. The completion of the final, comprehensive human genome sequence, published across six papers in the April 1, 2022, issue of "Science," marked a pivotal moment in biotechnology [33]. This achievement not only signifies our ability to decode the intricate blueprint of human life but also represents a critical leap forward in our capacity to manipulate this genetic code through gene editing technologies. The release of the complete human genome sequence has ushered in a new era of biotechnological possibilities, enabling researchers to explore and potentially modify the genetic underpinnings of life with unprecedented precision. This milestone underscores the transformative power of genomics in shaping the future of medicine, agriculture and beyond [34,35]. Over the past three decades, genome-editing strategies have undergone significant evolution. Currently, four types of "programmable" nucleases are utilized worldwide, each with distinct characteristics and applications [36]. Mega nucleases, for example, are endonucleases that can recognize large DNA target sites spanning 12 to 45 base pairs [37,38]. Zinc finger nucleases, on the other hand, are artificial restriction enzymes created by fusing a zinc finger DNA-binding domain with a DNA-cleavage domain, providing a high degree of specificity in targeting [39,40]. Transcription activator-like effector nucleases(TALEN) are engineered restriction enzymes that offer precise editing capabilities [41,42]. The clustered regularly interspaced short palindromic repeats (CRISPR)/CRISPR-associated protein 9 (Cas9) system, perhaps the most well-known, allows for highly efficient and versatile genome editing by utilizing RNA-guided Cas9 nucleases to target specific DNA sequences [42-44]. Each of these technologies has its unique advantages and limitations, shaping the landscape of genome editing applications across various fields such as medicine, agriculture and biotechnology [45-47].

Gene editing is a potent instrument, especially advantageous when aimed at deleterious genes that present health hazards to organisms like humans, animals, or plants and their progeny [48]. In agriculture, gene editing facilitates the creation of crops that resist pests and diseases, thereby bolstering food security and diminishing dependency on chemical pesticides [49]. Additionally, gene editing shows potential in tackling food allergens, potentially eradicating risks linked to allergic responses [50]. In healthcare, gene editing has the potential to revolutionize the treatment of genetic disorders. Monogenic disorders, such as Duchenne Muscular Dystrophy (DMD), which affects approximately one in 3,500 young boys and often leads to early death, could benefit significantly from gene editing [51-53]. By targeting and correcting disease-causing mutations, gene editing offers hope for more effective treatments and, potentially, cures for such devastating conditions. Furthermore, the adaptability of gene editing technologies, such as CRISPR-Cas9, enables the precise and effective alteration of genetic material. For instance, CRISPR-Cas9 has been employed in numerous research endeavors to modify genes linked to ailments such as cancer and genetic disorders, showcasing its promise in targeted gene therapy [54-56]. This accuracy heralds fresh avenues for personalized medicine, wherein therapies can be customized to suit individual genetic compositions, thus optimizing effectiveness and minimizing adverse effects [57].

Human genome editing technologies have the potential to target different types of cells, each with its own implications and applications [58-60]. Somatic cell editing targets non-reproductive cells and is non-heritable, meaning any changes made will not be passed on to future generations [61]. This approach holds promise

for treating diseases by directly addressing the genetic causes within an individual's body, potentially curing or slowing down the spread of diseases. Germ line cell editing, on the other hand, can be divided into two categories: Editing of germ line cells not intended for reproduction and editing of germ line cells intended for reproduction [62]. Editing germ line cells not intended for reproduction can have therapeutic benefits by correcting genetic abnormalities that may affect an individual's health but will not be passed on to their offspring [63,64]. For example, studies have demonstrated that engineered nucleases, particularly CRISPR/Cas9, can be readily employed to edit genes in mammalian embryos, including those of mice, rats and even monkeys [65].

Current applications of genome editing: Advancements and implications

This section of the article offers a comprehensive examination of the cutting-edge advancements in genome editing technologies, exploring their multifaceted applications. It illuminates the diverse array of disciplines benefiting from these technologies, ranging from the medical realm, where they are revolutionizing the treatment of genetic disorders, to agriculture, where they are driving innovation in crop improvement. Additionally, the section explores the burgeoning impact of genome editing in biotechnology, showcasing its potential to reshape industries and address pressing global challenges. For example, in the medical field, sickle-cell disease (SCD) is a common inherited blood disorder that affects more than 6 million people worldwide, with about 75 percent of cases occurring in sub-Saharan Africa, where childhood mortality rates are high [66]. Recent clinical trials are exploring the potential of CRISPR/Cas9 gene editing as a treatment for SCD and transfusion-dependent ß-thalassemia (TDT) [67,68]. One such trial involved the use of CTX001, CRISPR/Cas9-edited CD34+ hematopoietic stem and progenitor cells (HSPCs), in two patients, one with TDT and the other with SCD [69]. The trial demonstrated early, significant and sustained increases in fetal hemoglobin levels, with more than 99 percent pan cellularity during a 12-month observational period. This suggests that the CRISPR-Cas9-edited HSPCs successfully engrafted and maintained adequate levels of fetal hemoglobin, highlighting the potential of CRISPR/Cas9 gene editing as a promising therapeutic approach for these inherited diseases.

Moreover, tumor evolution involves genetic mutations in genes like proto-oncogenes and tumor suppressor genes, which can be identified through genome sequencing technology [70]. These mutations serve as targets for the CRISPR/Cas9 system, forming the basis for CRISPR/Cas9-based clinical trials aimed at suppressing tumor metastasis in humans [71]. Furthermore, to address the limited application of patient-specific autologous CAR-T (chimeric antigen receptor T cells) cell therapy for treating cancer in a larger population, researchers have developed allogeneic universal CAR-T cells [72,73]. These cells are designed to be a one-size-fits-all solution, where the donor T lymphocytes undergo gene editing to eradicate their T cell receptor (TCR) and human leukocyte antigen (HLA). This modification reduces the risk of graft-versus-host disease (GVHD) by preventing the donor's CAR-T cells from reacting against the recipient's tissues. Instead, these engineered CAR-T cells can efficiently target and attack cancer cells, enhancing the effectiveness of the treatment [74]. While genome editing of disease-causing genes in non-reproductive somatic cells to treat human illnesses is widely accepted in the medical field, human heritable germ line genome editing (GGE) presents significant ethical, legal and social concerns [75]. These concerns have sparked intense debates and controversies, particularly in regions lacking clear regulatory frameworks, following the controversial case of the first "gene-edited babies." In this incident, researchers utilized in vitro fertilization (IVF) to edit the genomes of embryos using CRISPR/Cas9, targeting the CCR5 (C-C chemokine receptor type 5) gene to confer resistance to HIV [76]. The incident has prompted discussions about the ethical implications of using human GGE as a routine medical intervention in the future, with varying perspectives on its appropriateness and potential risks. In biotechnology and agriculture, the application of genome editing is crucial, especially in the face of challenges posed by climate change and microbial pathogens to agricultural systems, food security and human nutrition [77,78]. To combat these challenges, significant efforts have been directed towards gene editing in crops and livestock to improve their performance in traits essential for adapting to climate change. Successful applications of gene editing include using CRISPR/Cas9 to knockout OsRR22, a gene linked to salt susceptibility in rice [79]. Additionally, CRISPR/Cas9 has been used to modify flowering-related genes like Hd2, 4, and 5 in rice, resulting in plants that flower earlier, enhancing their ability to thrive in regions with long day lengths and cool temperatures, such as those at northern latitudes [80]. Another strategy involves inserting an alternative maize promoter before the ARGOS8 gene to enhance drought resistance in plants. Furthermore, CRISPR/Cas9 has been employed to knockout OsSWEET13 in rice, a gene responsible for encoding sucrose transporters that pathogens exploit for pathogenesis, leading to improved disease resistance [81,82]. Similarly, deleting the eIF4e (Eukaryotic translation initiation factor 4E) gene in cucumber using CRISPR/Cas9 has proven effective in preventing viral infections [83,84]. These examples underscore the potential of genome editing technologies in bolstering agricultural resilience to climate change and combating microbial pathogens, thereby contributing significantly to global food security and nutrition [85].

Societal implications of genome editing: Ethical considerations and cultural perspectives

The most compelling argument in support of the clinical application of human germ line genome editing is its potential to help parents with severe genetic diseases avoid passing them on to their children [86]. This technology also holds promise for reducing the risk of common diseases like cancer, diabetes, heart disease and multiple sclerosis [87]. Additionally, genome editing could be used for biomedical enhancement, such as introducing rare genetic features to enhance human capabilities, including extended lifespan, improved intelligence quotient and increased endurance [88]. However, biomedical enhancement involves making multiple edits, altering native gene expression and in many cases, replacing pieces of native DNA with synthetic DNA, which is currently not technically feasible in human embryos [89]. Biomedical enhancement presents ethical challenges distinct from those of repairing disease-causing

mutations in somatic or reproductive cells and requires careful consideration by society. Professional organizations, ethics boards and advisory panels, including the United States national academies of sciences, engineering, and medicine, support the therapeutic use of genome editing but oppose enhancement [89]. Moreover, enhancing complex traits like intelligence through genome editing is technically challenging, as intelligence is influenced by a large number of networked genes. This complexity increases the risk of "off-target" effects of gene editing systems [29].

For example, editing the normal CCR5 gene to confer immunity to HIV infection could potentially impact cognitive traits and psychosocial makeup, as CCR5 is known to play a role in cognitive functions such as memory [90]. Furthermore, any error in germ line genome editing to correct disease-causing genes or variants could have severe negative implications for future individuals. The consequences of genetic mosaicism, where cells within the same person have different genetic compositions, resulting from germ line genome editing, are difficult to predict and could pose significant risks [91,92]. GGE, particularly when aimed at biomedical enhancement, reignites the moral debate surrounding human genome editing, which has its roots in the eugenics movement of the 1950s [93,94]. This movement suggested that desirable genetic traits were not limited to specific races, ethnicities, or social classes but could be found across all groups. It advocated for the improvement of the human species by promoting reproduction among individuals with favorable traits and limiting reproduction among those with less desirable qualities. This perspective supports the idea of polygenic enhancements as the blueprint for human personalities and traits [95].

The debate over the permissibility of GGE to introduce new traits into embryos using synthetic DNA, which they would not naturally carry, remains unresolved. In contrast, correcting a mutated allele to a healthy "wild type" version, a process that occurs naturally in the human population, seems more logistically feasible and ethically appropriate [89]. Furthermore, the distinction between somatic and germ line gene editing has led to the emergence of bioethicists, who emphasize four critical public values: Beneficence (benefiting others), nonmaleficence (avoiding harm), respect for autonomy and justice [96]. According to Theodore Friedmann, a pioneer in somatic gene therapy, the need for efficient disease control or prevention, particularly in early development or inaccessible cells, may eventually justify germ line therapy [97]. For example, editing the somatic cells in a person's brain may be challenging due to the inaccessibility of brain cells. In contrast, modifying an embryo to have a genetically modified, disease-free brain would be more feasible [98]. Thus, bioethics values such as beneficence and nonmaleficence equally support both somatic modification to correct genetic diseases and germ line intervention to prevent them.

The evolving regulatory landscape: Navigating the complexities of genome editing

Implementing genome-editing technology in humans poses significant ethical challenges, considering various considerations such as pragmatic, sociopolitical and categorical issues. Pragmatic considerations focus on the medico-technological aspects, including safety, efficacy, risk–benefit ratio and alternative interventions. Sociopolitical aspects address the societal impact, aiming to reduce health interventional inequalities and address power asymmetries. Categorical considerations highlight barriers to certain aspects of technology implementation [11,12,17,18]. For instance, obtaining consent to modify human nature through genome editing may be challenging, regardless of technological advancements or changing sociopolitical conditions [99]. Therefore, policies regarding the use of genome editing should be guided by identifiable public interests, subjected to critical examination and achieve consensus democratically through broad and inclusive societal debate. One of the main societal concerns surrounding human gene editing, in addition to the safety of genomic changes, is the potential for increased disease burden among the population, especially affecting the economically, disadvantaged due to the high costs involved. This disparity raises fears that only the wealthy will have access to genome editing, leading to concerns that germ line editing could create a class of genetically privileged individuals. There is also uncertainty about whether health insurance companies would cover the costs of gene editing treatments, which could affect a broader segment of society [100,101].

The Nuffield report highlights two key principles for the use of germ line gene editing: protecting the welfare of future individuals and promoting social justice and solidarity [13]. Because germ line gene editing impacts future generations, there is a moral obligation to protect those not yet born. Social justice aims to ensure an equitable distribution of health interventions so that socially disadvantaged groups do not receive an unfair share of health benefits. Solidarity recognizes that society as a whole benefits when all individuals thrive [102]. Additionally, global perspectives on creating and altering life vary widely. Some countries' views are deeply influenced by their histories and religious traditions, with human control over genetics being a contentious issue. Despite its association with eugenics, the profound impact of genetics on lives can generate skepticism among many in society. As a result, the use of gene editing is likely to proceed at varying rates among countries, depending on their cultural and regulatory frameworks [11-15]. Additionally, germ line gene editing might contribute to a rise in medical tourism, where individuals seek more cost-effective treatment in countries with less stringent regulations [103]. Nonetheless, this trend could pose health hazards if treatments are offered prematurely and irresponsibly. Reproductive travel also raises concerns about legal obligations, such as liability for reproductive procedures performed in other countries in the event of complications [99].

The challenges are particularly evident in the context of biomedical enhancement through germ line gene editing, which necessitates strict regulatory supervision in the assisted reproductive technology (ART) clinics of the destination country to mitigate the heightened risk of adverse effects associated with polygenic interventions required for enhancements [100]. It is crucial that humanitarian considerations rather than market pressures guide decisions regarding the utilization of advanced technologies like human genome editing.

Conclusion and Future Direction

Despite the multitude of challenges and considerations associated with implementing genome editing technology for the human population, along with speculation regarding its potential as a mainstream health intervention, its successful implementation could have significant impacts on society. These impacts include: Population diversity- genome editing could potentially reduce or even eliminate some serious inherited diseases from a population; Perceptions of reproductive choices - Individuals initially hesitant to use genome editing may reconsider their reproductive options based on their expectations for their future children, leading to behavioral shifts; Attitudes towards disabled people - Techniques like pre-implantation genetic diagnosis (PGD), which provide information about genetic disorders to help with the selection of embryos or termination of pregnancies, can potentially impact the perception and treatment of disabled individuals in society [101-102].

Genome editing has experienced remarkable growth in recent years, holding significant promise for various medical applications such as cancer immunotherapy, infectious disease prevention and the treatment of hematological, metabolic, neurodegenerative and ocular disorders. The advent of different genome editing nucleases has revolutionized genomic engineering, enabling easy manipulation of the mammalian genome. However, despite the initial excitement surrounding CRISPR/Cas9 as a powerful gene editing tool, our understanding of its off-target effects remains limited, warranting further investigation. Another critical question is whether the body's immune system will accept or reject foreign genetic elements introduced during editing.

To fully realize the benefits of gene-editing technology, it requires support from governments, stakeholders, scientists, and physicians. This support is crucial for advancing healthcare and addressing challenges such as improving crop yields, enhancing nutritional values and combating food production losses due to climate change. These efforts align with Sustainable Development Goals (SDGs) aimed at reducing poverty (SDG1), improving human health (SDG3), increasing crop yield, enhancing nutrition (SDG2), and promoting sustainability, with a target achievement date of 2030 [103].

Moreover, there is a need for uniform international governance of genome editing to minimize the risk of misuse, especially in regions with limited regulatory oversight. A unified governance framework, led by the World Health Organization, can help harness the full potential of genome editing for the benefit of global society.

Conflict of Interest

The authors declare that there are no conflicts of interest regarding this work. The research was conducted without any commercial or financial relationships that could be perceived as potential conflicts of interest.

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References

1. Xu Y, Li Z (2020) CRISPR-Cas systems: Overview, innovations and applications in human disease research and gene therapy. Comput Struct Biotechnol J 18: 2401-2415.
2. Zhu Y (2022) Advances in CRISPR/Cas9. Biomed Res Int 2022: 9978571.
3. Ansori AN, Antonius Y, Susilo RJ, Hayaza S, Kharisma VD, et al. (2023) Application of CRISPR-Cas9 genome editing technology in various fields: A review. Narra J 3(2): e184.
4. Li C, Brant E, Budak H, Zhang B (2021) CRISPR/Cas: A Nobel prize award-winning precise genome editing technology for gene therapy and crop improvement. J Zhejiang Univ Sci B 22(4): 253-284.
5. Joung JK, Sander JD (2013) TALENs: A widely applicable technology for targeted genome editing. Nat Rev Mol Cell Biol 14(1): 49-55.
6. Khalil AM (2020) The genome editing revolution: Review. J Genet Eng Biotechnol 18(1): 68.
7. Watters KE, Kirkpatrick J, Palmer MJ, Koblentz GD (2021) The CRISPR revolution and its potential impact on global health security. Pathog Glob Health 115(2): 80-92.
8. Ebrahimi S, Khosravi MA, Raz A, Karimipoor M, Parvizi P (2023) CRISPR-Cas technology as a revolutionary genome editing tool: Mechanisms and biomedical applications. Iran Biomed J 27(5): 219-246.
9. Liu W, Li L, Jiang J, Wu M, Lin P (2021) Applications and challenges of CRISPR-Cas gene-editing to disease treatment in clinics. Precis Clin Med 4(3): 179-191.
10. Park SH, Bao G (2021) CRISPR/Cas9 gene editing for curing sickle cell disease. Transfus Apher Sci 60(1): 103060.
11. Ayanoğlu FB, Elçin AE, Elçin YM (2020) Bioethical issues in genome editing by CRISPR-Cas9 technology. Turk J Biol 44(2): 110-120.
12. Cribbs AP, Perera SMW (2017) Science and bioethics of CRISPR-Cas9 gene editing: An analysis towards separating facts and fiction. Yale J Biol Med 90(4): 625-634.
13. Halpern J, O'Hara SE, Doxzen KW, Witkowsky LB, Owen AL (2019) Societal and ethical impacts of germline genome editing: How can we secure human rights? CRISPR J 2(5): 293-298.
14. Conley JM, Davis AM, Henderson GE, Juengst ET, Meagher KM, et al. (2020) A new governance approach to regulating human genome editing. N C J Law Technol 22(2): 107-141.
15. Barbosa S, Pare TL, Thizy D, Vaz M, Carter L (2021) Engagement and social acceptance in genome editing for human benefit: Reflections on research and practice in a global context. Wellcome Open Res 5: 244.
16. Davies G, Gorman R, McGlacken R, Peres S (2022) The social aspects of genome editing: Publics as stakeholders, populations and participants in animal research. Lab Anim 56(1): 88-96.
17. Peng Y, Lv J, Ding L, Gong X, Zhou Q (2022) Responsible governance of human germline genome editing in China†. Biol Reprod 107(1): 261-268.
18. (2017) National academies of sciences, engineering, and medicine; national academy of medicine; national academy of sciences; committee on human gene editing: Scientific, medical, and ethical considerations. Human genome editing: science, ethics, and governance. Washington (DC): National Academies Press (US), USA.
19. Townsend BA (2020) Human genome editing: How to prevent rogue actors. BMC Med Ethics 21(1): 95.
20. Carroll D, Charo RA (2015) The societal opportunities and challenges of genome editing. Genome Biol 16: 242.
21. Parsaeimehr A, Ebirim RI, Ozbay G (2022) CRISPR-Cas technology a new era in genomic engineering. Biotechnol Rep (Amst) 34: e00731.
22. Liu Q, Yang F, Zhang J, Liu H, Rahman S, et al. (2021) Application of CRISPR/Cas9 in crop quality improvement. Int J Mol Sci 22(8): 4206.

23. Gajardo HA, Gómez EO, Boscariol FP, Carrer H, Bravo LA (2023) The Potential of CRISPR/Cas technology to enhance crop performance on adverse soil conditions. Plants (Basel) 12(9): 1892.

24. Bulger RE, Meyer BE, Fineberg HV (1995) Society's choices: Social and ethical decision making in biomedicine. Institute of Medicine (US) committee on the social and ethical impacts of developments in biomedicine. Washington (DC): National academies press (US). The Ethical, legal, and social implications program of the national center for human genome research: A missed opportunity?

25. Dolan DD, Lee SS, Cho MK (2022) Three decades of ethical, legal and social implications research: Looking back to chart a path forward. Cell Genom 2(7): 100150.

26. Lino CA, Harper JC, Carney JP, Timlin JA (2018) Delivering CRISPR: A review of the challenges and approaches. Drug Deliv 25(1): 1234-1257.

27. Rothschild J (2020) Ethical considerations of gene editing and genetic selection. J Gen Fam Med 21(3): 37-47.

28. Petraitytė G, Preikšaitienė E, Mikštienė V (2021) Genome editing in medicine: Tools and challenges. Acta Med Litu 28(2): 205-219.

29. Guo C, Ma X, Gao F, Guo Y (2023) Off-target effects in CRISPR/Cas9 gene editing. Front Bioeng Biotechnol 11: 1143157.

30. Critchley C, Nicol D, Bruce G, Walshe J, Treleaven T, et al. (2019) Predicting public attitudes toward gene editing of germlines: The impact of moral and hereditary concern in human and animal applications. Front Genet 9: 704.

31. Wilson BJ, Nicholls SG (2015) The human genome project, and recent advances in personalized genomics. Risk Manag Healthc Policy 8: 9-20.

32. Nurk S, Koren S, Rhie A, Rautiainen M, Bzikadze AV, et al. (2022) The complete sequence of a human genome. Science 376(6588): 44-53.

33. Hofker MH, Fu J, Wijmenga C (2014) The genome revolution and its role in understanding complex diseases. Biochim Biophys Acta 1842(10): 1889-1895.

34. Gonzaga JC, Lupski JR, Gibbs RA (2012) Human genome sequencing in health and disease. Annu Rev Med 63: 35-61.

35. Phan HTL, Kim K, Lee H, Seong JK (2023) Progress in and prospects of genome editing tools for human disease model development and therapeutic applications. Genes(Basel) 14(2): 483.

36. Epinat JC, Arnould S, Chames P, Rochaix P, Desfontaines D, et al. (2003) A novel engineered meganuclease induces homologous recombination in yeast and mammalian cells. Nucleic Acids Res 31(11): 2952-2962.

37. Zheng N, Li L, Wang X (2020) Molecular mechanisms, off-target activities and clinical potentials of genome editing systems. Clin Transl Med 10(1): 412-426.

38. Carroll D (2011) Genome engineering with zinc-finger nucleases. Genetics 188(4): 773-782.

39. Schierling B, Dannemann N, Gabsalilow L, Wende W, Cathomen T, et al. (2012) A novel zinc-finger nuclease platform with a sequence-specific cleavage module. Nucleic Acids Res 40(6): 2623-2638.

40. Forsyth A, Weeks T, Richael C, Duan H (2016) Transcription activator-like effector nucleases (TALEN)-mediated targeted DNA insertion in potato plants. Front Plant Sci 7: 1572.

41. Nemudryi AA, Valetdinova KR, Medvedev SP, Zakian SM (2014) TALEN and CRISPR/Cas genome editing systems: Tools of discovery. Acta Naturae 6(3): 19-40.

42. Kato IT, Takahashi G, Hsu S, Miyaoka Y (2018) Clustered regularly interspaced short palindromic repeats (CRISPR)/ CRISPR-associated protein 9 with improved proof-reading enhances homology-directed repair. Nucleic Acids Res 46(9): 4677-4688.

43. Alamillo JM, López CM, Martínez RFJ, Torralbo F, Bulut M, et al. (2023) Clustered regularly interspaced short palindromic repeats/CRISPR-associated protein and hairy roots: A perfect match for gene functional analysis and crop improvement. Curr Opin Biotechnol 79: 102876.

44. Zhou W, Yang J, Zhang Y, Hu X, Wang W (2020) Current landscape of gene-editing technology in biomedicine: Applications, advantages, challenges, and perspectives. MedComm 3(3): e155.

45. Wei X, Pu A, Liu Q, Hou Q, Zhang Y, et al. (2022) The bibliometric landscape of gene editing innovation and regulation in the worldwide. Cells 11(17): 2682.

46. Hsu PD, Lander ES, Zhang F (2014) Development and applications of CRISPR-Cas9 for genome engineering. Cell 157(6): 1262-1278.

47. De Graeff N, Jongsma KR, Johnston J, Hartley S, Bredenoord AL (2019) The ethics of genome editing in non-human animals: A systematic review of reasons reported in the academic literature. Philos Trans R Soc Lond B Biol Sci 374(1772): 20180106.

48. Komal J, Desai HR, Samal I, Mastinu A, Patel RD, et al. (2023) Unveiling the genetic symphony: Harnessing CRISPR-Cas genome editing for effective insect pest management. Plants (Basel) 12(23): 3961.

49. Brackett NF, Pomés A, Chapman MD (2022) New frontiers: Precise editing of allergen genes using CRISPR. Front Allergy 2: 821107.

50. Hotta A (2015) Genome editing gene therapy for Duchenne muscular dystrophy. J Neuromuscul Dis 2(4): 343-355.

51. Hanson B, Wood MJA, Roberts TC (2021) Molecular correction of Duchenne muscular dystrophy by splice modulation and gene editing. RNA Biol 18(7): 1048-1062.

52. Chey YCJ, Arudkumar J, Aartsma RA, Adikusuma F, Thomas PQ (2023) CRISPR applications for Duchenne muscular dystrophy: From animal models to potential therapies. WIREs Mech Dis 15(1): e1580.

53. Ding S, Liu J, Han X, Tang M (2023) CRISPR/Cas9-mediated genome editing in cancer therapy. Int J Mol Sci 24(22): 16325.

54. Lu X, Zhang M, Li G, Zhang S, Zhang J, et al. (2023) Applications and research advances in the delivery of CRISPR/Cas9 systems for the treatment of inherited diseases. Int J Mol Sci 24(17): 13202.

55. Begagić E, Bečulić H, Đuzić N, Džidić KA, Pugonja R, et al. CRISPR/Cas9-mediated gene therapy for glioblastoma: A scoping review. Biomedicines 12(1): 238.

56. Strianese O, Rizzo F, Ciccarelli M, Galasso G, D'Agostino Y, et al. (2020) Precision and personalized medicine: How genomic approach improves the management of cardiovascular and neurodegenerative disease. Genes (Basel) 11(7): 747.

57. Alagoz M, Kherad N (2020) Advance genome editing technologies in the treatment of human diseases: CRISPR therapy (Review). Int J Mol Med 46(2): 521-534.

58. Morshedzadeh F, Ghanei M, Lotfi M, Ghasemi M, Ahmadi M, et al. (2024) An update on the application of CRISPR Technology in clinical practice. Mol Biotechnol 66(2): 179-197.

59. Lotfi M, Morshedi RD, Mashhadi SS, Ashouri A, Mojarrad M, et al. (2023) Recent advances in CRISPR/Cas9 delivery approaches for therapeutic gene editing of stem cells. Stem Cell Rev Rep 19(8): 2576-2596.

60. Ishii T (2017) Germ line genome editing in clinics: The approaches, objectives and global society. Brief Funct Genomics 16(1): 46-56.

61. Rubeis G, Steger F (2018) Risks and benefits of human germline genome editing: An ethical analysis. Asian Bioeth Rev 10(2): 133-141.

62. Kang Y, Chu C, Wang F, Niu Y (2019) CRISPR/Cas9-mediated genome editing in nonhuman primates. Dis Model Mech 12(10): dmm039982.

63. Grosse SD, Odame I, Atrash HK, Amendah DD, Piel FB, et al. (2011) Sickle cell disease in Africa: a neglected cause of early childhood mortality. Am J Prev Med 41(6 Suppl 4): S398-405.

64. Abdelnour SA, Xie L, Hassanin AA, Zuo E, Lu Y (2021) The potential of CRISPR/Cas9 gene editing as a treatment strategy for inherited diseases.

Front Cell Dev Biol 9: 699597.

65. Frangoul H, Altshuler D, Cappellini MD, Chen YS, Domm J, et al. (2021) CRISPR-Cas9 gene editing for sickle cell disease and β-thalassemia. N Engl J Med 384(3): 252-260.

66. Germino WP, Hinds M, Le A, Chu R, Liu X, et al. (2022) Hematopoietic stem cell gene-addition/editing therapy in sickle cell disease. Cells 11(11): 1843.

67. Ciriello G, Magnani L, Aitken SJ, Akkari L, Behjati S, et al. (2024) Cancer evolution: A multifaceted affair. Cancer Discov 14(1): 36-48.

68. White MK, Khalili K (2016) CRISPR/Cas9 and cancer targets: Future possibilities and present challenges. Oncotarget 7(11): 12305-12317.

69. Ayala CM, Khericha M, Harris CM, Puig SC, Chen YY (2024) CAR-T cell manufacturing: Major process parameters and next-generation strategies. J Exp Med 221(2): e20230903.

70. Lonez C, Breman E (2024) Allogeneic CAR-T therapy technologies: Has the promise been met? Cells 13(2): 146.

71. Tang TCY, Xu N, Nordon R, Haber M, Micklethwaite K, et al. (2022) Donor T cells for CAR T cell therapy. Biomark Res 10(1): 14.

72. Ormond KE, Mortlock DP, Scholes DT, Bombard Y, Brody LC, et al. (2017) Human germline genome editing. Am J Hum Genet 101(2): 167-176.

73. Chen Q, Ma Y, Labude M, Schaefer GO, Xafis V, et al. (2021) Making sense of it all: Ethical reflections on the conditions surrounding the first genome-edited babies. Wellcome Open Res 5: 216.

74. Atia M, Jiang W, Sedeek K, Butt H, Mahfouz M (2024) Crop bioengineering via gene editing: Reshaping the future of agriculture. Plant Cell Rep 43(4): 98.

75. Hamdan MF, Karlson CKS, Teoh EY, Lau SE, Tan BC (2022) Genome editing for sustainable crop improvement and mitigation of biotic and abiotic stresses. Plants (Basel) 11(19): 2625.

76. Sheng X, Ai Z, Tan Y, Hu Y, Guo X, et al. (2023) Novel salinity-tolerant third-generation hybrid rice developed via CRISPR/Cas9-mediated gene editing. Int J Mol Sci 24(9): 8025.

77. Kishchenko O, Zhou Y, Jatayev S, Shavrukov Y, Borisjuk N (2020) Gene editing applications to modulate crop flowering time and seed dormancy. aBIOTECH 1(4): 233-245.

78. Shi J, Gao H, Wang H, Lafitte HR, Archibald RL, et al. (2017) ARGOS8 variants generated by CRISPR-Cas9 improve maize grain yield under field drought stress conditions. Plant Biotechnol J 15(2): 207-216.

79. Erdoğan İ, Cevher KB, Bilir Ö, Hong Y, Tör M (2023) Recent developments in CRISPR/Cas9 genome-editing technology related to plant disease resistance and abiotic stress tolerance. Biology (Basel) 12(7): 1037.

80. Chandrasekaran J, Brumin M, Wolf D, Leibman D, Klap C, et al. (2016) Development of broad virus resistance in non-transgenic cucumber using CRISPR/Cas9 technology. Mol Plant Pathol 17(7): 1140-11453.

81. Fidan H, Calis O, Ari E, Atasayar A, Sarikaya P, et al. (2023) Knockout of elF4E using CRISPR/Cas9 for large-scale production of resistant cucumber cultivar against WMV, ZYMV, and PRSV. Front Plant Sci 14: 1143813.

82. Smyth SJ (2022) Contributions of genome editing technologies towards improved nutrition, environmental sustainability and poverty reduction. Front Genome Ed 4: 863193.

83. Ranisch R, Trettenbach K, Arnason G (2023) Initial heritable genome editing: Mapping a responsible pathway from basic research to the clinic. Med Health Care Philos 26(1): 21-35.

84. Cwik B (2019) Moving beyond 'Therapy' and 'enhancement' in the ethics of gene editing. Camb Q Healthc Ethics 28(4): 695-707.

85. Zhou M, Greenhill S, Huang S, Silva TK, Sano Y, et al. (2016) CCR5 is a suppressor for cortical plasticity and hippocampal learning and memory. Elife 5: e20985.

86. Thorpe J, Osei OIA, Avigdor BE, Tupler R, Pevsner J (2020) Mosaicism in human health and disease. Annu Rev Genet 54: 487-510.

87. Queremel Milani DA, Chauhan PR (2023) Genetics, mosaicism. StatPearls [Internet]. Treasure Island (FL), USA.

88. Evans JH (2021) Setting ethical limits on human gene editing after the fall of the somatic/germline barrier. Proc Natl Acad Sci USA 118(22): e2004837117.

89. Allen GE (1989) Eugenics and American social history, 1880-1950. Genome 31(2): 885-889.

90. Sanchez RS, Gray JC, MacKillop J, Chen CH, Palmer AA (2018) The genetics of human personality. Genes Brain Behav 17(3): e12439.

91. Cheraghi R, Valizadeh L, Zamanzadeh V, Hassankhani H, Jafarzadeh A (2023) Clarification of ethical principle of the beneficence in nursing care: An integrative review. BMC Nurs 22(1): 89.

92. McCain J (2005) The future of gene therapy. Biotechnol Healthc 2(3): 52-60.

93. Saha K, Sontheimer EJ, Brooks PJ, Dwinell MR, Gersbach CA, et al. (2021) The NIH somatic cell genome editing program. Nature 592(7853): 195-204.

94. Koralesky KE, Sirovica LV, Hendricks J, Mills KE, Von KMAG, et al. (2023) Social acceptance of genetic engineering technology. PLoS One 18(8): e0290070.

95. Subica AM (2023) CRISPR in public health: The health equity implications and role of community in gene-editing research and applications. Am J Public Health 113(8): 874-882.

96. Witkowsky L, Norstad M, Glynn AR, Kliegman M (2023) Towards affordable CRISPR genomic therapies: A task force convened by the Innovative Genomics Institute. Gene Ther 30(10-11): 747-752.

97. Ruger JP (2004) Health and social justice. Lancet 364(9439): 1075-1080.

98. Rosemann A, Balen A, Nerlich B, Hauskeller C, Sleeboom FM, et al. (2019) Heritable genome editing in a global context: National and international policy challenges. Hastings Cent Rep 49(3): 30-42.

99. Storrow RF (2011) Assisted reproduction on treacherous terrain: The legal hazards of cross-border reproductive travel. Reprod Biomed Online 23(5): 538-545.

100. Macpherson I, Roqué MV, Segarra I (2019) Ethical challenges of germline genetic enhancement. Front Genet 10: 767.

101. Eyisoy ÖG, Özgökçe Ç, Uygur L, Eriç ÖM, Taşdemir Ü, et al. (2023) Clinical and genetic aspects of termination of pregnancy; tertiary center experience. Turk J Obstet Gynecol 20(3): 234-241.

102. Flinter FA (2001) Preimplantation genetic diagnosis. BMJ 322(7293): 1008-1009.

103. Zhao W, Yin C, Hua T, Meadows ME, Li Y, et al. (2022) Achieving the sustainable development goals in the post-pandemic era. Humanit Soc Sci Commun 9(1): 258.