



REVIEW ARTICLE

Precision Genome Editing for Smarter, Inclusive, and Nutritious Crops: Emerging Tools, Omics Integration, and Global Perspectives

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ABSTRACT

Sustaining a rising human population amidst a changing climate and dwindling resources calls for a next-generation crop set that's high-yielding, climate-resistant, and nutritionally enriched. Precision editing of the genome through CRISPR systems now lets us make precise and efficient changes in traits in crops like rice, maize, and wheat. At the same time, development in omics sciences, genomics, transcriptomics, proteomics, and metabolomics is speeding the discovery of gene-linked traits so that we can make better and targeted edits. Latest developments like base and prime editors have supplemented the toolbox, making single-nucleotide editing and complex insertions possible without double-strand breaks. These have already been used extensively in cereals, legumes, and horticultural crops for traits ranging from disease resistance and stress tolerance to nutrient biofortification. Multi-omics integration has also enhanced the identity and verification of editing targets through improvement in predictive trait engineering by machine learning and systems biology. Global rollout continues apace, with numerous countries making a regulatory distinction between gene-edited crops and GMOs where they are transgene-free. Case studies from Kenya, Nigeria, and Argentina demonstrate regulatory progress and public-sector breeding initiatives. Future development will move from single gene editing toward complex reprogramming of the genome through structural variations, epigenome modulation, and multiplexed stacking of genes. Still lacking are delivery systems, efficiency of editing in polyploidy crops, reduction of off-target effects, and harmonization of policy requirements. These will be crucial if access is to be democratized and benefits equitably shared in agriculture worldwide.

Key words: Biofortification; Abiotic stress tolerance; Multiplex genome editing; Systems biology; Regulatory frameworks; Food security.

INTRODUCTION

Global food demand is increasing fast with the growth in the world's population and the evolving food habits of consumers, and it is causing tremendous pressure on agricultural production systems to deliver increased quantity and quality crops. Existing breeding practices are very important in crop improvement, but take years and might prove to be too slow to deal with the immediate threats given by climate change, limited input availability, and shifting consumers' needs. (Sharma *et al.*, 2023). Recent progress in the field of biotechnology has unveiled genome editing as a revolutionary method in crop improvement. Genome editing technologies, specifically CRISPR/Cas systems, support the accurate and targeted editing of plant

genomes and possess the potential to increase the yield and nutritional value, as well as resistance to environmental stresses, more efficiently and accurately than the traditional breeding method or the previous genetic modification techniques (Ku & Ha, 2020). Genome editing technologies, including CRISPR/Cas9, TALENs, and zinc finger nucleases, have transformed plant breeding through the ability to insert, delete, or modify targeted areas of the DNA sequence. These technologies have also been used successfully to enhance a number of agronomic attributes, such as yield, stress tolerance, and nutritional value in both staple and horticultural crops. (Nagamine & Ezura, 2022).

One feature with the greatest promise is the potential to produce non-transgenic crops, potentially

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sidestepping the regulatory and public perception barriers in the case of genetically modified organisms (GMOs). Utilisation of CRISPR/Cas9-mediated editing has produced crops with improved shelf life and flavor and nutritional content, and higher levels of beneficial compounds, including vitamins and minerals, and healthy fat in staple crops. (Yang *et al.*, 2022). With the use of the adaptive immune system of bacteria in the CRISPR/Cas9 system, the Cas9 endonuclease is targeted to genomic sites through the guide RNA and cuts the double strands therein. These are then repaired through the use of the plant cell's native machinery to obtain gene disruption and substitution or insertion-specific mutations. This method enabled the development of crops with improved photosynthesis efficiency, enhanced nutrient acquisition and utilization, and improved tolerance towards both biotic and abiotic stresses, the effects being improved production and nutritional value. (Dongariyal *et al.*, 2023).

Recent advances in genome editing technologies, including base editing and prime editing, have pushed the boundaries and specificity of genetic editing further forward. The latter enables the fine-tuning of biosynthetic and storage metabolic pathways and biofortification with micronutrients and the elimination of anti-nutritional compounds in crops. Because genome editing promises nutritional deficiency and food security solutions at the international level. (Abdallah *et al.*, 2015). Though its potential to revolutionize crop improvement exists, the use of genome editing to achieve this is challenged by a number of issues. These include the technological limitations presented by off-target effects, the requirement for high-efficiency delivery mechanisms, and the multifaceted nature of the polygenic traits responsible for yield and nutritional quality. There are also ethical, regulatory, and public perception concerns for the careful management of the deployment of genome-edited crops. (Chen *et al.*, 2024). Further research and the combination of genome editing with other new technologies are expected to boost the production of resilient, high-yielding, and nutrient-enriched crops. Genome editing will increasingly become the key to developing sustainable agricultural production systems to address the needs of a larger and health-focused world population as the technology evolves. (Xu *et al.*, 2019). Despite the excellent potential for genome editing in agriculture, several important roadblocks hinder its application at a large scale. Owing to inefficient transformation techniques and the lack of well-documented genomes, numerous important crops, including sugarcane, are polyploid and genetically complex and are hard targets for editing. Also limiting the accurate genetic improvements are a lack of understanding about the gene functions behind the complex nutritional attributes such as vitamin fortification and mineral availability. The problem of integrating extensive genomic, phenotypic, and

environmental facts is yet another important hurdle. Using genome editing and optimizing the crop effectively is very hard without the advanced management of the data itself. Also hindering are varying public attitudes and regulations across different countries, and developers and scientists find the landscape unclear. Off-target activity persists as a distinct concern and strengthens the need to do more targeted research work. Editing a wider range of species will be achievable if the efficient transformation techniques are designed specifically to target resistant and polyploid crops. To make more targeted and beneficial edits possible, functional research work in the field of genomics needs to make the gene functions behind nutritional quality explicit. In order to manage and analyse diverse datasets properly, advanced data management platforms need to be installed. Standardising international regulatory environments will make granting approval and the uptake of genome-edited crops easier at a wider basis. Finally, and importantly, enhancing the tools to genome edit and reduce off-targeting will increase public trust and safety and enable more confident application of the technologies in sustainable agriculture.

Importance of Enhancing Crop Yield and Nutritional Quality

Enhancing crop yield and nutritional quality is critical for addressing global food security and malnutrition. With the world population expanding and the nutritional demands increasing, enhancing the quantity and quality of food crops is vital. As figure 1. Shows that conventional breeding methods face significant limitations in meeting these urgent challenges.

Global Food Security and Malnutrition

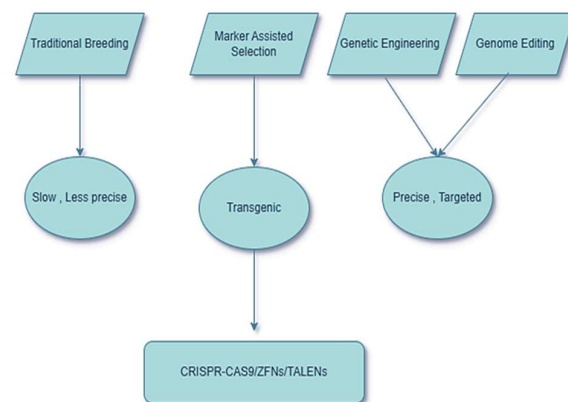


Fig. 1: Tools Used in Precision Genome Editing.

Prevalence of Malnutrition

There are more than two billion people around the planet who are malnourished, and mostly so because staple crops lack essential micronutrients or are cultivated in nutrient-deficient soil (Koul & Tiwari, 2020).

Deficiencies in micronutrients or “hidden hunger” are more common in developing nations and cause dire health issues (Jha *et al.*, 2022). Population expansion and altered patterns of consumption are pushing the need for principal crops such as wheat and rice, and making it crucial to maximize both nutritional content and production to secure food (Mondal *et al.*, 2016). Biofortification (enhancing the micronutrient content in crops) and minimizing the anti-nutritional compounds are significant methods through which malnutrition can be addressed and nutrient intake can be enhanced (Jha *et al.*, 2022).

Limitations of Conventional Breeding

Traditional breeding techniques take more than a decade to produce new cultivars with the desired characters and are too slow to address food security needs urgently (Koul & Tiwari, 2020). Combining more than one beneficial character (e.g., stress tolerance, nutritional value, and high yield) in a single type is difficult and uneconomical owing to limitations in screening techniques and low chances of combining good alleles (Imam *et al.*, 2024). Though adequate genetic variability and appropriate selection techniques are available for some characters, combining high-yielding with improved nutritional value makes the breeding programme expensive and complex. Conventional breeding alone cannot cope with the fast development of new pathogens, climate change, and the requirement of climate-resistance and nutrient-dense crops (Thudi *et al.*, 2020). New techniques such as genomics-assisted breeding, marker-assisted selection, and genome editing are being increasingly required to expedite genetic gains and come up with crops meeting both the production and nutritional targets (Gaikwad *et al.*, 2020).

Multi-Omics Integration in Crop Genome Editing

Genome editing technologies have revolutionized the capacity to edit plant genomes with precision and introduce targeted enhancements to crop quality and yield. There are various significant genome editing platforms currently available with different mechanisms, strengths, and limitations.

CRISPR-Cas9

CRISPR-Cas9, as illustrated in Figure 2, guides the Cas9 nuclease using a guide RNA to a target DNA sequence, where it creates a double-stranded cut, and the cell's own repair mechanisms cause targeted genetic modification (Schulze & Lammers, 2020). Very efficient, user-friendly, inexpensive, and versatile to use in many organisms. The guide RNA alone needs to be altered to target other genes, making it more versatile compared to the older techniques such as ZFNs and TALENs (Gupta *et al.*, 2019). Most commonly used in gene knockouts, gene regulation, live cell labelling, and high-throughput screening in plants and other organisms (Janik *et al.*, 2020). May have off-target effects, although these can be reduced using improved design and the use of paired nickases (Smith *et al.*, 2014).

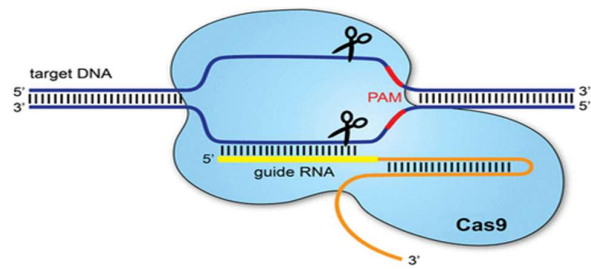


Fig. 2: CRISPR Cas mechanism (Redman *et al.*, 2016).

The CRISPR/Cas9 system.1. Clustered regularly interspaced palindromic repeats (CRISPR) refers to sequences in the bacterial genome. They afford protection against invading viruses when combined with a series of CRISPR-associated (Cas) proteins. Cas9, one of the associated proteins, is an endonuclease that cuts both strands of DNA. Cas9 is directed to its target by a section of RNA. This can be synthesized as a single strand called a synthetic single guide RNA (sgRNA); the section of RNA which binds to the genomic DNA is 18–20 nucleotides. In order to cut, a specific sequence of DNA between 2 and 5 nucleotides (the exact sequence depends upon the bacteria that produce the Cas9) must lie at the 3' end of the guide RNA; this is called the protospacer adjacent motif (PAM). Repair after the DNA cut may occur via two pathways: non-homologous end joining, typically leading to a random insertion/deletion of DNA, or homology-directed repair, where a homologous piece of DNA is used as a repair template. It is the latter which allows precise genome editing: the homologous section of DNA with the required sequence change may be delivered with the Cas9 nuclease and sgRNA, theoretically allowing changes as precise as a single base-pair. (Redman *et al.*, 2016)

CRISPR-Cas12a (Cpf1)

Cas12a (Cpf1) is yet another RNA-guided nuclease in the CRISPR family and a Type V system. As can be observed from Figure 3, it identifies other DNA sequences than Cas9 and forms staggered (sticky) ends instead of blunt ends (Tang & Fu, 2018). Increases the targetable range of DNA sequences, provides other cutting patterns, and can be more targeted in some settings (Tang & Fu, 2018). Utilized in genome editing, gene regulation, and detection and increasingly used in plant biotechnology (Tang & Fu, 2018).

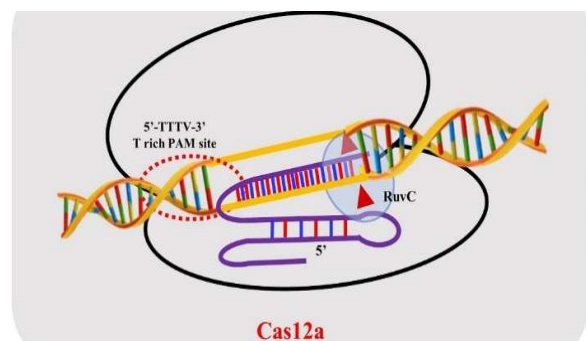


Fig. 3: Schematic representation of Cas12a crRNA with the target strand DNA association. (Anindya *et al.*, 2020).

Genome Editing Tools

Base and prime editing are newer tools that facilitate precise base change without making double-strand breaks and minimizing unwanted mutations. Previous tools, TALENs and ZFNs, involve the use of engineered nucleases, making targeted breaks but being time-consuming and less adaptable. Table 1 discusses methods to create a multifarious toolkit for precision crop enhancement.

Applications in Crop Yield Improvement

Yield-Related Gene Targets

Key TF (transcription factors) family genes such as *NAC*, *MYB*, *WRKY*, *Bzip*, and *ERF/DREB* are pivotal in modulating genes related to yield and stress tolerance. Modulation or overexpression of TF genes in crop species such as wheat, rice, maize, and barley has the potential to enhance yield during stress conditions (Baillio *et al.*, 2019; Manna *et al.*, 2020). MiRNAs are small RNA genes that regulate gene expression post-transcriptionally. They fine-tune the expression of stress-and-yield-associated genes, and their overexpression or knockdown can increase crop yield and tolerance (Chaudhary *et al.*, 2021). Both regulatory genes (regulating the expression of other genes) and structural genes (coding proteins with a direct role in stress tolerance) are vital targets. Gene editing through CRISPR/Cas9 or other tools can directly regulate yield by enhancing plant growth and productivity in adverse conditions (Sedeek *et al.*, 2019).

Stress Tolerance and Climate Resilience

Genes responsible for drought tolerance, salinity tolerance, high temperature tolerance, and heavy metal tolerance are the keys to sustaining yield during climatic stress conditions. CRISPR/Cas9 and other

genome editing systems have been utilized to edit the mentioned genes to produce crops more resistant to abiotic stresses (Karunaratne *et al.*, 2023). TFs, including *Bzip*, *DREB*, *DOF*, *HSF*, *MYB*, *NAC*, *TCP*, and *WRKY*, are the primary regulatory proteins in stress-responsive pathways. Genetic modification through TFs can boost drought tolerance, salinity tolerance, and temperature tolerance, directly maintaining the stability of the yield in fluctuating climates (Baillio *et al.*, 2019). Overexpression of certain miRNA species, like *Os-miR408* in drought tolerance and *OsmiR535A* in salinity tolerance, has enhanced tolerance to stress and the efficiency of photosynthesis and increased the yield even during stress conditions (Chaudhary *et al.*, 2021). Genomics and transcriptomics integration identifies and validates stress-responsive genes and regulatory networks and aids in the accurate genome editing of stress resilience and increased yield (Kamali and Singh, 2023). Table.2. shows strategies collectively enable the development of high-yield, climate-resilient crops through targeted genome editing. More than 150 potential key genes responsible for stress tolerance have been targeted for editing in barley. In wheat, CRISPR/Cas9 facilitates the production of enhanced drought tolerance, salinity tolerance, and high temperature tolerance in the crops and maintains the stability of the yield in the worst conditions (Trono and Pecchioni, 2022).

Yield-Related Gene Targets

Enhancing crop yield and building resilience to environmental stresses are central goals in modern crop improvement. Recent research highlights specific gene targets and strategies that directly address these challenges through advanced breeding and genome editing.

Table 1: The table summarizes some of the important tools of genome editing used in crop biotechnology.

Genome Editing Tool	Description	Citations
Base Editing	Engineered proteins that convert one DNA base to another (e.g., C→T or A→G) without double-stranded breaks. Includes CBEs and ABEs. Reduces indels and is useful for correcting SNVs and improving traits.	Kantor <i>et al.</i> , 2020
Prime Editing	Uses a modified Cas9 with reverse transcriptase and pegRNA to perform insertions, deletions, and all base conversions without double-stranded breaks. Offers high precision with fewer byproducts.	Anzalone <i>et al.</i> , 2020
TALENs	Engineered proteins that bind specific DNA sequences and create double-stranded breaks via FokI. Known for high specificity, but are labour-intensive to construct.	Schulze & Lammers, 2020
Zinc Finger Nucleases (ZFNs)	Fusion of zinc finger DNA-binding domains with FokI nuclease for targeted DNA cleavage. Early genome editing tool with good specificity but limited flexibility.	Janik <i>et al.</i> , 2020

Table 2: The following strategies collectively enable the development of high-yield, climate-resilient crops through targeted genome editing.

Application Area	Key Targets/Approaches	Example Crops	Impact on Yield/Resilience	Citation
Genomic/Transcriptomic Integration	Omics-guided gene identification/editing	Multiple	Precise trait improvement, resilience	Sedeek <i>et al.</i> (2019).
Yield-Related Gene Targets	TFs (<i>NAC</i> , <i>MYB</i> , <i>WRKY</i> , etc.), miRNAs	Wheat, rice, maize	Improved yield under stress	Chaudhary <i>et al.</i> (2021).
Abiotic Stress Tolerance	Structural/regulatory genes, CRISPR	Wheat, barley	Enhanced drought, salinity, temp. tolerance	Karunaratne <i>et al.</i> (2023).
MiRNA-Mediated Engineering	Overexpression/knockout of miRNAs	Rice, barley	Increased stress tolerance, photosynthesis	Chaudhary <i>et al.</i> (2021).

Yield-Related Gene Targets

Various QTLs and genes have been discovered and stacked to boost yield and tolerance to stress in crops such as rice. QTLs *Qdty1.1*, *Qdty2.1*, *Qdty3.1*, and *Qdty12.1* (for drought), and genes *Sub1* (tolerance to submergence), *Pig* and *Pita2* (resistance to blast), and *Xa4*, *xas5*, *xa13*, *Xa21*, and *Xa23* (resistance to bacterial blight) are cases in point and have successfully been pyramided through genomics-assisted breeding to produce high-yielding, multi-stress-tolerant lines (Yadav *et al.*, 2021). The NAC family of transcription factors is essential to manage the potential at the grain production stage, seed size, biomass, and stress management. Genetic manipulation of the NAC genes can increase plant survivability, the quantity and quality of the grain produced, and tolerance to several stresses (Singh *et al.*, 2021). Both are significant targets. Structural genes produce proteins directly responsible for conferring tolerance to stress, while regulatory genes manage the expression of other genes related to stress and the grain production processes. Targeting the genes with CRISPR/Cas9 and other allied technologies can produce crops with enhanced yield and resistance to stress (Zafar *et al.*, 2020).

Stress Tolerance and Climate Resilience

Genome editing technologies such as CRISPR/Cas9 are employed to knock out or alter stress-responsive genes to confer advantageous crop characteristics such as increased tolerance against drought and salinity stress, temperature extremes, and diseases without adding any extraneous DNA (Riaz *et al.*, 2025). Small RNAs such as miRNAs are used to regulate the expression of numerous stress-responsive genes at the post-transcriptional level. Manipulating miRNAs can modify the abiotic and biotic stress response in plants and make them good targets to design stress-tolerant crops (Chaudhary *et al.*, 2021). Genes such as *OsSRDP* (one member of the *DUF740* family in rice) have proved to impart increased tolerance against drought stress, salinity stress, cold stress, and particular diseases when overexpressed and are evidence enough to reveal the utility of stress-inducible gene expression in climate resilience (Jayaraman *et al.*, 2023). These techniques confirm and identify stress-responsive genes and regulatory networks and assist with accurate genome editing towards enhanced stress resilience (Kamali and Singh, 2023).

Applications in Nutritional Quality Enhancement

Enhancing the nutritional quality of crops is a key strategy to combat malnutrition and “hidden hunger” worldwide. Biofortification; through breeding, genetic engineering, and agronomic practices targets the enrichment of vitamins, minerals, amino acids, and the reduction of anti-nutrients in staple foods, offering a sustainable solution for improving public health, especially in regions with limited dietary diversity.

Vitamin Biofortification

Biofortified crops like “Golden Rice,” cassava rich in provitamin A, bananas, and fruits such as mango and papaya have been bred to combat vitamin A deficiency,

high rates of preventable blindness, and immune system malfunctioning being a significant reason for it (Kaya, 2025). Folate and B vitamins in crops have been enhanced through genetic and metabolic engineering, while agronomic biofortification also enhances the amounts of vitamin C and vitamin A in horticultural crops (Kathi *et al.*, 2023). Genetic modification and conventional breeding are both employed to introduce or boost the biosynthesis pathway of vitamins in crops with minimal effect on other nutritional characters (Dwivedi *et al.*, 2023).

Mineral Enrichment

More than 400 zinc and iron-rich crop cultivars (wheat, rice, beans, and fruits) have been released to benefit millions of households in the Global South (Zulfiqar *et al.*, 2024). Efforts are also made to biofortify calcium, magnesium, iodine, selenium, and copper in vegetables and fruits through both agronomic means (application of fertilizer and soil amendments) and genetics (Consentino *et al.*, 2023). They aim not just to raise the mineral content but also to enhance their bioavailability, bio accessibility, and utilization in the human body (Dwivedi *et al.*, 2023).

Improvement of Amino Acid Profiles

Metabolic engineering and biofortification have enriched the content of vital amino acids such as tryptophan, glycine, tyrosine, phenylalanine, glutamic acid, and proline in crops and enhanced their quality and nutritional value (Kaya, 2025). Nanoselenium treatment in *Siraitia grosvenorii* remarkably enhanced amino acid content and proved the efficacy of targeted treatments in amino acid enrichment (Zhou *et al.*, 2022).

Anti-nutrient Reduction

These modern breeding and gene editing methods are employed to decrease anti-nutrients such as phytates, the absorption-inhibiting compounds, thus increasing the nutritional efficacy of the biofortified crops (Zulfiqar *et al.*, 2024). Integration of nutrient fortification and anti-nutrient reduction also means the increased utilization of the incorporated vitamins and minerals in the body since their absorption will not be hindered by the anti-nutrients (Zulfiqar *et al.*, 2024).

Advances in Editing Recalcitrant and Orphan Crops

Recent technological advances in genome editing are making potential breakthroughs achievable in enhancing recalcitrant and orphan crops, those crops that are recalcitrant to genetic modification or have received scant attention in the past. These crops, such as the majority of millets, pulses, and cassava, are important sources of food security in marginal environments but are technically demanding, particularly with complex or polyploid genomes.

Challenges with Polyploid Genomes

Polyploid crops like potato and finger millet possess more than one set of chromosomes, and genome assembly, gene targeting, and improvement through

desirable traits are more complex compared to diploid species. Polyploidy makes it difficult to identify and edit all the gene copies (homeologs), and this is sometimes essential to achieve desired phenotypes (Nadakuduti *et al.*, 2018). Advanced sequencing and hybrid assembly pipelines have also been created to address the complexities presented by polyploidy. A case study is the use of multiple hybrid de novo assemblies to successfully assemble the finger millet genome and resolve the majority of homeologs and form the basis for accurate editing (Hatakeyama *et al.*, 2017). Genome editing tools such as CRISPR/Cas9 and TALENs have still been used in polyploid crops like potato to target traits such as cold-induced sweetening, processing efficiency, and herbicide tolerance (Nadakuduti *et al.*, 2018).

Editing in Different Crops

Table 3 documents significant advances in genome editing across different crop groups, such as millets, cassava, recalcitrant, and orphan crops. Landmark techniques such as CRISPR/Cas9 and Agrobacterium-mediated transformation have rendered targeted enhancement in quality attributes such as herbicide tolerance, stress resistance, and architectural modification feasible. Recently developed techniques, such as DNA-free editing in recalcitrant crops, have further widened the scope towards universal crop improvement. Such advances also indicate the utility value of comparative analysis in the selection of the appropriate method based on efficiency, scalability, and crop compatibility.

Efficiency and Specificity

CRISPR/Cas Systems

CRISPR/Cas9 is well-known for precision, accuracy, and efficiency in targeted genome editing. Engineered Cas9 mutants (e.g., eCas9-NG and Cas9-NG) increase target site compatibility and can optimize editing efficacy in crops such as rice (Manghwar *et al.*, 2020). CRISPR/Cas9 is also unique in its potential to minimize off-target effects when compared to the previous tools

(Manzoor *et al.*, 2024). Other tools include ZFN and TALENs, are powerful yet typically more complex and less efficient than CRISPR/Cas systems (Ahmadikhah *et al.*, 2025). Base editors, e.g., cytosine base editors (CBEs), deliver accurate single-nucleotide changes with low off-target activity when properly constructed (Randall *et al.*, 2021). Carefully constructed guide RNAs and enhanced Cas9 mutants are capable of maintaining high specificity, with off-target alterations being minimal and commonly lower than rates of natural or induced mutation rates (Manghwar *et al.*, 2020).

Cost, Scalability, and Crop Compatibility

CRISPR/Cas9 is simpler to design and use and more cost-effective than both ZFN and TALENs, each of whose targets necessitates complex protein engineering (Ali *et al.*, 2024). CRISPR/Cas9's simplicity and multiplexing ability make it very feasible to scale up the editing of many genes or large populations (Manzoor *et al.*, 2024). CRISPR/Cas9 and variants are widely used across a range of crops with complex genomes and are more widely used than ZFN and TALENs, albeit with technological hurdles (Zeng *et al.*, 2019).

Off-target effects and mitigation techniques

Off-target effects are problematic, particularly with CRISPR/Cas systems. Advanced computer tools and sequencing techniques enable the detection and assessment of off-target effects to be successfully achieved (Manghwar *et al.*, 2020). Off-target activity can be minimized using high-fidelity variants of Cas9, optimizing guide RNA design, and implementing regulatory switches to modulate nuclease activity (Guha *et al.*, 2017). Selection and breeding methods further minimize the risk of accidental mutations in the production of commercial crops (Hamdan *et al.*, 2022). Certain base editors introduce minimal or no sgRNA-dependent off-target mutation but can have low-level sgRNA-independent effects (Randall *et al.*, 2021).

Table 3: This table discusses the recent Advances in Genome Editing Across Diverse Crop Categories and their Applications

Crop Category	Key Advancements	Techniques Used	Notable Outcomes	Citation
Millets	Genome editing systems have been established in broomcorn millet and finger millet.	Agrobacterium-mediated transformation, CRISPR/Cas9	Herbicide-resistant and visually selectable mutants were created. Editing of stress-resistance gene orthologs is suggested.	Hatakeyama <i>et al.</i> , 2017;
Cassava	Efficient gene editing demonstrated by targeting MePDS gene.	CRISPR/Cas9	High rates of targeted mutations and visible phenotypes were achieved, proving feasibility.	Odipto <i>et al.</i> , 2017
Recalcitrant Crops	Barriers to transformation are overcome with direct delivery of editing tools.	DNA- and marker-free editing (Cas9-GRNA delivery)	Efficient genome editing without transgene integration in difficult genotypes like maize.	Yamada <i>et al.</i> , 2024
Orphan Crops	Traits like architecture, yield, and stress tolerance being improved using genome editing.	Gene targeting via CRISPR and translation from model crops	Rapid trait enhancement in lesser-known, underutilized crops like groundcherry.	Venezia & Krainer, 2021
Comparative Analysis	Highlights the importance of comparing editing tools based on efficiency, specificity, cost, scalability, compatibility, and off-target management.	General analysis across tools (e.g., CRISPR, TALENs)	Helps select appropriate tools for crop-specific genome editing strategies.	—

Regulatory Approaches and International Outlook

Regulatory environments and the public attitudes towards genome editing differ extensively across the world and mirror variations in legal, ethical, and societal norms. While genome editing technologies continue to progress, different countries and regions are formulating unique policies and holding ongoing discussions about their applications and responsible use in agriculture, medicine, and human healthcare.

Country-specific Policies Regarding Genome Editing

Several countries illustrated in Table 4 have created or are reforming regulatory environments for genome-edited organisms, and more specifically, crops. Certain genome-edited products are exempted from conventional GMO regulations in some countries, while having stricter controls in other countries. Even within the same regions, in this case the European Union, regulatory advice can significantly vary between the member states (Sprink *et al.*, 2022; Ševcová, 2024).

Public Perception and Ethical Considerations

Genome editing triggers important ethical, safety, and moral concerns, particularly when considering human use. The main concerns are the risks of unforeseen effects, effects in future generations, and the requirement for strict monitoring in the clinic and agriculture (Xue and Shang, 2022). Public polls in places such as Costa Rica indicate high levels of support for regulation, emphasizing the value of open, accessible communication and education to frame societal fears and concerns (Hernández-Soto and Gatica-Arias, 2024). Effective governance relies upon the contributions of scientists, regulators, patient groups, and the wider public. Open discussion, good science communication, and multi-level engagement are advocated to combat misinformation and enable responsible innovation (Nordberg *et al.*, 2020). Policymakers are encouraged not to overextend regulation and restrict research prematurely but to support adaptable and flexible rules to enable responsible innovation while maintaining sound standards of ethics (Coller, 2019).

Case Studies from Developing Countries

Success Stories and Field Applications

Genome editing using CRISPR/Cas techniques has proved promising in developing countries in the improvement of crop quality and yield. CRISPR/Cas-based

genome editing is presently being used in Africa to generate staple crops with improved attributes. They include disease-resistant banana, maize resistant to necrosis lethality, and Striga-resistant sorghum and nutritional quality sorghum. The products are being developed specifically for farmers in Africa to address the region's food and nutritional security concerns. Genome editing adoption is also eased by the fact that crops are not regulated as GMOs in several countries if they are edited without the inclusion of foreign genes. This eases market access and approval. Besides, Nigeria and Kenya have advanced their national biosafety provisions and guidelines guiding the regulation of gene editing in the region. This bodes well for wider adoption and field use in the continent (Tripathi *et al.*, 2022).

Challenges for Smallholder Adoption

Despite such progress, the wide adoption of genome-edited crops by smallholder farmers in developing countries is being impeded by a number of impediments. Principal among these is the requirement for enabling environments through well-articulated, science-based regulatory systems, still in the process of being developed in many parts of the world. There are also technical impediments in the form of the requirement for efficient delivery vehicles and the potential for off-target effects, limiting the access and consistency of genome editing for small-scale production (Chen *et al.*, 2024). Public perception is also a factor since debates over the safety and ethics of genome-edited crops can sway policy and market behaviour (Tripathi *et al.*, 2022). Smallholder farmers might also find the technology out of reach in terms of limited assets, infrastructure, and technological competency despite the relatively low barrier to entering genome editing versus the conventional genetic modification (Ku & Ha, 2020). Overcoming the impediments will need to involve complementary action across policy-making, education, and capacity development to ensure the benefits from genome editing are available to and make a difference to smallholder farmers and are available to support sustainable agricultural development in developing countries.

Table 4: The table encapsulates the regulatory framework for genome editing in major geographies. While Latin America boasts product-centric regulations, the EU and South Africa comprise policy fragmentation. Global non-harmonization hampers trading, innovations, and global collaborations.

Region/Country	Regulatory Highlights	Current Focus/Challenges	Citation
Latin America	Countries like Argentina, Brazil, Colombia, Chile, Paraguay, Honduras, and Guatemala pioneered regulation based on whether foreign DNA is in the final product.	Emphasis on product-based evaluation. Updates in Costa Rica, El Salvador, Ecuador, Uruguay, and Colombia aim to balance innovation, safety, and global compliance.	Recent Hernández-Soto & Gatica-Arias, 2024
European Union	The regulatory system struggles to keep up with rapid advancements in genomic techniques.	Harmonization efforts are ongoing, with debates centred on ethics, safety, and modernization of legislation.	Ševcová, 2024
South Africa	The regulatory environment is inconsistent and fragmented.	Reforms are needed to address public concerns and bring policies in line with global perspectives.	Townsend & Shozi, 2021
Global Harmonization	No globally unified regulatory framework exists for genome editing.	This complicates trade and international research partnerships; harmonization remains a long-term goal.	Sprink <i>et al.</i> , 2022

Research Gaps and Future Directions

Genome editing holds great promise for enhancing crop yield and nutritional quality, but several research gaps and technical challenges remain. Addressing these issues is crucial for realizing the full potential of genome editing in crop improvement.

Gaps in Gene Knowledge Regarding Nutrition

Several starch, lipid, protein, and other functional compound genes have been targeted for editing, with complex regulatory networks and incomplete understanding controlling the corresponding characters. Present research aims to map and define the networks but with areas still to cover, particularly those influenced by more than one gene and the environment (Wei *et al.*, 2023). One gene may result in varying phenotypic results based on the status of the environment, and thus the nutritional characters are difficult to predict and manipulate with certainty (Weckwerth *et al.*, 2020).

Technical Challenges in Editing Complex Traits

These agronomically and nutritionally important traits are regulated by several genes and involve interactions between genes through epistasis and pleiotropy. This makes it hard to find and edit all the genes involved to obtain the desirable trait (Liu & Yan, 2018). Functional testing of candidate genes in species with complex genomes, such as maize, is still a bottleneck. The development of high-throughput CRISPR/Cas9 pipelines is in progress to make the process easier and faster, but further improvement is required (Liu *et al.*, 2020). Making accurate and off-target-free edits, particularly in polyploid or heavily heterozygous crops, remains a technical bottleneck (Abdallah *et al.*, 2015).

Need for Improved Data Integration and Functional Validation

In order to fully understand and manipulate nutritional traits, genomic, transcriptomic, proteomic, metabolomic, and epigenetic information needs to be put together. This combined “PANOMICS” strategy can make predictions more accurate and assist in the choice of traits but needs sophisticated analytical tools and big carefully curated data sets (Weckwerth *et al.*, 2020). Large-scale and high-throughput testing of gene function is needed to verify the roles played by putative genes in nutritional quality and quantity. Genome editing combined with speed breeding and deep learning can make this happen more rapidly, but practical application is still in the process of emerging (Tsakirpaloglou *et al.*, 2023).

Vision for the Future

Technological breakthroughs in genome editing, artificial intelligence, and synthetic biology are redefining the future of agriculture through the production of climate-resilient and nutrient-dense crops. Such breakthroughs are poised to meet food

security needs, ensure sustainability, and achieve equitable access to food supplies, particularly as the world grapples with climate change and increased population pressure.

Integration of AI and Synthetic Biology

Plant sciences are being revolutionized through the use of AI and machine learning to identify species with accuracy, detect disease early, and predict and optimize precision agriculture through the use of genomic, phenotypic, and environmental information in AI models, thereby increasing breeding cycles and predictive accuracy for desirable attributes (Wójcik-Gront *et al.*, 2024). Synthetic biology uses the principles of engineering to redesign biological networks and organisms to add value through enhanced drought tolerance, nutrient biosynthesis, and the ability to fix nitrogen. Synthetic biology enables the design of novel metabolic routes and the design of plant-microbiota networks to optimize the use of nutrients and lower the requirement for fertilizer use (Ahlawat *et al.*, 2024). Synthetic biology in combination with the use of AI speeds up the design and optimization of engineered crops, facilitates the production of proteins and phytochemicals, and facilitates quick function checks through deep learning-driven predictors (Iram *et al.*, 2024).

Climate-Resilient, Nutrient-Dense Crops

Genome editing and synthetic biology streamline the development of crops with tolerance to abiotic and biotic stresses, such as drought, high temperatures, and pathogens, enabling production across fluctuating climates (Tariq, 2024). Engineering techniques are employed to enhance the nutritional quality of crops through increased nutrient content and the synthesis of health-enhancing compounds. These activities are important in the management of malnutrition and the enhancement of global health (Roell & Zurbruggen, 2019). Phenomics through the use of AI and high-throughput phenotyping make it efficient to screen plant traits, fine-tuning conditions and use of resources for sustainable agriculture and high production (Kaya, 2025).

Policy and innovation for equitable access

Global initiatives and partnerships, e.g., CGIAR and AGRA, play a key role in sharing knowledge, resources, and technologies, especially with developing countries. Programs to build capacities and transfer technology are also required for the general adoption (Ahlawat *et al.*, 2024). Overcoming regulatory barriers, public opinion, and ethics is instrumental to responsible deployment. Standardized data harmonization, open AI practices, and participant-inclusive policy will make the technologies available equally to all (Wójcik-Gront *et al.*, 2024). Prioritization of conservation, sustainable use of genetic diversity, and interdisciplinary research will enable the production of robust, nutrient-dense crops available to all stakeholders (Roell & Zurbruggen, 2019).

Precision, Efficiency, and Delivery Systems in Genome Editing

Advances in genome editing rely significantly upon the accuracy, efficacy, and delivery of editing instruments into plant cells. New delivery systems are important to broaden the use of genome editing, particularly in crop species that are recalcitrant when transformed through common tissue culture techniques.

Nanoparticle-based Delivery

Nanoparticles such as lipid, polymer, hybrid, and inorganic are proving to be extremely potent non-viral vectors to deliver CRISPR/Cas9 and other genome editing elements. They possess benefits such as targeted delivery, protection against the degradation of genetic material, enhanced cellular delivery, and lower cytotoxicity (Dizaj *et al.*, 2014). Engineered nanoparticles from lentivirus-derived nanoparticles (LVNPs) have been created to deliver CRISPR/Cas ribonucleoprotein complexes to enable efficient support of base and prime editing with significant on-target activity and diminished off-target effects. LVNPs have proved successful in gene editing *in vivo*, including proof-of-concept interventions in animal models (Haldrup *et al.*, 2023). Lipid nanoparticles have facilitated the effective delivery of mRNA and CRISPR/Cas9 for gene editing in different organs such as the liver and lungs and are promising for multiplex editing and viral-free gene therapy (Hajj *et al.*, 2020). Polyester nanoparticles such as PLGA and PLA are also being considered based on their safety and versatility to deliver genome editing reagents (Piperno *et al.*, 2021).

Virus-induced Gene Editing

Bioengineered virus-like nanoparticles (reBiosomes) have also been developed to deliver genes in a highly efficient manner with lowered immunogenicity and increased specificity towards target tissues. These platforms have exhibited very strong therapeutic effects in disease models through the delivery of gene editing and gene silencing systems (Bao *et al.*, 2023). Hybrid delivery strategies utilizing viral vectors (such as adeno-associated virus delivery of sgRNA and repair templates) and non-viral delivery vehicles (such as lipid nanoparticles for delivery of Cas9 mRNA) have produced accurate gene editing and disease correction in animal models and proved the potential utilization of synergistic delivery platforms (Yin *et al.*, 2016).

Tissue Culture-Free Transformation

Plant transformation is being addressed with nanoparticle and virus-based delivery systems to eliminate the tissue culture bottleneck in the process. Such technologies are potentially capable of delivering genome editing reagents directly to the tissue or cells of plants, simplifying the editing process and widening the array of crops amenable to transformation (Dizaj *et al.*,

2014). Further advances in the design of nanoparticles and virus-like particles are predicted to further enhance the efficiency, specificity, and scalability of tissue culture-free genome editing in plants (Raguram *et al.*, 2022).

Bioinformatics and AI in Genome Editing

Bioinformatics and AI are revolutionizing genome editing through accurate targeting, effective guide RNA design, and accurate pre-screening for off-target effects. Improved targeting, accurate off-target prediction, and high-throughput screening are essential for maximizing crop productivity and reducing off-target toxicity from CRISPR-based crop breeding strategies.

Artificial Intelligence for Predicting Target Genes

Artificial intelligence, including conventional machine learning and deep learning, is extensively employed for predicting the best target genes and guide RNAs for genome editing. Algorithms like recurrent neural networks and convolutional neural networks examine vast databases and provide predictions for ideal target sites as well as for editing efficiency (Sherkatghanad *et al.*, 2023). AI platforms can consider sequence context, mismatches, and structural elements and enhance the specificity in predicting target genes along with accurate modulation of gene expression (Cheng *et al.*, 2023).

CRISPR Design Tools and Databases

Cloud-based web resources and web-based tools like Elevation and TIGER offer end-to-end solutions for the design of guide RNAs, including predictions for on-target as well as off-target activities. These web-based platforms rely on pre-calculated information and complex algorithms, fast-tracking the design and making them available to researchers all around the world (Listgarten *et al.*, 2018). Systematic reviews and benchmarking investigations review the performance of different deep learning-based CRISPR design tools across different datasets and edit scenarios, discussing their strengths and weaknesses (Sherkatghanad *et al.*, 2023).

Off-target effect prediction

Models driven by AI such as Elevation, CRISPR-DIPOFF, CRISPR-Net, and CrisprBERT have greatly enhanced off-target prediction accuracy through analysis of sequence mismatches, insertions, deletions, and contextual information (Sari *et al.*, 2024). New models like CrispAI do not just provide point predictions but also uncertainty quantification for off-target activity, enabling a holistic risk evaluation for selecting guide RNA (Özden & Minary, 2024). A few models include interpretability elements like integrated gradients and sensitivity analysis for researchers to know the contributing factors for off-target predictions and enhance the transparency of models (Toufikuzzaman *et al.*, 2023).

Epigenome Editing and Gene Regulation

Epigenome editing enables precise regulation of gene expression without altering the underlying DNA sequence. The use of nuclease-dead Cas9 (dCas9) has opened new possibilities for targeted transcriptional regulation and epigenetic modification, offering powerful tools for both basic research and crop improvement. Figure 4. Shows the step-by-step process from gene identification to crop improvement.

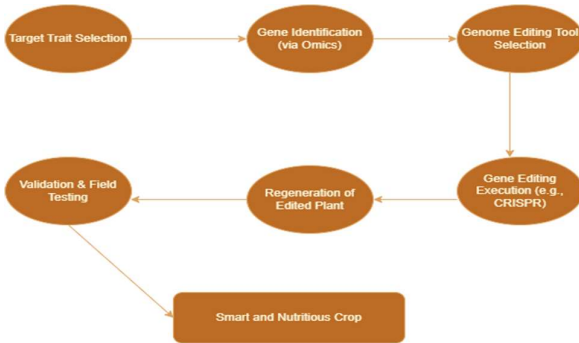


Fig.4: Flowchart of Precision Genome Editing Process.

DCas9 for Transcriptional Regulation

dCas9, which does not possess DNA-cutting capability, can be combined with transcriptional activators or repressors in order to modulate gene expression. With fusion using activator domains (for example, EDLL, TAL, or VP64), dCas9 can activate target genes (CRISPRa). With fusion using repressor domains (for example, KRAB, SRDX, or TEN), dCas9 can suppress gene expression (CRISPRi) (Piatek *et al.*, 2015). DCas9-based systems have been employed successfully in plants, animals, and human cells for activating or suppressing native genes for functional genomics analysis and trait development without making double-stranded breaks (Xu & Qi, 2019). Recent developments include inducible dCas9 platforms, where gene regulation can be regulated externally through light, small molecules, or oligonucleotides, enabling spatiotemporal specificity in gene expression (Wu *et al.*, 2021).

Epigenetic Modification Without Cutting DNA

dCas9 can be joined to epigenetic effector domains, including DNA methyltransferases (e.g., DNMT3A), demethylases (e.g., TET1), or histone-modifying enzymes (e.g., PAD for citrullination), in order to add or subtract epigenetic marks at targeted genomic loci (Vojta *et al.*, 2016). These changes can cause heritable changes in gene expression, such as targeted DNA methylation or demethylation, or histone modification, without changing the DNA itself. For instance, dCas9-DNMT3A can cause targeted CpG methylation, which results in permanent gene silencing, whereas dCas9-TET1 causes demethylation and gene activation (Vojta *et al.*, 2016). DCas9-KRAB-MeCP2 fusion proteins can cause long-term gene silencing irrespective of DNA

methylation and broaden the scope of available epigenetic regulatory mechanisms for use in research and possible therapeutic purposes (Ding *et al.*, 2022).

Socioeconomic and Gender Effects of Genomically Edited Crops

The potential exists for genome-edited crops to redefine farming, especially in resource-constrained environments, as they enhance productivity and bring in new traits. Yet, their socioeconomic and gender dimensions will rely on their implementation and regulation.

Contribution toward Empowering Women Farmers

Social inequalities like gender inequality play a major role in determining global food security. Genome editing as part of overall agricultural innovation provides an avenue for redressing these inequalities through enabling crops for increased yield and resilience, which could benefit female farmers who lack equal access to technology and resources (Lassoued *et al.*, 2021). With properly targeted policies and equitable implementation, genome-edited crops would be capable of empowering women through access to enhanced seed and technology, which has a potential for boosting their productivity and financial independence (Lassoued *et al.*, 2021).

Lessening Inequality in Resource-Poor Environments

Genome editing allows for accelerated development of traits and reduced costs for research and development, enabling crops that can be developed for resource-poor farmers' needs. This could assist in reducing inequality and poverty through improved agricultural productivity and environmental stress resilience (Kalaitzandonakes *et al.*, 2022). While technology has progressed, there remains a potential for smallholder and resource-poor farmers not to benefit from genome-edited crops if socioeconomic concerns are not considered. Access, affordability, and facilitation for adoption are essential for equitable benefits (Toledo-Hernández *et al.*, 2021). Unclear regulatory frameworks and societal uncertainty will restrict genome-edited crop market development and access, particularly across developing regions. Transparent, inclusive policies should facilitate these innovations reaching marginal communities (Lassoued *et al.*, 2021).

Industry Collaborations and Startups

The CRISPR revolution has altered modes of entrepreneurship, as numerous genome editing companies spin off from universities. This has promoted a fivefold growth in investment in bioenterprise, as these businesses vie for complete intellectual property holdings and speedy commercialization of products (Brinegar *et al.*, 2017). Industry collaborations, such as those between official research organizations, private corporations, and global consortia, are growing in scale and scope. These collaborations enable technology

transfer, regulatory management, and the creation of market-valued traits in plants (Ricroch, 2019). The first genome-modified crops have entered commercial markets, and research operations are spreading across the world. Firms are targeting traits such as insect resistance, yield enhancement, and climate resilience, complemented by commercialization through advances in regulation and industrial associations (Menz *et al.*, 2020).

Patent Landscape and Commercialization Trends

The commercial trends and patent environment for agricultural genome editing are fast-changing, propelled by advances in technology, investment around the world, and regulatory environments in flux. CRISPR and associated technology are now at the epicentre of innovation, having a tremendous impact in terms of industry collaboration and startup formation.

Patents for Global Genome Editing in Agriculture

Since its advent around 2012, CRISPR has been preeminent in agricultural genome editing patents. International CRISPR patents across 13 nations from 2015 to 2022 have been found to exhibit a high positive relationship between agricultural economic efficiency improvements and an increase in CRISPR patents, indicating its strategic potential for crop resilience, drought tolerance, and nutritional traits (Zhu *et al.*, 2025). The United States and China are at the fore in terms of research into crop genome edit and patent applications for crops, while other regions like Nigeria lead in sub-Saharan Africa through research networks (Ricroch, 2019). Commercialization of genome-edited crops is directly associated with regulatory clarity. Over recent years, a number of nations primarily in the Americas have implemented guidelines or modified legislation for the promotion of genome editing, whereas others continue arguing about legal categorizations, which affects commercializing and patent moments (Tachikawa & Matsuo, 2024).

Recommendations for Policy and Education

Policy and education are essential for responsible use and adaptation of genome editing technology. Closing the gap between advances in science and policy and enhancing people's understanding are crucial in order to benefit from ethical, secure, and equitable genome editing in society.

Bridging the Science–Policy Gap

Effective policy frameworks need to be guided by a wide range of values, such as ethical, social, and economic ones. Policymakers need to consult various stakeholders, such as scientists, ethicists, and the general population, in order to develop adaptive, multilayered models for governing that can be sensitive to changing scientific and societal needs (Iacomussi, 2019). Harmonized global regulation is needed because

regulatory strategies for genome editing vary considerably between nations. International organizations like the WHO have come up with frameworks for directing national policies, but further coordination and discourse are needed to cater for crossborder threats and for normalizing use (Sprink *et al.*, 2022). Policy formulation should not be left to scientists alone; rather, it should actively facilitate public involvement and discussion. This promotes trust-building, ensures policies align societally, and enhances regulatory decision legitimacy (Xue & Shang, 2022).

Public Awareness and Genome Literacy

Developing genome literacy is critical for making informed public discussion and decision-making possible. Public and targeted groups, including farmers, patients, and policymakers, should be targeted through education as part of explaining the benefits, harms, and ethical considerations of genome editing (Peng *et al.*, 2022). Accurate, easily understandable information about genome editing technology, applications, and regulatory affairs is required in order to counteract misconceptions and generate informed views. This should comprise timely knowledge updates about policy developments and societal consequences (Schiemann *et al.*, 2020). Policies should facilitate grassroots participation and education, enabling local communities to join discussions and decision-making processes for issues relevant within their location and environment (Xue & Shang, 2022).

Conclusions

This review identifies that integration of advanced genome editing tools and holistic integration of omics has the potential to revolutionize crop improvement. Advanced platforms (CRISPR/Cas9, Cas12a, base editors, prime editors, TALENs) already are enabling targeted enhancement of stress tolerance, yield, and nutritional content across cereal, leguminous, and fruit and vegetable boundaries (Jaganathan *et al.*, 2018). Rice and maize varieties are being developed for increased nutrient content and environmental tolerance, and soybeans and tomatoes for quality traits (Singh *et al.*, 2024). Nevertheless, critical bottlenecks still remain; off-target mutagenesis, suboptimal performance under editing (specifically on complex genomes), bottlenecks for delivery, and dispersed regimes of regulatory control are hindering wide-scale deployment (Shim *et al.*, 2017). Overcoming all of them – through technological innovations, robust regulatory regimes, and inclusive research agendas – promises a next-generation series of "smart" crops which will be climatic-resilient and nutritionally dense (Zenda *et al.*, 2021). Such success would represent an enormous leap toward food and nutrition security at an international scale, meeting the needs of mixed farming systems and agricultural diversity without environmental sustainability loss (Waha *et al.*, 2022).

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REFERENCES

- Jaganathan, D., Ramasamy, K. M., Sellamuthu, G., Jayabalan, S., & Venkataraman, G. (2018). CRISPR for Crop Improvement: An Update Review. *Frontiers in Plant Science*, 9. <https://doi.org/10.3389/fpls.2018.00985>
- Shim, G., Kim, D., Park, G. T., Jin, H., Suh, S., & Oh, Y. (2017). Therapeutic gene editing: Delivery and regulatory perspectives. *Acta Pharmacologica Sinica*, 38, 738–753. <https://doi.org/10.1038/aps.2017.2>
- Singh, P. K., Devanna, B. N., Dubey, H., Singh, P., Joshi, G., & Kumar, R. (2024). The potential of genome editing to create novel alleles of resistance genes in rice. *Frontiers in Genome Editing*, 6. <https://doi.org/10.3389/fgeed.2024.1415244>
- Waha, K., Accatino, F., Godde, C., Rigolot, C., Bogard, J., Domingues, J. P., Gotor, E., Herrero, M., Martin, G., Mason-D'Croz, D., Tacconi, F., & Wijk, M. van. (2022). The benefits and trade-offs of agricultural diversity for food security in low- and middle-income countries: A review of existing knowledge and evidence. *Global Food Security*. <https://doi.org/10.1016/j.gfs.2022.100645>
- Zenda, T., Liu, S., Dong, A., Li, J., Wang, Y., Liu, X., Wang, N., & Duan, H. (2021). Omics-Facilitated Crop Improvement for Climate Resilience and Superior Nutritive Value. *Frontiers in Plant Science*, 12. <https://doi.org/10.3389/fpls.2021.774994>
- Abdallah, N., Prakash, C., & McHughen, A. (2015). Genome editing for crop improvement: Challenges and opportunities. *GM Crops & Food*, 6(4), 183–205. <https://doi.org/10.1080/21645698.2015.1129937>
- Anzalone, A., Koblan, L., & Liu, D. (2020). Genome editing with CRISPR–Cas nucleases, base editors, transposases and prime editors. *Nature Biotechnology*, 38, 824–844. <https://doi.org/10.1038/s41587-020-0561-9>
- Baillo, E., Kimotho, R., Zhang, Z., & Xu, P. (2019). Transcription factors associated with abiotic and biotic stress tolerance and their potential for crop improvement. *Genes*, 10(10), 701. <https://doi.org/10.3390/genes10100701>
- Chaudhary, S., Grover, A., & Sharma, P. (2021). MicroRNAs: Potential targets for developing stress-tolerant crops. *Life*, 11(4), 289. <https://doi.org/10.3390/life11040289>
- Chen, F., Chen, L., Yan, Z., Xu, J., Feng, L., He, N., ... & Liu, C. (2024). Recent advances of CRISPR-based genome editing for enhancing staple crops. *Frontiers in Plant Science*, 15. <https://doi.org/10.3389/fpls.2024.1478398>
- Dongriyal, A., Chandra, A., Dongriyal, A., Kumar, A., & Sharma, P. (2023). Tending genome editing via CRISPR/Cas9-induced mutagenesis: Opportunity and challenges for yield, quality and nutritional improvement of fruit crops. *Scientia Horticulturae*, 311, 111790. <https://doi.org/10.1016/j.scienta.2022.111790>
- Gaikwad, K., Rani, S., Kumar, M., Gupta, V., Babu, P., Bainsla, N., & Yadav, R. (2020). Enhancing the nutritional quality of major food crops through conventional and genomics-assisted breeding. *Frontiers in Nutrition*, 7. <https://doi.org/10.3389/fnut.2020.533453>
- Gupta, D., Bhattacharjee, O., Mandal, D., Sen, M., Dey, D., Dasgupta, A., ... & Ghosh, D. (2019). CRISPR-Cas9 system: A new-fangled dawn in gene editing. *Life Sciences*, 116636. <https://doi.org/10.1016/j.lfs.2019.116636>
- Imam, Z., Sultana, R., Parveen, R., Singh, D., Sinha, S., & Sahoo, J. (2024). Understanding the concept of speed breeding in crop improvement: Opportunities and challenges towards global food security. *Tropical Plant Biology*. <https://doi.org/10.1007/s12042-024-09353-5>
- Janik, E., Niemcewicz, M., Ceremuga, M., Krzowski, L., Saluk-Bijak, J., & Bijak, M. (2020). Various aspects of a gene editing system—CRISPR–Cas9. *International Journal of Molecular Sciences*, 21(24), 9604. <https://doi.org/10.3390/ijms21249604>
- Jha, R., Yadav, H., Raiya, R., Singh, R., Jha, U., Sathee, L., ... & Tripathi, S. (2022). Integrated breeding approaches to enhance the nutritional quality of food legumes. *Frontiers in Plant Science*, 13. <https://doi.org/10.3389/fpls.2022.984700>
- Kantor, A., McClements, M., & MacLaren, R. (2020). CRISPR-Cas9 DNA base-editing and prime-editing. *International Journal of Molecular Sciences*, 21(17), 6240. <https://doi.org/10.3390/ijms21176240>
- Koul, B., & Tiwari, S. (2020). Microbe-mediated genetic engineering for enhancement of nutritional value in food crops. In *Microbial Biotechnology* (pp. 19–53). https://doi.org/10.1007/978-981-15-2817-0_2
- Ku, H., & Ha, S. (2020). Improving nutritional and functional quality by genome editing of crops: Status and perspectives. *Frontiers in Plant Science*, 11. <https://doi.org/10.3389/fpls.2020.577313>
- Mondal, S., Rutkoski, J., Velu, G., Singh, P., Crespo-Herrera, L., Guzmán, C., ... & Singh, R. (2016). Harnessing diversity in wheat to enhance grain yield, climate resilience, disease and insect pest resistance and nutrition through conventional and modern breeding approaches. *Frontiers in Plant Science*, 7. <https://doi.org/10.3389/fpls.2016.00991>
- Nagamine, A., & Ezura, H. (2022). Genome editing for improving crop nutrition. *Frontiers in Genome Editing*, 4. <https://doi.org/10.3389/fgeed.2022.850104>
- Schulze, S., & Lammers, M. (2020). The development of genome editing tools as powerful techniques with versatile applications in biotechnology and medicine. *ChemTexts*, 6. <https://doi.org/10.1007/s40828-020-00126-7>

- Sharma, P., Pandey, A., Malviya, R., Dey, S., Karmakar, S., & Gayen, D. (2023). Genome editing for improving nutritional quality, post-harvest shelf life and stress tolerance of fruits, vegetables, and ornamentals. *Frontiers in Genome Editing*, 5. <https://doi.org/10.3389/fgeed.2023.1094965>
- Smith, C., Gore, A., Yan, W., Abalde-Atristain, L., Li, Z., He, C., ... & Ye, Z. (2014). Whole-genome sequencing analysis reveals high specificity of CRISPR/Cas9 and TALEN-based genome editing in human iPSCs. *Cell Stem Cell*, 15(1), 12–13. <https://doi.org/10.1016/j.stem.2014.06.011>
- Tang, Y., & Fu, Y. (2018). Class 2 CRISPR/Cas: An expanding biotechnology toolbox for and beyond genome editing. *Cell & Bioscience*, 8. <https://doi.org/10.1186/s13578-018-0255-x>
- Thudi, M., Palakurthi, R., Schnable, J., Chitkineni, A., Dreisigacker, S., Mace, E., ... & Varshney, R. (2020). Genomic resources in plant breeding for sustainable agriculture. *Journal of Plant Physiology*, 257, 153351. <https://doi.org/10.1016/j.jplph.2020.153351>
- Xu, J., Hua, K., & Lang, Z. (2019). Genome editing for horticultural crop improvement. *Horticulture Research*, 6. <https://doi.org/10.1038/s41438-019-0196-5>
- Yang, Y., Xu, C., Shen, Z., & Yan, C. (2022). Crop quality improvement through genome editing strategy. *Frontiers in Genome Editing*, 3. <https://doi.org/10.3389/fgeed.2021.819687>
- Zafar, S., & Xu, J. (2023). Recent advances to enhance nutritional quality of rice. *Rice Science*. <https://doi.org/10.1016/j.rsci.2023.05.004>
- Zafar, S., Zaidi, S., Gaba, Y., Singla-Pareek, S., Dhankher, O., Li, X., Mansoor, S., & Pareek, A. (2020). Engineering abiotic stress tolerance via CRISPR-Cas mediated genome editing: Progress and prospects.
- Chaudhary, S., Grover, A., & Sharma, P. (2021). MicroRNAs: Potential targets for developing stress-tolerant crops. *Life*, 11(4), 289. <https://doi.org/10.3390/life11040289>
- Consentino, B., Ciriello, M., Sabatino, L., Vultaggio, L., Baldassano, S., Vasto, S., Rouphael, Y., La Bella, S., & De Pascale, S. (2023). Current acquaintance on agronomic biofortification to modulate the yield and functional value of vegetable crops: A review. *Horticulturae*, 9(2), 219. <https://doi.org/10.3390/horticulturae9020219>
- Dwivedi, S., Garcia-Oliveira, A., Govindaraj, M., & Ortiz, R. (2023). Biofortification to avoid malnutrition in humans in a changing climate: Enhancing micronutrient bioavailability in seed, tuber, and storage roots. *Frontiers in Plant Science*, 14, 1119148. <https://doi.org/10.3389/fpls.2023.1119148>
- Ghosh, S. (2024). Current approaches and future potential for delivering CRISPR/Cas components in oilseeds and millets. *The Nucleus*. <https://doi.org/10.1007/s13237-024-00486-2>
- Hatakeyama, M., Aluri, S., Balachadran, M., Sivarajan, S., Patrignani, A., Grüter, S., Poveda, L., Shimizu-Inatsugi, R., Baeten, J., François, K., Nataraja, K., Reddy, Y., Phadnis, S., Ravikumar, R., Schlappbach, R., Sreeman, S., & Shimizu, K. (2017). Multiple hybrid de novo genome assembly of finger millet, an orphan allotetraploid crop. *DNA Research*, 25(1), 39–47. <https://doi.org/10.1093/dnares/dsx036>
- Jayaraman, K., Sevanthi, A., Raman, K., Jiwani, G., Solanke, A., Mandal, P., & Mohapatra, T. (2023). Overexpression of a DUF740 family gene (LOC_Os04g59420) imparts enhanced climate resilience through multiple stress tolerance in rice. *Frontiers in Plant Science*, 13, 947312. <https://doi.org/10.3389/fpls.2022.947312>
- Jha, A., Jayswal, D., Shikha, D., Kumar, A., & Ahmad, F. (2025). Empowering vital fruit crops with enhanced nutritional contents. *Frontiers in Plant Science*. <https://doi.org/10.3389/fpls.2025.1519673>
- Kamali, S., & Singh, A. (2023). Genomic and transcriptomic approaches to developing abiotic stress-resilient crops. *Agronomy*, 13(12), 2903. <https://doi.org/10.3390/agronomy13122903>
- Karunaratne, S., Walker, E., Sharma, D., Li, C., & Han, Y. (2023). Genetic resources and precise gene editing for targeted improvement of barley abiotic stress tolerance. *Journal of Zhejiang University - Science B*, 24, 1–24. <https://doi.org/10.1631/jzus.B2200552>
- Kathi, S., Laza, H., Singh, S., Thompson, L., Li, W., & Simpson, C. (2023). A decade of improving nutritional quality of horticultural crops agronomically (2012–2022): A systematic literature review. *The Science of the Total Environment*, 168665. <https://doi.org/10.1016/j.scitotenv.2023.168665>
- Kaya, C. (2025). Plant metabolic engineering for enhanced nutrition and food security during climate uncertainty. *Food and Energy Security*. <https://doi.org/10.1002/fes3.70060>
- Liu, Y., Cheng, Z., Chen, W., Wu, C., Chen, J., & Sui, Y. (2024). Establishment of genome-editing system and assembly of a near-complete genome in broomcorn millet. *Journal of Integrative Plant Biology*. <https://doi.org/10.1111/jipb.13664>
- Manghwar, H., Li, B., Ding, X., Hussain, A., Lindsey, K., Zhang, X., & Jin, S. (2020). CRISPR/Cas systems: Emerging tools for genome engineering in plants. *Trends in Plant Science*, 25(10), 884–905. <https://doi.org/10.1016/j.tplants.2020.06.005>
- Nadakuduti, S., Buell, C., Voytas, D., Starker, C., & Douches, D. (2018). Genome editing for crop improvement – Applications in clonally propagated polyploids with a focus on potato (*Solanum tuberosum* L.). *Frontiers in Plant Science*, 9, 1607. <https://doi.org/10.3389/fpls.2018.01607>
- Odipto, J., Alicai, T., Ingelbrecht, I., Nusinow, D., Bart, R., & Taylor, N. (2017). Efficient CRISPR/Cas9 genome editing of phytoene desaturase in cassava. *Frontiers in Plant Science*, 8, 1780. <https://doi.org/10.3389/fpls.2017.01780>
- Riaz, A., Uzair, M., Raza, A., Inam, S., Iqbal, R., Jameel, S., Bibi, B., & Khan, M. (2025). Enhancing the productivity and resilience of rice (*Oryza sativa*) under environmental stress conditions using clustered regularly interspaced short palindromic repeats (CRISPR) technology. *Functional Plant Biology*, 52(3). <https://doi.org/10.1071/fp24101>
- Singh, S., Koyama, H., Bhati, K., & Alok, A. (2021). The biotechnological importance of the plant-specific NAC transcription factor family in crop improvement. *Journal of Plant Research*, 134(3), 475–495. <https://doi.org/10.1007/s10265-021-01270-y>
- Venezia, M., & Krainer, K. (2021). Current advancements and limitations of gene editing in orphan crops. *Frontiers in Plant Science*, 12, 742932. <https://doi.org/10.3389/fpls.2021.742932>
- Yadav, S., Sandhu, N., Dixit, S., Singh, V., Catolos, M., Mazumder, R., Rahman, M., & Kumar, A. (2021). Genomics-assisted breeding for successful development of multiple-stress-tolerant, climate-smart rice for southern and southeastern Asia. *The Plant Genome*, 14(1), e20074. <https://doi.org/10.1002/tpg2.20074>
- Yamada, H., Kato, N., Ichikawa, M., Mannen, K., Kiba, T., Osakabe, Y., Sakakibara, H., Matsui, M., & Okamoto, T.

- (2024). DNA- and selectable-marker-free genome-editing system using zygotes from recalcitrant maize inbred B73. *Plant & Cell Physiology*. <https://doi.org/10.1093/pcp/pcae010>
- Zafar, S., Zaidi, S., Gaba, Y., Singla-Pareek, S., Dhankher, O., Li, X., Mansoor, S., & Pareek, A. (2020). Engineering abiotic stress tolerance via CRISPR-Cas mediated genome editing. *Journal of Experimental Botany*, 71(17), 4706–4723. <https://doi.org/10.1093/jxb/erz476>
- Zhou, C., Zhang, J., Wu, Y., Cheng, H., Pang, Q., Xiao, Y., Li, D., & Pan, C. (2022). Metabolomic analysis on the mechanism of nanoselenium biofortification improving the *Siraitia grosvenorii* nutritional and health value. *Foods*, 11(19), 3019. <https://doi.org/10.3390/foods11193019>
- Zulfiqar, U., Khokhar, A., Maqsood, M., Shahbaz, M., Naz, N., Sara, M., Maqsood, S., Sahar, S., Hussain, S., & Ahmad, M. (2024). Genetic biofortification: Advancing crop nutrition to tackle hidden hunger. *Functional & Integrative Genomics*, 24(2), 34. <https://doi.org/10.1007/s10142-024-01308-z>
- Ahmad, M. Z., Rahman, M. U., Ahmed, H., Altaf, M. A., & Naveed, M. (2021). Genome editing using CRISPR/Cas9—A way forward to achieve sustainable agriculture. *Frontiers in Plant Science*, 12, 690279. <https://doi.org/10.3389/fpls.2021.690279>
- Alok, A., & Banerjee, A. (2023). Genome editing in crops: current innovations, applications and future scope. *Journal of Genetics*, 102(1), 6. <https://doi.org/10.1007/s12041-023-01392-w>
- Anzalone, A. V., Koblan, L. W., & Liu, D. R. (2020). Genome editing with CRISPR-Cas nucleases, base editors, transposases and prime editors. *Nature Biotechnology*, 38(7), 824–844. <https://doi.org/10.1038/s41587-020-0561-9>
- Sedeek, K. E. M., Mahas, A., & Mahfouz, M. (2019). Plant genome engineering for targeted improvement of crop traits. *Frontiers in Plant Science*, 10, 114. <https://doi.org/10.3389/fpls.2019.00114>
- Brinegar, K., Yetisen, A., Choi, S., Vallillo, E., Ruiz-Esparza, G., Prabhakar, A., Khademhosseini, A., & Yun, S. (2017). The commercialization of genome-editing technologies. *Critical Reviews in Biotechnology*, 37, 924–932. <https://doi.org/10.1080/07388551.2016.1271768>
- Cheng, X., Li, Z., Shan, R., Li, Z., Wang, S., Zhao, W., Zhang, H., Chao, L., Peng, J., Fei, T., & Li, W. (2023). Modeling CRISPR-Cas13d on-target and off-target effects using machine learning approaches. *Nature Communications*, 14. <https://doi.org/10.1038/s41467-023-36316-3>
- Ding, L., Schmitt, L., Brux, M., Sürün, D., Augsburg, M., Lansing, F., Mircetic, J., Theis, M., & Buchholz, F. (2022). DNA methylation-independent long-term epigenetic silencing with dCRISPR/Cas9 fusion proteins. *Life Science Alliance*, 5. <https://doi.org/10.26508/lsa.202101321>
- Iacomussi, S. (2019). Regulating genome editing technologies: A comparison of expert recommendations in the U.K. and in the U.S.A...
- Kalaitzandonakes, N., Willig, C., & Zahringer, K. (2022). The economics and policy of genome editing in crop improvement. *The Plant Genome*, 16. <https://doi.org/10.1002/tpg2.20248>
- Lassoued, R., Phillips, P., Macall, D., Hessel, H., & Smyth, S. (2021). Expert opinions on the regulation of plant genome editing. *Plant Biotechnology Journal*, 19, 1104–1109. <https://doi.org/10.1111/pbi.13597>
- Lin, J., Zhang, Z., Zhang, S., Chen, J., & Wong, K. (2020). CRISPR-Net: A Recurrent Convolutional Network Quantifies CRISPR Off-Target Activities with Mismatches and Indels. *Advanced Science*, 7. <https://doi.org/10.1002/advs.201903562>
- Listgarten, J., Weinstein, M., Kleinstiver, B., Sousa, A., Joung, K., Crawford, J., Gao, K., Hoang, L., Elibol, M., Doench, J., & Fusi, N. (2018). Prediction of off-target activities for the end-to-end design of CRISPR guide RNAs. *Nature Biomedical Engineering*, 2, 38–47. <https://doi.org/10.1038/s41551-017-0178-6>
- Menz, J., Modrzejewski, D., Hartung, F., Wilhelm, R., & Sprink, T. (2020). Genome Edited Crops Touch the Market: A View on the Global Development and Regulatory Environment. *Frontiers in Plant Science*, 11. <https://doi.org/10.3389/fpls.2020.586027>
- Özden, F., & Minary, P. (2024). Learning to quantify uncertainty in off-target activity for CRISPR guide RNAs. *Nucleic Acids Research*, 52, e87. <https://doi.org/10.1093/nar/gkae759>
- Piatek, A., Ali, Z., Baazim, H., Li, L., Abulfaraj, A., Al-Shareef, S., Aouida, M., & Mahfouz, M. (2015). RNA-guided transcriptional regulation in planta via synthetic dCas9-based transcription factors. *Plant Biotechnology Journal*, 13(4), 578–589. <https://doi.org/10.1111/pbi.12284>
- Ricroch, A. (2019). Global developments of genome editing in agriculture. *Transgenic Research*, 28, 45–52. <https://doi.org/10.1007/s11248-019-00133-6>
- Sari, O., Liu, Z., Pan, Y., & Shao, X. (2024). Predicting CRISPR-Cas9 off-target effects in human primary cells using bidirectional LSTM with BERT embedding. *Bioinformatics Advances*, 5. <https://doi.org/10.1093/bioadv/vbae184>
- Sherkatghanad, Z., Abdar, M., Charlier, J., & Makarenkov, V. (2023). Using traditional machine learning and deep learning methods for on- and off-target prediction in CRISPR/Cas9: a review. *Briefings in Bioinformatics*, 24. <https://doi.org/10.1093/bib/bbad131>
- Tachikawa, M., & Matsuo, M. (2024). Global regulatory trends of genome editing technology in agriculture and food. *Breeding Science*, 74, 3–10. <https://doi.org/10.1270/jsbbs.23046>
- Toledo-Hernández, M., Lander, T., Bao, C., Xie, K., Atta-Boateng, A., & Wanger, T. (2021). Genome-edited tree crops: mind the socioeconomic implementation gap. *Trends in Ecology & Evolution*. <https://doi.org/10.1016/j.tree.2021.08.007>
- Toufikuzzaman, M., Abul, M., Samee, H., & Rahman, M. (2023). CRISPR-DIPOFF: an interpretable deep learning approach for CRISPR Cas-9 off-target prediction. *Briefings in Bioinformatics*, 25. <https://doi.org/10.1101/2023.08.05.552139>
- Vojta, A., Dobrinčić, P., Tadić, V., Bočkor, L., Korać, P., Julg, B., Klasić, M., & Zoldoš, V. (2016). Repurposing the CRISPR-Cas9 system for targeted DNA methylation. *Nucleic Acids Research*, 44, 5615–5628. <https://doi.org/10.1093/nar/gkw159>
- Wu, H., Wang, F., & Jiang, J. (2021). Inducible CRISPR-dCas9 Transcriptional Systems for Sensing and Genome Regulation. *ChemBioChem*, 22. <https://doi.org/10.1002/cbic.202000723>
- Xu, X., & Qi, L. (2019). A CRISPR-dCas9 Toolbox for Genetic Engineering and Synthetic Biology. *Journal of Molecular Biology*, 431(1), 34–47. <https://doi.org/10.1016/j.jmb.2018.06.037>
- Xue, Y., & Shang, L. (2022). Governance of Heritable Human Gene Editing World-Wide and Beyond. *International Journal of Environmental Research and Public Health*, 19. <https://doi.org/10.3390/ijerph19116739>
- Zhu, H., Wu, X., Zheng, R., & Zhu, Y. (2025). The impact of gene editing technology on agricultural economic efficiency: An empirical analysis based on international CRISPR patent data. *Molecular & Cellular Biomechanics*. <https://doi.org/10.62617/mcb1031>