OPEN ACCESS

Middle East Research Journal of Medical Sciences
ISSN: 2789-7699 (Print) & ISSN: 2958-2024 (Online)
Frequency: Bi-Monthly
DOI: https://doi.org/10.36348/merjms.2026.v06i05.001

KUWAIT SCHOLARS PUBLISHER
Website: http://www.kspublisher.com/
Email: office@kspublisher.com

Artificial Intelligence Integration into Gene Editing: Prospects, Challenges and Therapeutic Applications: Review Article

Hussein R. Mahmood[1*]
[1]Dept. of Pathological Analyses, College of Sciences, University of AI-Qadisiyah, Diwaniyah, Iraq

Abstract: In gene editing, CRISPR-Cas9 has revolutionized the field and led to advancements such as base editing and prime editing. This decade's most significant advancement was the creative convergence of these technologies with artificial intelligence (AI) techniques, particularly deep learning and large language models. The goal of this comprehensive review article is to review the key aspects of accelerated integration, including how to design sgRNA, predict off-target effects, engineer Cas proteins, and discover new genomic editors designed with generative artificial intelligence. In addition, it explores practical therapeutic applications, including regulatory-approved treatments like Casgevy for sickle cell anemia, as well as the ethical and regulatory issues related to this convergence. Accumulating evidence suggests that AI is no longer merely an aid but a fundamental pillar in the entire gene editing development cycle, with promising prospects for virtual cell models and the complete automation of gene editing experiments.

Keywords: Gene editing, CRISPR-Cas9, Artificial Intelligence, Deep Learning, Baseline Editing, Large Language Models, AlphaFold, Gene Therapy.

Review Paper

***Corresponding Author:**
Hussein R. Mahmood
Dept. of Pathological Analyses, College of Sciences, University of AI-Qadisiyah, Diwaniyah, Iraq

How to cite this paper:
Mahmood, H. R. (2026). Artificial Intelligence Integration into Gene Editing: Prospects, Challenges and Therapeutic Applications: Review Article. *Middle East Res J. Med. Sci, 6*(5), 302-307. https://doi.org/10.36348/merjms.2026.v06i05.001

Article History:
| Submit: 25.07.2026 |
| Accepted: 27.08.2026 |
| Published: 02.09.2026 |

1. INTRODUCTION

Gene editing is one of the most dynamic fields in contemporary molecular biology. Since the advent of CRISPR-Cas9, described in 2012 by Jennifer Doudna and Emmanuelle Charpentier [1], who were awarded the 2020 Nobel Prize in Chemistry for this discovery. Genome editing has transformed into a well-established technology with broad medical, agricultural, and industrial applications. Tools have rapidly evolved to include baseline and major editing, as well as Cas12 and Cas13 systems with distinct properties [2]. With the increasing volume of genomic data and the growing complexity of precise design requirements, artificial intelligence (AI) has become an indispensable partner. As a result of AI, not only have existing tools been improved, but also a number of unprecedented possibilities have opened up, including the design of entirely new Cas proteins [3, 4], the prediction of editing outcomes before experimental implementation [5, 6], and the automation of the entire experimental design process [7]. The AlphaFold protein structure prediction system, which won the Nobel Prize in Chemistry in 2024, is one example of how AI can revolutionize biology [8, 9]. The purpose of this review is to provide a comprehensive and systematic review of the intersection between artificial intelligence (AI) and gene editing, drawing on peer-reviewed papers (Nature, Nature Reviews Genetics, Science, Advanced Science, The Lancet, etc.), while also exploring ethical and regulatory issues related to the emerging field.

2. GENOME EDITING TOOLS

CRISPR-Cas9: Principles and Evolution

In CRISPR-Cas9 systems, two main components are crucial to their operation: double nuclease Cas9 proteins, and single-stranded guide RNAs (sgRNAs) that direct the proteins towards target genes [1]. DNA double-cuts are repaired using either mutagenic non-heterozygous end joining (NHEJ) or directed DNA repair (HDR). As a result of rapid advances in the field, a second generation of tools has been developed, including base editing, which modifies specific nitrogenous bases without causing a double break, as well as prime editing, which uses Cas9 nexase activity and reverse transcriptase to achieve precise modifications without breaking the two strands completely [10]. By editing messenger RNA (mRNA), the CRISPR-Cas13 system can target gene expression

directly below the genome, opening up new therapeutic possibilities.

Fundamental Challenges of Genome Editing

Despite its enormous potential, genome editing technologies face fundamental challenges that limit their widespread clinical application. Foremost among these are off-target effects, where breaks in sequences similar to the target can occur, leading to serious mutations [5, 6]. Added to this are the challenges of delivery within living cells and tissues, and the need to improve the design of sgRNAs to increase their effectiveness against the target. These very challenges have made artificial intelligence a pivotal partner in the development cycle [12-14].

3. ARTIFICIAL INTELLIGENCE METHODOLOGIES IN GENE EDITING

Deep Learning and SgRNA Design

Doench *et al*., (2016) [5], laid the methodological foundation for sgRNA optimization using logistic regression models, before DeepCRISPR (Chuai *et al.,* 2018) [6]. Brought convolutional neural networks (CNNs) to higher predictive accuracy. The AttnToMismatch_CNN model (Li *et al*., 2019) [15] added attention mechanisms to predict off-target effects, while a review by Winter *et al*., (2025) [12], found that modern Transformer models improve on-target editing rates by 30–60% compared to manual design.

Engineering Cas Proteins with Structure Models

The AlphaFold2 (Jumper *et al*., 2021) [8], winner of the 2024 Nobel Prize in Chemistry – revolutionized the prediction of the three-dimensional structure of proteins, a feat extended with AlphaFold3 (Abramson *et al*., 2024) [9], to include Cas-sgRNA-DNA complex interactions. In the engineering field, ProMEP (Cheng *et al*., 2024) [16], employed a language model trained on 160 million proteins to guide Cas9 mutations and improve baseline editing efficiency, while Madugula *et al*., (2025) [17], revealed allotropic response networks in Cas9 using structural machine learning, paving the way for high-precision variants with low side effects.

Generative Design and Discovery of New Editors

Ruffolo and Madani (2024) [18], employed large-scale language models to generate OpenCRISPR-1, a functional gene editor that carries hundreds of mutations compared to its nearest natural counterpart while maintaining or exceeding its efficiency. In Nature 2025, the same team documented the generation of 4.8 times the diversity of natural CRISPR-Cas proteins. In the discovery field, Altae-Tran *et al*., (Science 2023) [19], revealed previously unknown CRISPR systems using terabyte-scale clustering, while Yoon *et al*., (Science 2024) [20], identified ancestral Cas13 ribonucleases using structural guidance.

Experimental Automation: Agentic AI

The CRISPR-GPT system (Qu *et al*., 2025) [7], represents a significant step toward automating the genome editing research cycle. The system utilizes sequentially operating LLM agents that automatically analyze the researcher's request, select the appropriate genetic target, design the sgRNA, determine the optimal delivery method, and interpret experimental results [7]. In independent evaluation, the system has demonstrated performance comparable to or exceeding that of human experts in standard design tasks, thereby reducing barriers to specialization and accelerating the scientific discovery cycle.

Table 1: The most prominent artificial intelligence tools used in genome editing

Tool/Model	Type	Main Function	Reference
DeepCRISPR	CNN(ML)	Efficiency prediction and design optimization sgRNA	[6] Chuai *et al.,* 2018
Rule Set 2 (RS2)	ML (Logistic regression)	Optimization for sgRNA SpCas9	Doench *et al.,*[5] 2016
AttnToMismatch_CNN	CNN+Attension mechanism	Off-target effects predicyion	Liu [15] *et al.,* 2019
AlphaFold 2	Transformer/Diffusion model	Protein three dimensional structure prediction	Jumper *et al.,*[8] 2021
AlphaFold 3	Developed difussion models	Protein, RNA, DNA and ligands structure prediction and interaction	Abramson *et al.,*[9] 2024
ProteinMPNN	Graph neural networks (GNN)	Novel protein sequences design	Dauparas *et al.,*[22] 2022
RFdiffusion	Difussion models	Design of de novo Protein structure	Watson *et al.,* [21] 2023
ProMEP	Protein language model	Mutation effects prediction and Cas9 engineering	Cheng *et al.,* 2024 [16]
OpenCRISPR-1	LLM(Large language model)	CRISPReditors de nova design	Ruffolo & Madani, 2024 [18]

CRISPR-GPT	LLM (Agentic)	Automation of genome editing experiment design	[7] Qu *et al.,* 2025

4. THERAPEUTIC APPLICATIONS: FROM THE LABORATORY TO THE HOSPITAL BED

Sickle Cell Anemia and Beta Thalassemia — the First Approved CRISPR Treatments

December 2023 marked a turning point when the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) approved Casgevy (exagamglogene autotemcel) for the treatment of sickle cell anemia and beta thalassemia [23, 24]. This treatment works by inhibiting the erythroid enhancer of the BCL11A gene in hematopoietic stem cells (HSCs), leading to increased production of fetal hemoglobin (HbF), which compensates for the defective hemoglobin. Sickle cell anemia is caused by a single point mutation (A→T) in the beta globin gene that results in the substitution of glutamate for valine, leading to the formation of hemoglobin polymers and blood vessel blockage [25].

Basal Editing in T-ALL Treatment

In 2022–2023, a UK research group performed a pioneering treatment on two children with T-cell acute lymphoblastic leukemia (T-ALL) using basally edited CAR-T cells [12]. The procedure involved simultaneous multiple modifications to several genes: removal of the endogenous T cell receptor to avoid graft-versus-host disease (GvHD), inactivation of the CD7 surface antigen gene, and inhibition of autolysis among the treatment cells. This type of multiple modification requires extensive computational support with artificial intelligence to ensure that the different sgRNAs do not interfere and to predict intercellular interactions [12-26]. Both cases achieved complete remission without the development of graft-versus-host disease or acute toxicity.

Gene Therapy for Hereditary Deafness (OTOF)

The Lancet published in May 2024 the results of a clinical trial by Lv *et al*., [27], in which gene insertion using an AAV viral vector approach was used to treat spontaneous hereditary deafness (DFNB9) caused by mutations in the OTOF gene in six children aged 1 to 6 years [27]. A single viral injection into the cochlea resulted in restored hearing and significant improvement in speech perception in five children (83.3%) without serious side effects. Artificial intelligence models contributed to the analysis of genomic outcomes, the assessment of delivery safety, and the optimization of the AAV vector's operational design.

Oncology Therapy — the Next Horizon

Although CRISPR therapy has shown remarkable success in hematology, solid tumors remain difficult to treat due to delivery hurdles inside the tumor and complex immune microenvironments [6-26]. Artificial intelligence (AI) can assist in identifying optimal genetic targets for each tumor as part of a precision medicine approach, as well as designing enhanced CAR-T modalities that adapt to the immune response of the tumor [26], according to the report Computers in Biology and Medicine (2024). Using AI with multilevel data (Multiomics) can help predict tumor response to gene therapy.

Table 2: The most prominent therapeutic applications of AI-assisted genome editing

Disease	Technology	AI role	Regulation state	Reference
Sickle Cell Anemia	CRISPR-Cas9 (Casgevy)	Off-target effects prediction and sgRNAoptimization for BCL11A	FDA/EMA 2023	[23,24]
Beta Thalassemia	CRISPR-Cas9 (Casgevy)	Editiong proficiency and safty improvement	FDA/EMA 2023	[24]
T-ALL	Base editing+ CAR-T	Multiplex simultanous edits design	Sucessful clinical experiments	[12]
OTOF	Gen addition (AAV)	Genomic results analysis and safty assessment	Lancet 2024	[27]
Solid tumors	CRISPR + CAR-(AI) T	Identification of targets and therapeutic cell optimization	Continous clinical experiments	[6,26]
Duchenne muscular dyatrophy(DMD)	CRISPR Exon Skipping	Design of sgRNA and efficiency optimization	clinical experiments	[10]

5. ETHICAL AND ORGANIZATIONAL CHALLENGES AND CONSIDERATIONS

Technology Challenges

Off-target effects present a key technical challenge. There have been significant advances in prediction models [5-11], but detecting all effects within the full genomic context of a living cell remains a challenge. Dixit *et al*., (2024), it was found that bias in training data causes AI models to be less generalizable, since they are trained on datasets that represent a limited number of human cells or disease types. Further, explainability is still a significant problem, because deep

models often omit to explain what drives their recommendations, which makes them unsuitable for clinical settings [20-28]. Drug safety professionals face unique challenges when it comes to pharmacovigilance when dealing with gene therapies since delayed side effects may occur with short clinical trials that go undetected, according to the Drug Safety Report (2025). The report presents an AI-based pharmacovigilance model that detects salivary signals early by analyzing real-world data.

Ethical Challenges

Increasing automation and simplicity in gene editing contribute to fundamental ethical concerns. Gene editing of germ cells is highly sensitive both from an ethical and philosophical perspective. During 2018, He Jiankui was the subject of controversy, illustrating the inadequacy of current governance frameworks to keep up with rapid technological advancements [30]. Casgevi is more expensive than its competitor, Levgenia, between US$3.1 and US$3.5 million per patient [31]. In low- and middle-income countries with sickle cell disease and thalassemia, treatment access appears to be limited [29]. The World Health Organization recommends a comprehensive governance system to ensure equitable access to treatment. A major challenge with gene therapies is getting informed consent from patients, because they may not understand all the technical complexities associated with permanent gene editing, as noted by Patel and Ko (Curious, 2025). A further question arises when artificial intelligence is integrated into medical decision-making: Is the algorithm accountable for errors or is it the physician?

Privacy of Genomic Data

Informed consent and careful data management are required when training AI models on large-scale genomic data [28]. Since the human genome contains information about an individual, their family, and future generations, genomic data raises exceptional privacy concerns. In genomic data banks, races and ethnicities are underrepresented, which causes bias in AI models and undermines their generalizability [26-28].

6. FUTURE PROSPECTS

Virtual Cell Models

Computer models that are capable of simulating how a living cell responds to a specific gene modification, including its effects on transcription, translation, signaling networks within the cell, and gene-gene interactions, represent the pinnacle of this integration. A review by Winter *et al*., [12], indicates that these models will enable the selection of target genes and the prediction of modification outcomes within the context of the whole cell, reducing the need for extensive experimental testing prior to animal studies [6]. This vision complements initiatives to reduce the use of animals in biomedical research (the principles of substitution, reduction, and optimization).

AI-Powered Precision Genomic Medicine

The integration of artificial intelligence with multi-level individual patient data (genomics, proteome, metabolome, and microbiome) leads to the diagnosis of disease-causing mutations with unprecedented accuracy and the design of personalized gene-editing protocols for each patient [13-28]. This approach forms the core of the future of precision genomic medicine, where intervention success rates increase and side effects decrease as a result of precisely tailored protocols.

Discovering New Generations of Genome Editing Tools

The biological landscape still abounds with vast families of unexplored Cas proteins. Artificial intelligence, through the analysis of massive (terabyte) metagenomic data, enables the discovery of new CRISPR-Cas systems [19], and allows for pushing beyond the limits of natural evolution to design editing tools with ideal properties: small size for easy viral delivery (AAV encapsulation), high accuracy, and modifiability with small molecular catalysts [3, 4]. This capability is crucial in overcoming the size limitations that restrict the delivery of the large SpCas9 protein by AAV vectors.

7. FINDINGS AND CONCLUSION

Based on the findings of this comprehensive review, the integration of artificial intelligence with genome editing represents not merely an incremental improvement, but a structural change in the course of scientific research and therapeutic development. As part of the entire genome editing lifecycle from tool design to therapeutic application, AI provides predictive efficiency, generative discovery, and rapid development. This integration has moved beyond theoretical promise to practical realization in human patients with Casgevy approval, basal editing successes, and gene therapy successes. The scientific leap, on the other hand, requires rigorous ethical and regulatory oversight: ensuring equitable access to expensive treatments, making AI algorithms transparent, ensuring genomic data governance transparent, and establishing effective international frameworks. The most powerful guarantee that this science will deliver on its promises in a just, sustainable, and responsible manner remains the ongoing dialogue between scientists, clinicians, policymakers, and the communities concerned. An unregulated technological arms race poses the greatest dangers.

RECOMMENDATIONS

- The development of gene-editing models that can be explained should be prioritized over black boxes, which have risks in medical settings.
- Expanding and diversifying genomic databases: Current AI models tend to favor European and American genomes. The recommendation is to build databases that represent all races and ethnicities, especially African, Asian, and Arab communities, which suffer from diseases such as sickle cell anemia and thalassemia.
- Studies of off-target effects should be intensified: In order to develop more accurate and comprehensive models of off-target effects within the whole-cell genomic context, with systematic experimental validation of these models across multiple cell types, specialized research should be funded. Enhancing Virtual Cell Models: Research should focus on developing comprehensive cell simulators that will allow gene-editing results to be tested in a computational environment before moving forward with human or animal trials. In this way, animal models are reduced in cost and reliance.
- Opening Scientific Resources and AI Tools: It is recommended to adopt the principles of Open Science in this field. Making AI models and datasets available to the wider scientific community, similar to Profluent's release of OpenCRISPR-1, will accelerate discovery and reduce the disparity between large and small research centers.

REFERENCES

1. Doudna JA, Charpentier E. A programmable dual-RNA-guided DNA endonuclease in adaptive bacterial immunity. Science. 2012;337:816–821. https://doi.org/10.1126/science.1225829
2. Anzalone AV, Koblan LW, Liu DR. Genome editing with CRISPR-Cas nucleases, base editors, transposases and prime editors. Nat Biotechnol. 2020;38(7):824–844. doi:10.1038/s41587-020-0561-9.
3. Ruffolo JA, Madani A. Designing proteins with language models. Nat Biotechnol. 2025;43:396–405. doi:10.1038/s41587-024-02123-4.
4. Ruffolo JA, Nayfach S, Gallagher J, Bhatnagar A, Beazer J, Hussain R, et al. Design of highly functional genome editors by modelling CRISPR–Cas sequences. Nature. 2025;645:518–525. doi:10.1038/s41586-025-09298-z.
5. Doench JG, Fusi N, Sullender M, Hegde M, Vaimberg EW, Donovan KF, *et al.,* Optimized sgRNA design to maximize activity and minimize off-target effects of CRISPR–Cas9. Nat Biotechnol. 2016;34(2):184–191. doi:10.1038/nbt.3437.
6. Chuai G, Ma H, Yan J, Chen M, Hong N, Xue D, *et al.,* DeepCRISPR: optimized CRISPR guide RNA design by deep learning. Genome Biol. 2018;19:80. doi:10.1186/s13059-018-1459-4.
7. Qu Y, *et al.,* CRISPR-GPT for Agentic Automation of Gene Editing Experiments. bioRxiv. 2025. doi:10.1101/2024.04.25.591003.
8. Jumper J, Evans R, Pritzel A, Green T, Figurnov M, Ronneberger O, *et al.,* Highly accurate protein structure prediction with AlphaFold. Nature. 2021;596(7873):583–589. doi:10.1038/s41586-021-03819-2.
9. Abramson J, Adler J, Dunger J, Evans R, Green T, Pritzel A, *et al.,* Accurate structure prediction of biomolecular interactions with AlphaFold 3. Nature. 2024;630(8016):493–500. doi:10.1038/s41586-024-07487-w.
10. Anzalone AV, Koblan LW, Liu DR. Genome editing with CRISPR-Cas nucleases, base editors, transposases and prime editors. Nat Biotechnol. 2020;38:824–844. https://doi.org/10.1038/s41587-020-0561-9
11. Cox DBT, Gootenberg JS, Abudayyeh OO, Franklin B, Kellner MJ, Joung J, *et al.,* RNA editing with CRISPR–Cas13. Science. 2017;358(6366):1019–1027. doi:10.1126/science.aaq0180.
12. Winter J, Shirguppe S, Perez-Pinera P. Harnessing artificial intelligence to advance CRISPR-based genome editing technologies. Nature Reviews Genetics. 2025. DOI: 10.1038/s41576-025-00907-1.
13. Li Z, *et al.,* From Code to Life: The AI-Driven Revolution in Genome Editing. Advanced Science. 2025;12:2417029. DOI: 10.1002/advs.202417029.
14. Pindi S, Palermo G. Computation and deep-learning-driven advances in CRISPR genome editing. Nature Structural & Molecular Biology. 2026. DOI: 10.1038/s41594-025-01739-7.
15. Liu Q, He D, Xie L. Prediction of off-target specificity and cell-specific fitness of CRISPR-Cas system using attention boosted deep learning and network-based gene feature. PLoS Comput Biol. 2019;15(10):e1007480. doi:10.1371/journal.pcbi.1007480.
16. Cheng Y, et al. AI-guided Cas9 engineering provides an effective strategy to enhance base editing. Mol Syst Biol. 2025. https://doi.org/10.1038/s44320-025-00142-0
17. Madugula SS, *et al.,* Structure-Based Classification of CRISPR/Cas9 Proteins: A Machine Learning Approach to Elucidating Cas9 Allostery. bioRxiv. 2025. https://doi.org/10.1101/2025.04.05.647395
18. Ruffolo JA, Madani A. Designing proteins with language models. Nat Biotechnol. 2024;43:396–4051. https://doi.org/10.1038/s41587-024-02123-4
19. Altae-Tran H, *et al.,* Uncovering the functional diversity of rare CRISPR–Cas systems with deep terascale clustering Science. 2023;382:eadi1910. https://doi.org/10.1126/science.adi1910
20. Yoon PH, *et al.,* Structure-guided discovery of ancestral CRISPR–Cas13 ribonucleases. Science.

2024;385:538543. https://doi.org/10.1126/science.adk9018
21. Watson JL, Juergens D, Bennett NR, *et al.,* De novo design of protein structure and function with RFdiffusion. Nature. 2023;620:108989–1100. https://doi.org/10.1038/s41586-023-06415-8
22. Dauparas J, Anishchenko I, Bennett N, et al. Robust deep learning–based protein sequence design using ProteinMPNN. Science. 2022;378:49–56. https://doi.org/10.1126/science.add2187
23. Patel A, Kuo A. The Ethics of Gene Therapy for Sickle Cell Disease. Cureus. 2025;17(3):e81037. https://doi.org/10.7759/cureus.81037
24. Bhatt DL, *et al.,* Realising gene therapy: a biomedical challenge. eBioMedicine. 2024;105:105299 https://doi.org/10.1016/j.ebiom.2024.105299
25. World Health Organization. Human genome editing: recommendations of the WHO Expert Advisory Committee. Geneva: World Health Organization; 2021. ISBN 978-92-4-003038-1. Available from: https://www.who.int/publications/i/item/9789240030381
26. Dixit S, Kumar A, Srinivasan K, Patel V, Sharma A, *et al.,* Advancing genome editing with artificial intelligence: opportunities, challenges, and future directions. Front Bioeng Biotechnol. 2024;11:1335901. doi:10.3389/fbioe.2023.1335901.
27. Lv J, *et al.,* Hearing restoration in children with hereditary deafness using adeno-associated virus gene therapy [OTOF]. The Lancet. 2024.
28. Al-Kahtani A, *et al.,* Integration of Artificial Intelligence and Genome Editing System for Determining the Treatment of Genetic Disorders. Balkan Med J. 2024. PMC11589204.
29. Schwarzbich M-A, *et al.,* Pharmacovigilance in Cell and Gene Therapy: Evolving Challenges in Risk. Management. Drug Saf. 2025. https://doi.org/10.1007/s40264-025-01596-9
30. Swiss Institute of AI. Gene Editing Access at a Crossroads: From Breakthroughs to a Public Playbook202. https://siai.org
31. U.S. Food and Drug Administration. FDA approves first gene therapies to treat patients with sickle cell disease. FDA Press Release. December 8, 2023. Available from: https://www.fda.gov/news-events/press-announcements/fda-approves-first-gene-therapies-treat-patients-sickle-cell-disease.