



CRISPR-CAS9 and Artificial Intelligence: Shaping the Future of Precision Crop Improvement

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ABSTRACT

The increasing demand for sustainable and resilient crop production has accelerated the development of precision breeding technologies. Conventional breeding remains essential, but limited genetic diversity, complex traits and lengthy breeding cycles highlight the need for complementary approaches. CRISPR-based genome editing enables targeted genetic modification, while advances such as base editing, prime editing, promoter editing and multiplex editing have expanded its potential in crop improvement. Artificial intelligence (AI) and machine learning can complement these technologies by analysing genomic, phenotypic and multi-omics datasets, identifying candidate targets, assisting guide RNA design and predicting editing outcomes. This article reviews the emerging integration of AI with CRISPR-based genome editing for precision crop improvement, with applications in climate resilience, disease resistance, nutritional quality, yield-related traits and de novo domestication. A recent rice study using an AI-designed OpenCRISPR-1 nuclease highlights the growing potential of computational approaches in plant genome engineering. The article also discusses current challenges, including data quality, model reliability, biological complexity, delivery, experimental validation and regulatory considerations. Overall, integrating AI with genomics and genome editing could provide a more precise and data-driven framework for crop improvement, provided that computational predictions are supported by rigorous experimental and field validation.

Keywords: Artificial intelligence, base editing, CRISPR-Cas9, genome editing, guide RNA design, machine learning, prime editing.

1. Introduction

Global agricultural production has increased considerably over recent decades with wheat, maize, rice and soybean contributing substantially to global food calories (FAO, 2017; Cassman & Grassini, 2020). Conventional breeding has contributed greatly to yield improvement but limited genetic diversity and long breeding cycles can restrict further progress (Searchinger *et al.*, 2019; Gao, 2021). As yield gains in major crops begin to slow, advanced technologies such as genomics, CRISPR-based genome editing and artificial intelligence are gaining importance for developing improved and resilient crops (Saini *et al.*, 2025; Tuncel *et al.*, 2025).

Among these technologies, CRISPR-Cas systems have become important tools for plant genome engineering. CRISPR-Cas9 can introduce targeted changes in DNA and has been applied to investigate gene function and modify agriculturally important traits. The CRISPR toolbox has also expanded to include base editing, prime editing, promoter editing and other approaches for more precise genome modification (Tuncel *et al.*, 2025).

At the same time, artificial intelligence (AI) and machine learning are providing new methods for analysing large biological datasets. Their integration with genome editing can support target identification, guide RNA design, prediction of editing outcomes and analysis of complex gene–trait relationships (Saini *et al.*, 2025).

2. CRISPR-Cas9 and plant genome editing

CRISPR-Cas9 is a genome-editing system in which a guide RNA directs the Cas9 nuclease to a complementary DNA sequence. Cas9 introduces a DNA break at the selected site, after which the cell's repair machinery can generate a genetic modification (Bhalerao *et al.*, 2025).

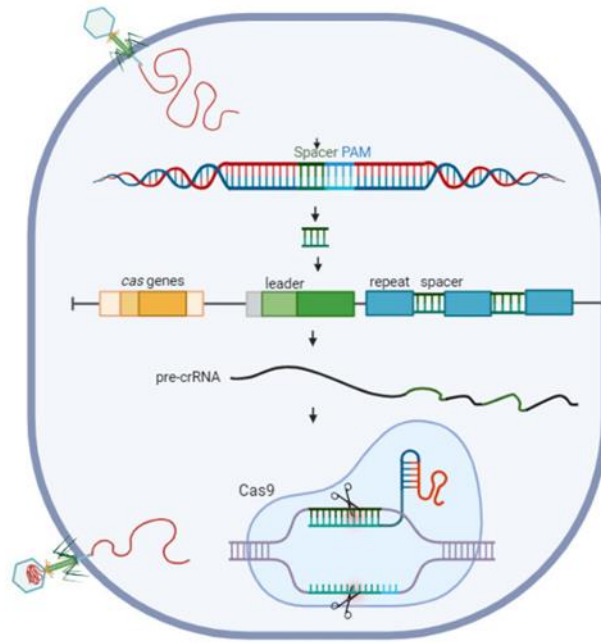


Fig. 1: Molecular Basis of CRISPR/Cas9-Mediated Genome Editing (Bhalerao *et al.*, 2025)

The programmability and versatility of CRISPR-Cas9 have made it a valuable tool for plant functional genomics and crop improvement. Genome editing can be used to investigate genes associated with disease resistance, abiotic stress responses, plant architecture, nutritional quality and other agronomic traits. Modern genome editing is no longer limited to small insertions or deletions. Base editors can introduce selected nucleotide substitutions, while prime editors provide opportunities for more flexible sequence changes. Promoter editing can also modify gene expression without necessarily altering the protein-coding region (Li *et al.*, 2024; Tuncel *et al.*, 2025).

Table 1: Major CRISPR-based approaches in plant improvement

Genome-editing approach	Main principle	Potential application	References
CRISPR-Cas9	Targeted DNA cleavage and repair	Gene knockout and functional studies	Liu <i>et al.</i> (2016); Wada <i>et al.</i> (2020)
Multiplex editing	Simultaneous targeting of multiple sites	Modification of multiple genes or pathways	Abdelrahman <i>et al.</i> (2021)
Base editing	Direct nucleotide conversion	Precise point mutations	Azameti and Dauda (2021); Li <i>et al.</i> (2023)
Promoter editing	Modification of regulatory regions	Alteration of gene expression	Shi <i>et al.</i> (2023); Tang and Zhang (2023)
Prime editing	Template-guided sequence modification	Precise sequence changes	Vats <i>et al.</i> (2024); Vu <i>et al.</i> (2024)

These technologies provide researchers with a wider range of strategies for studying and improving plant traits.

3. Role of artificial intelligence in crop improvement

Artificial intelligence (AI) refers to computational methods that can learn patterns from complex datasets and support prediction and decision-making. In plant science, AI can help integrate information from genomic sequences, gene expression, phenotypic traits, metabolomics and environmental data to identify relationships relevant to crop improvement. Machine learning and deep learning can help identify relationships between genotype, phenotype and environment. Such approaches may support prediction of traits such as yield, disease response and stress tolerance. AI can also help analyse large datasets that would be difficult to interpret using conventional methods alone (Li *et al.*, 2025).

AI is particularly relevant to genome editing because successful editing requires appropriate target selection and guide RNA design. Computational models can evaluate candidate guide sequences and estimate factors such as editing activity and potential off-target effects.

4. AI-assisted CRISPR-Cas9 design

The selection of an effective guide RNA (gRNA) is an important step in CRISPR-based genome editing. Multiple potential target sequences may be available within a genomic region, but they can differ in predicted editing activity and specificity. AI and machine-learning models can analyse sequence features and experimental datasets to help identify gRNAs with desirable characteristics. These approaches are also being used to predict editing outcomes and improve the performance of genome-editing systems (Thomson *et al.*, 2026).

The integration of artificial intelligence with CRISPR-Cas technology is creating new opportunities to improve the design and efficiency of genome editing. AI-based models can assist in selecting suitable guide RNAs, predicting potential off-target sites and evaluating the performance of candidate editing targets. Recent studies have also demonstrated the use of machine learning to analyse large CRISPR-Cas sequence datasets and identify or design Cas proteins with desirable properties (Kim *et al.*, 2025; Ruffolo *et al.*, 2025).

AI is also being explored for de novo molecular design, in which computational models generate and optimize new molecules with desired properties. Lamanna *et al.* (2023) developed GENERA, a computational approach that combines deep learning with a genetic algorithm for target-oriented de novo molecular design. Although their study focused on medicinal chemistry rather than crop improvement, it demonstrates the potential of AI to generate and optimize novel molecular candidates. Similar approaches may, in the future, contribute to the design or optimization of biomolecules and regulatory components relevant to plant biotechnology. However, such applications in crop improvement remain an emerging area and require plant-specific models and experimental validation.

Table 2: Potential roles of AI in genome-editing workflows

Stage	Role of AI	Reference
Gene identification	Analysis of genomic and functional datasets	Li <i>et al.</i> (2025)
Target selection	Prioritization of candidate genes or genomic regions	Li <i>et al.</i> (2025); Thomson <i>et al.</i> (2026)
Guide RNA design	Prediction of suitable guide sequences	Kim & Kim (2026); Thomson <i>et al.</i> (2026)
Off-target analysis	Identification of potential unintended targets	
Editing prediction	Estimation of editing outcomes	
Phenotype prediction	Analysis of genotype–phenotype relationships	Li <i>et al.</i> (2025); MacNish <i>et al.</i> (2025)
Data interpretation	Integration of multi-omics and phenotypic datasets	Li <i>et al.</i> (2025)

Thus, AI can support several stages from gene discovery to experimental validation.

5. Applications in precision crop improvement

The integration of AI and genome editing has potential applications in several areas of crop improvement.

5.1. Climate resilience:

Drought, salinity, heat and other environmental stresses can substantially affect crop productivity. AI can analyse genomic and environmental information to identify candidate genes and pathways associated with stress responses. Genome editing can subsequently be used to investigate selected targets.

5.2. Disease resistance:

Disease resistance is an important target of molecular breeding. Genome editing can be used to modify genes involved in plant–pathogen interactions, while AI can assist in analysing genomic and transcriptomic information to identify potential targets.

5.3. Improved nutritional quality:

Genes involved in metabolic pathways can be investigated and modified to alter the nutritional composition of crops. Integration of AI with metabolomic and genomic datasets may help identify promising targets for further experimental testing.

5.4. Yield-related traits:

Yield is a complex trait influenced by multiple genes and environmental conditions. AI-based prediction models can integrate genomic and phenotypic information to identify relationships that may be difficult to detect using individual datasets.

5.5. *De novo domestication*:

Genome editing can also be used to introduce selected domestication traits into plants with useful characteristics. This approach may provide an alternative route for developing improved plant materials from diverse genetic resources (Tuncel *et al.*, 2025).

6. Case Study: AI-designed genome editing in rice

Das *et al.* (2026) developed Plant OpenCRISPR-1 (POC1), an AI-designed genome-editing platform based on the OpenCRISPR-1 (OC1) nuclease, at ICAR–Central Rice Research Institute, Cuttack. In rice, POC1 achieved 10.0–16.8% editing efficiency at selected target loci, showing performance comparable to SpCas9. The system was further adapted for adenine base editing, cytosine base editing, and prime editing, demonstrating its versatility for targeted DNA modification. In regenerated rice plants, POC1 produced targeted genetic alterations, including a 573-bp deletion in *OsCYP75B4*. These findings demonstrate the potential of AI-designed nucleases as alternative platforms for crop genome engineering, while further validation across diverse crops and assessment of off-target effects remain necessary (Das *et al.*, 2026).

7. Integration of AI, genomics and CRISPR

AI and genome editing are increasingly being viewed as complementary technologies rather than independent approaches. AI can analyse biological data and generate predictions, while genome editing provides an experimental method for testing those predictions.

Gao *et al.* (2026) proposed a reciprocal relationship in which AI supports guide-RNA design, editing-outcome prediction and target selection, while genome-editing experiments generate biological data that can subsequently improve predictive models.

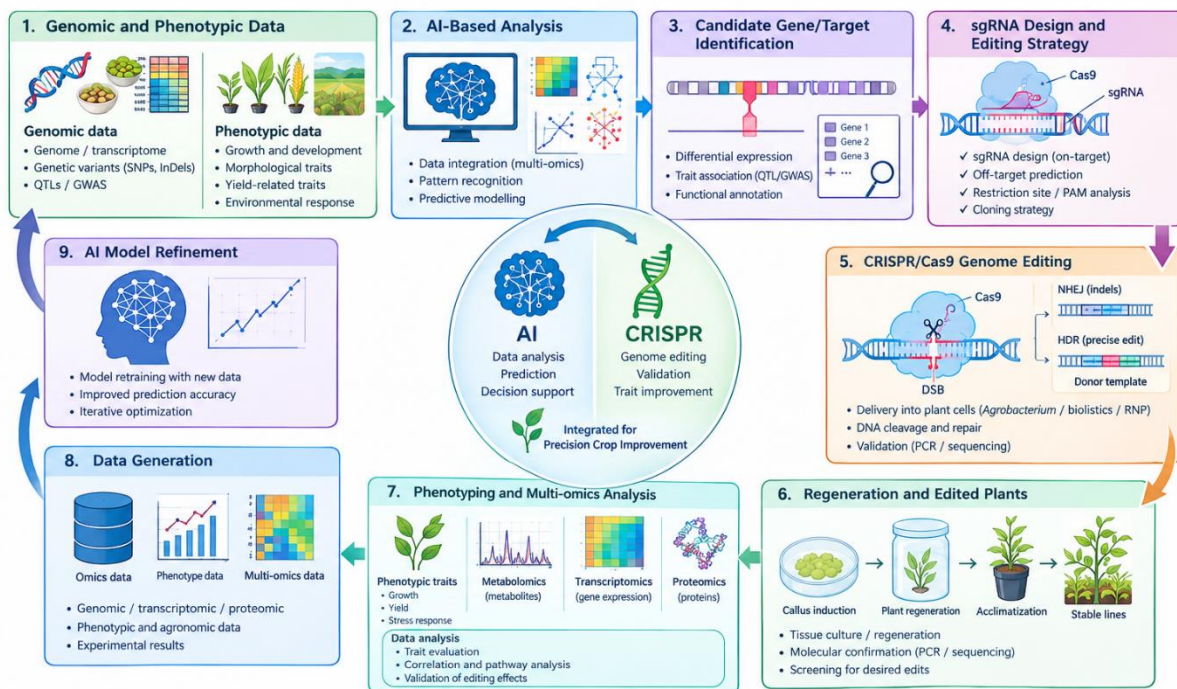


Fig. 2: Conceptual workflow of AI-assisted precision crop improvement

This type of iterative workflow could contribute to a more predictive approach to crop improvement.

8. Advantages of AI-integrated genome editing

Integrating AI with genome editing can improve the efficiency of crop-improvement workflows by helping researchers prioritize promising genes and editing targets before experimental testing. AI-based analysis can also facilitate the interpretation of large genomic, phenotypic and multi-omics datasets, while prediction models may assist in evaluating guide-RNA performance, potential off-target effects and possible editing outcomes. The integration of AI with genome editing, multi-omics and high-throughput phenotyping may therefore support more data-driven and efficient crop-improvement strategies (Li *et al.*, 2025; Thomson *et al.*, 2026).

9. Challenges and limitations

Despite its potential, the integration of AI with genome editing faces several challenges. The accuracy of AI-based predictions depends strongly on the quality, size and diversity of training datasets. Many available datasets are generated from limited plant species, genotypes or experimental conditions, which can reduce the reliability of predictions when models are applied to other crops or genetic backgrounds (Li *et al.*, 2025; Gao *et al.*, 2026).

Plant traits are also influenced by complex interactions among genes, regulatory networks and environmental conditions. Consequently, computational predictions of gene function or phenotype may not always correspond to the responses observed experimentally. In genome editing, differences in editing efficiency, off-target activity, transformation efficiency and plant regeneration can further affect experimental outcomes (Tsakirpaloglou *et al.*, 2023).

Another limitation is the interpretability of some AI models, particularly complex machine-learning and deep-learning approaches. Understanding why a model makes a particular prediction is important when selecting genes or editing targets for biological experiments. In addition, genome-edited crops require appropriate assessment of genetic stability, unintended changes and agronomic performance before practical application. Regulatory requirements also differ among countries and technologies, creating additional considerations for the deployment of genome-edited crops (Tachikawa & Matsuo, 2024).

Therefore, AI-assisted genome editing should currently be considered a complementary approach in which computational predictions require appropriate molecular, phenotypic and, where relevant, field-level validation.

10. Future prospects

The future of precision crop improvement will increasingly involve the integration of artificial intelligence (AI) with genomics, multi-omics, genome editing and high-throughput phenotyping. AI can assist in identifying candidate genes, prioritizing editing targets, designing guide RNAs and predicting editing outcomes. Advances in base editing, prime editing, promoter editing and AI-designed genome-editing systems may further expand the precision and flexibility of crop genome engineering. However, plant-specific datasets, improved editing and delivery systems, and experimental and field validation will be essential for translating computational predictions into reliable crop-improvement outcomes. Iterative workflows in which AI predictions guide genome-editing experiments and experimental data improve subsequent models may provide a promising direction for future research (Li *et al.*, 2025; Gao *et al.*, 2026).

11. Conclusion

Artificial intelligence and CRISPR-based genome editing are complementary technologies with strong potential for precision crop improvement. AI can support target identification, guide-RNA design, prediction of editing outcomes and interpretation of complex biological datasets, while genome editing enables experimental modification of selected genomic regions. Their integration may contribute to the development of crops with improved resilience, disease resistance, nutritional quality and other desirable traits. Nevertheless, AI-assisted genome editing remains an emerging field, and computational predictions must be supported by laboratory and field validation. Continued integration of AI, genomics and advanced genome-editing technologies could provide more precise and data-driven approaches for future crop improvement.

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