Physical Education, Health and Social Sciences

https://journal-of-social-education.org E-ISSN: 2958-5996

P-ISSN: 2958-5988

CRISPR-Cas Genome Editing for Climate-Smart Agriculture: Molecular Tools, Stress Resilience, and Regulatory Horizons

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DOI: https://doi.org/10.63163/jpehss.v4i1.1716

Abstract

Global agriculture faces an unprecedented convergence of population growth and climate change, demanding a 25-60% increase in food production by 2050 while contending with rising temperatures, drought, salinity, and emerging phytopathogens. Conventional breeding and transgenesis have proven insufficient to meet these challenges due to genetic bottlenecks, lengthy timelines, and regulatory constraints. Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) and CRISPR-associated protein (Cas) systems have revolutionized plant biotechnology by enabling precise, targeted genome modifications directly within elite germplasm. This comprehensive review examines the molecular mechanics of CRISPR-Cas platforms, including SpCas9, Cas12a, base editing, prime editing, and epigenome editing, highlighting their applications in developing climate-resilient and high-yielding crop varieties. Key achievements include promoter engineering of maize *ARGOS8* that increased drought tolerance yields by 5 bushels per acre, susceptibility gene knockouts conferring resistance to powdery mildew, bacterial blight, and citrus canker, and multiplex editing enabling synthetic apomixis for hybrid vigor fixation. The review critically evaluates global regulatory frameworks, contrasting product-based models (United States, Brazil, Japan) with process-based approaches (European Union), and examines recent policy shifts toward exempting transgene-free edits from GMO oversight. Despite technical bottlenecks including tissue culture recalcitrance, off-target mutations, and complex polygenic trait engineering, emerging solutions such as morphogenic regulators, high-fidelity Cas variants, and integration with pangenomics and speed breeding promise to accelerate crop improvement. CRISPR-Cas technology represents a transformative paradigm for developing climate-smart agriculture, offering precise, efficient, and transgene-free pathways to enhance food security in an era of environmental uncertainty.

Keywords: CRISPR-Cas9, Genome Editing, Climate Resilience, Abiotic Stress Tolerance, Disease Resistance, Crop Improvement, Regulatory Frameworks, Food Security

1. Introduction

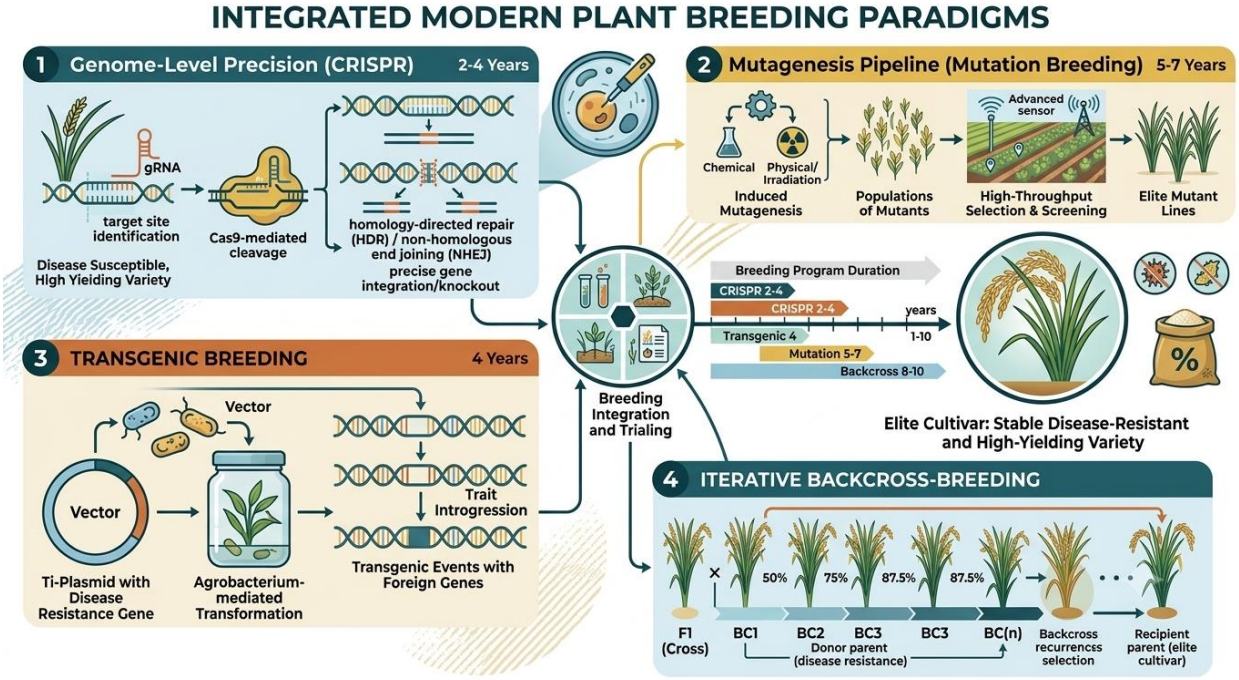
Global agriculture is facing an unprecedented convergence of demographic pressure and environmental instability. Demographic projections indicate that the human population will reach approximately 8.5 billion by 2030 and 9.6 billion by 2050, requiring an estimated 25% to 60% expansion in global food production to secure basic nutritional requirements. Concurrently, anthropogenic climate change is intensifying both the frequency and severity of abiotic and biotic stresses across major agricultural regions (Khatri et., 2024). Environmental models project localized

mean temperature increases of up to 8°C by the end of the twenty-first century, accompanied by hydrological shifts that could elevate the global average drought index from a baseline of 52.45 to 129. Thermodynamics dictates that for every 1°C increase in global mean temperature, atmospheric moisture capacity drives a 3% increase in average precipitation variability and a 7% increase in relative humidity, creating microclimatic conditions that accelerate phytopathogenic epidemics and insect pest proliferation (Chen & Frauenfeld, 2014).

The primary cereal crops rice (*Oryza sativa*), maize (*Zea mays*), and wheat (*Triticum aestivum*) form the foundation of global caloric supply. Rice alone serves as the primary staple for nearly half of the global population; however, approximately 90% of global rice production is concentrated in Asian agricultural basins that are increasingly vulnerable to drought, heat waves, salinity intrusion, and flash flooding (Awika, 2011). Conventional plant breeding strategies based on phenotypic selection and marker-assisted crossbreeding have driven historical yield gains, but they are increasingly limited by genetic bottlenecks, extended breeding cycles, and the complex polygenic inheritance of climate-adaptation traits. Transgenic approaches involving recombinant DNA technologies provided early solutions, but their widespread deployment remains constrained by lengthy developmental timelines, low public acceptance, and costly regulatory oversight (Ahmar et al., 2020).

In response to these challenges, Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) and CRISPR-associated protein (Cas) systems have established a novel paradigm in plant biotechnology. As a site-specific genome editing platform, CRISPR-Cas allows targeted nucleotide alterations, gene disruptions, cis-regulatory promoter engineering, and epigenomic modifications directly within elite germplasm. By enabling transgene-free editing of endogenous gene networks, CRISPR-Cas technology bypasses traditional breeding barriers to accelerate the development of climate-smart crop varieties optimized for yield stability, resource-use efficiency, and multi-stress resilience (Nazir et al., 2022).

Figure 1. Schematic representation of integrated modern plant breeding paradigms, contrasting genome-level precision (CRISPR), mutagenesis, transgenic methods, and iterative backcrossing timelines.



2. CRISPR-Cas Molecular Mechanics and Tool Expansion

The canonical SpCas9 system operates through a dual-component ribonucleoprotein complex consisting of a Cas9 endonuclease and a synthetic single-guide RNA (sgRNA). The sgRNA contains a 20-nucleotide spacer sequence that directs Cas9 to a complementary genomic locus positioned immediately 5' of a conserved Protospacer Adjacent Motif (PAM), typically 5'-NGG-3' for SpCas9. Upon target site binding and R-loop formation, the HNH and RuvC catalytic domains of Cas9 cleave opposite strands of the target DNA, generating a blunt-ended double-strand break (DSB) three base pairs upstream of the PAM site (Chandrashekhar, 2018). Plant cells repair these DSBs primarily through the endogenous Non-Homologous End Joining (NHEJ) pathway, an inherently error-prone repair mechanism that frequently introduces small insertions or deletions (indels) leading to frameshift mutations and functional gene knockouts. Alternatively, co-delivering an exogenous donor repair template allows the Homology-Directed Repair (HDR) or Microhomology-Mediated End-Joining (MHEJ) pathways to introduce targeted nucleotide substitutions, precise gene insertions, or promoter replacements (Cetin et al., 2021).

To overcome target site constraints and enhance editing precision, the molecular CRISPR toolbox has expanded beyond standard SpCas9 nucleases through natural ortholog mining and protein engineering:

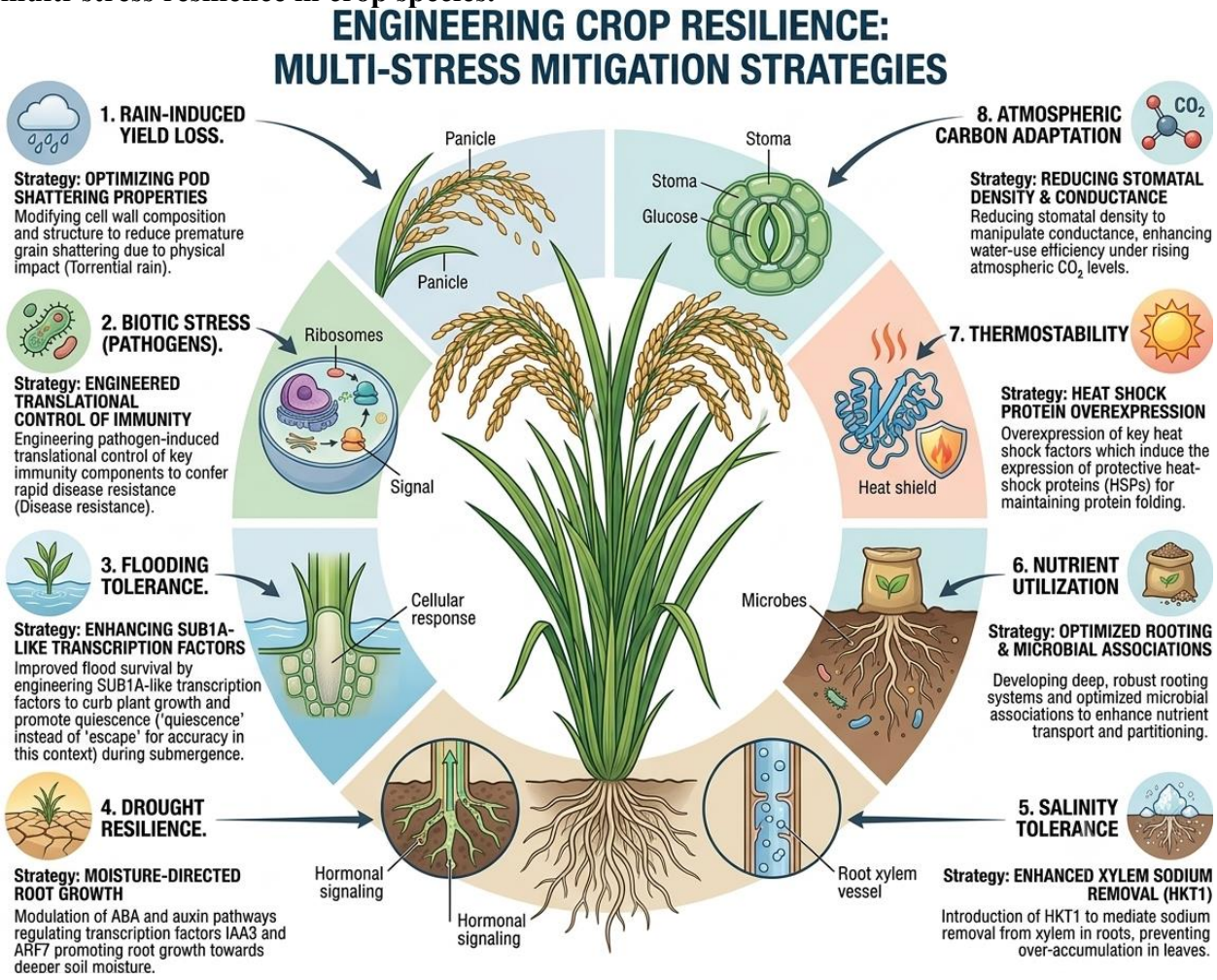
- **Cas12a (Cpf1) Orthologs**: Unlike Cas9, Cas12a recognizes thymine-rich PAM sequences (e.g., 5'-TTTV-3') and uses a single RuvC-like domain to generate staggered DSBs with 4- or 5-nucleotide 5' overhangs. These cohesive ends promote precise HDR-mediated knock-in events over NHEJ indels. Furthermore, Cas12a possesses intrinsic ribonuclease activity capable of processing single crRNA precursor arrays, enabling efficient single-vector multiplex genome editing across extended gene pathways (Parvathy, 2024).
- **Base Editing Systems**: Cytosine Base Editors (CBEs) and Adenine Base Editors (ABEs) combine a catalytically impaired Cas9 nickase (nCas9) or dead Cas9 (dCas9) with single-stranded DNA cytidine or adenosine deaminases. Base editors catalyze targeted $C \cdot G \rightarrow T \cdot A$ or $A \cdot T \rightarrow G \cdot C$ transition mutations within a narrow editing window without double-strand break generation or donor DNA templates, avoiding high indel rates (Molla & Yang, 2019).
- **Prime Editing (PE)**: Prime editors integrate an nCas9 fused to an engineered reverse transcriptase, guided by a prime editing guide RNA (pegRNA) that specifies the genomic target locus and encodes the desired edit sequence. Prime editing enables all twelve possible transition and transversion base conversions, targeted micro-insertions, and micro-deletions without donor DNA or DSBs (Zhao et al., 2023).
- **Epigenome Editing**: Fusing dCas9 to transcriptional activators, repressors, or chromatin-modifying enzymes allows locus-specific regulation of gene expression without altering the underlying genomic sequence. For example, coupling dCas9 to the catalytic domain of histone acetyltransferase (HAT) targets the promoter region of *AREB1* (ABRE-binding protein 1), inducing local histone acetylation. This structural chromatin opening increases promoter accessibility for endogenous transcription factors during water stress, upregulating downstream stress-responsive genes like *RD29A* without introducing permanent DNA mutations (Pulecio et al., 2017).

A major bottleneck in applying CRISPR technology across diverse agricultural cultivars remains the challenge of component delivery across cell walls and the reliance on tissue culture regeneration. While *Agrobacterium tumefaciens*-mediated transformation and biolistic bombardment remain the standard delivery methods, delivering pre-assembled Ribonucleoprotein (RNP) complexes avoids vector integration, yielding non-transgenic edited plants in the first generation (T_0). Emerging delivery formats including viral vectors like Tobacco Rattle Virus (TRV) and Haploid-Inducer Mediated Editing (HI-Edit / IMGE), which pairs a CRISPR expression cassette with a pollen-side haploid inducer line allow direct genome editing in commercial elite lines, bypassing traditional tissue culture steps (Cardi et al., 2023)

3. Engineering Abiotic Stress Resilience

Abiotic environmental drivers drought, soil salinity, thermal extremes, and nutrient scarcity cause cellular dehydration, reactive oxygen species (ROS) accumulation, photosynthetic disruption, and substantial yield losses. CRISPR-Cas technology provides a platform to systematically re-engineer stress-response pathways, balancing emergency survival mechanisms with agronomic productivity (Chaudhry & Sidhu, 2022).

Figure 1. Overview of physiological target pathways and cellular mechanisms for engineering multi-stress resilience in crop species.



3.1 Drought and Osmotic Stress Mitigation

In response to water deficits, plants synthesize abscisic acid (ABA) and ethylene, initiating stomatal closure, root remodeling, and osmotic adjustment networks. Ethylene plays a key role in mediating drought responses; however, elevated ethylene signaling during reproductive development causes silk desiccation, kernel abortion, and significant grain yield reductions. The maize *ARGOS8* gene functions as a negative regulator of cellular ethylene responses. Screenings across 400 native maize inbred lines indicated that natural variation in *ARGOS8* transcription was insufficient to limit ethylene sensitivity under severe drought conditions (Aslam et al., 2022).

Using CRISPR-Cas9 homology-directed repair, researchers inserted or replaced the native promoter of *ARGOS8* with the moderately constitutive, native maize *GOS2* promoter within its 5'-untranslated region (5'-UTR). This cis-regulatory engineering elevated *ARGOS8* transcription across both vegetative and reproductive tissues. In extensive field trials across drought-stressed environments

during flowering, the engineered *ARGOS8* variants produced an average yield increase of 5 bushels per acre over wild-type controls, while maintaining equivalent high yields under well-watered conditions (Shi et al., 2017).

Beyond *ARGOS8*, editing key transcription factors within the ABA signaling cascade such as AREBs/ABFs, SNF1-related protein kinase 2 (*SnRK2*), *DREB2A*, *ZmNAC111*, and *HaHB4* improves stomatal conductance, water retention, and root elongation. Knocking out selective negative regulators of ABA signaling enhances stomatal sensitivity during water deficits, preserving leaf water potential while limiting damaging ROS accumulation (Ayub et al., 2025).

3.2 Thermal, Salinity, and Heavy Metal Tolerance

Heat stress during reproductive growth disrupts metabolic homeostasis and causes spikelet sterility in cereal crops. Multiplex CRISPR editing targeting heat shock transcription factors (HSFs), ROS-scavenging pathways, and ethylene signaling components protects cellular structures under combined heat and drought conditions (Qian et al., 2025).

In saline soils, excess intracellular sodium (Na^+) disrupts K^+/Na^+ homeostatic ratios, inhibiting essential enzymatic functions. Targeted editing of high-affinity potassium transporters (such as *ZmHKT1* in maize) optimizes ion selectivity, preserving root xylem loading under high salt concentrations. In potato (*Solanum tuberosum*), editing translation initiation factors *eIF4E* and *eIF(iso)4E* mitigates cold-induced sweetening during cold storage, preserving tuber processing quality. Additionally, editing gibberellin biosynthesis genes like *ZmGA20ox3* generates semidwarf crop architectures with stronger lodging resistance under severe weather events (Wakeel, 2013).

4. Biotic Stress Resistance, Yield Architecture, and Domestication

Susceptibility Gene Engineering for Phytopathogen Resistance

Infectious plant diseases driven by fungi, bacteria, and viruses cause significant annual crop loss. Rather than inserting foreign resistance genes, CRISPR-Cas technology enables broad-spectrum resistance by knocking out endogenous Susceptibility (*S*) genes host targets required by pathogens for entry, colonization, or metabolic exploitation:

- **Powdery Mildew Resistance**: Targeted knockout of *EDR1* (Enhanced Disease Resistance 1) in hexaploid wheat (*Triticum aestivum*) confers resistance against *Blumeria graminis* f. sp. *tritici*. Similarly, knocking out *SlMLO1* in tomato (*Solanum lycopersicum*) blocks infection by *Oidium neolycopersici* (Dong & Fan, 2024).
- **Bacterial Blight and Speck Resistance**: In rice (*Oryza sativa*), mutating the promoter region of *OsSWEET13* prevents *Xanthomonas oryzae* pv. *oryzae* from hijacking host sucrose transporters, preventing bacterial blight development. In tomato, knocking out *SlJAZ2* prevents *Pseudomonas syringae* pv. *tomato* from using coronatine toxins to open stomata during entry (Kumari et al., 2021).
- **Citrus Canker Resistance**: Promoter editing of *CsLOB1* in grapefruit (*Citrus paradisi*) and sweet orange (*Citrus sinensis*) abolishes the binding site for the PthA4 effector secreted by *Xanthomonas citri*, establishing bacterial canker resistance (Huang et al., 2022).
- **Rice Blast Control**: Disruption of the transcription factor *OsERF922* in rice significantly increases host resistance against *Magnaporthe oryzae*.

Yield Architecture Optimization and Weed Management

Agronomic yield is a complex polygenic trait determined by sink-source dynamics, inflorescence architecture, kernel size, and nutrient allocation. CRISPR-Cas9 promoter editing targeting the *CLAVATA-WUSCHEL* signaling axis specifically members of the *CLE* (CLAVATA3/ESR-related) gene family modifies shoot apical meristem proliferation. Precise tuning of *CLE* promoter activity expands

shoot apical meristem size in maize and rice, increasing kernel row number and overall grain capacity per ear (Tefera & Debele, 2026).

Targeted knockouts of *Waxy* locus alleles alter endosperm amylose content, improving starch processing qualities. In addition, precise nucleotide modifications within the *ALS* (Acetolactate Synthase) and *EPSPS* (5-Enolpyruvylshikimate-3-Phosphate Synthase) genes across maize, wheat, potato, soybean, and cassava confer targeted herbicide resistance, supporting low-tillage, water-conserving weed management practices (Sun et al., 2017).

De Novo Domestication and Clonal Seed Production

Wild plant species and underutilized orphan crops possess natural stress resilience and genetic diversity, but they often exhibit poor agronomic traits such as fruit shattering, tall architectures, small seed size, and low yield. De novo domestication uses CRISPR editing to mutate classical domestication gene orthologs in wild germplasm, rapidly introducing yield-related traits while preserving native stress tolerance. A clear demonstration of this approach was achieved in groundcherry (*Physalis peruviana*), where CRISPR-Cas9 knockout of the self-pruning ortholog *SP5G* modified stem growth and flowering, driving a compact plant architecture and higher fruit yield (Chapman et al., 2022).

Another breakthrough in crop breeding is the artificial fixation of hybrid vigor (synthetic apomixis). F_1 crop hybrids display superior yield relative to inbred lines; however, genetic segregation during meiosis prevents farmers from saving F_2 seeds for replanting. By using CRISPR-Cas9 to simultaneously knock out three meiotic genes *REC8*, *PAIR1*, and *OSD1* researchers converted meiosis into a mitotic division (the MiMe phenotype). Combined with the targeted expression of a parthenogenesis factor, this system enables the production of clonal diploid seeds from F_1 hybrids, permanently fixing hybrid vigor across successive generations (Underwood & Mercier, 2022).

Table 1 summarizes representative applications of CRISPR-Cas technology targeting abiotic stress resilience, disease resistance, yield architecture, and domestication traits across major crop species.

Table 1. Representative CRISPR-Cas genomic modifications for climate resilience, yield enhancement, and pathogen resistance in crops.

Crop Species	Target Gene(s)	Editing Mechanism / Tool	Targeted Agronomic Phenotype / Trait
Maize (*Zea mays*)	*ARGOS8*	CRISPR-Cas9 (HDR promoter insertion)	Increases grain yield under drought during flowering (~5 bu/acre boost)
Maize (*Zea mays*)	*ZmGA20ox3*	CRISPR-Cas9 (NHEJ knockout)	Yields semidwarf architecture; increases stalk lodging resistance
Maize (*Zea mays*)	*CLE* family	CRISPR-Cas9 (Promoter editing)	Expands shoot meristem; increases kernel row number
Wheat (*Triticum aestivum*)	*EDR1*	CRISPR-Cas9 (NHEJ knockout)	Establishes broad-spectrum resistance to powdery mildew (*B. graminis*)
Rice (*Oryza sativa*)	*OsERF922*	CRISPR-Cas9 (NHEJ knockout)	Increases host defense against rice blast (*M. oryzae*)
Rice (*Oryza sativa*)	*OsSWEET13* promoter	CRISPR-Cas9 (Promoter deletion)	Blocks pathogen exploitation; confers bacterial blight resistance
Rice (*Oryza sativa*)	*REC8*, *PAIR1*, *OSD1*	Multiplex CRISPR-Cas9	Fixes hybrid vigor via clonal, apomictic seed production
Potato (*Solanum tuberosum*)	*eIF4E*, *eIF(iso)4E*	CRISPR-Cas9 (NHEJ knockout)	Reduces viral infection susceptibility and cold-induced sweetening

Tomato (*Solanum lycopersicum*)	*SlMLO1*	CRISPR-Cas9 (NHEJ knockout)	Establishes complete resistance to powdery mildew (*O. neolycopersici*)
Grapefruit (*Citrus paradisi*)	*CsLOB1* promoter	CRISPR-Cas9 (Promoter editing)	Disrupts effector binding; confers citrus canker resistance
Groundcherry (*Physalis peruviana*)	*SP5G*	CRISPR-Cas9 (NHEJ knockout)	Induces compact growth and fruit retention (de novo domestication)

5. Global Regulatory Architectures and Policy Harmonization

The commercial adoption of CRISPR-edited crops depends heavily on global biosafety frameworks and legal classifications. Genome editing techniques using Site-Directed Nucleases (SDNs) are classified internationally into three main categories based on the repair mechanism and whether exogenous DNA remains in the genome:

- **SDN-1**: Induces double-strand breaks repaired by endogenous NHEJ without donor DNA, generating small random insertions or deletions. These edits contain no foreign DNA and are genetically indistinguishable from natural spontaneous mutations or traditional physical/chemical mutagenesis (Movahedi et al., 2023).
- **SDN-2**: Uses a short donor DNA template via HDR or MHEJ to introduce precise nucleotide changes or substitutions without leaving recombinant foreign DNA.
- **SDN-3**: Uses a donor template to integrate large exogenous DNA sequences (transgenes or cisgenes) at a specific target locus. SDN-3 products are universally regulated under traditional Genetically Modified Organism (GMO) frameworks.

Global biosafety policies fall into two main approaches: product-based regulatory frameworks (focusing on the final trait risk profile) and process-based frameworks (regulating crops based on the techniques used to create them) (Alburquerque et al., 2016).

Product-Based Regulatory Paradigms

The United States leads the product-based regulatory model through the USDA-APHIS SEC (Sustainable, Ecological, Consistent) rule under the Coordinated Framework for Regulation of Biotechnology. Plants carrying single base changes, localized indels (SDN-1), or targeted edits achievable through conventional breeding (SDN-2) are exempt from biotechnology regulation, provided they contain no foreign DNA. Similar product-based policies exempting transgene-free SDN-1 and SDN-2 edits have been adopted across South America (e.g., Brazil under CTNBio Normative Resolution No. 16, Argentina), Japan, India, Australia, the United Kingdom (via the Genetic Technology Act 2023), the Philippines, Kenya, and Nigeria (Sagawa et al, 2023).

Process-Based Models and Policy Shifts

The European Union historically operated under a process-based model governed by Directive 2001/18/EC. A 2018 ruling by the Court of Justice of the European Union (CJEU, Case C-528/16) placed all directed mutagenesis products under existing GMO regulations, subjecting transgene-free gene-edited crops to extensive environmental risk assessments, strict traceability, and mandatory labeling. This framework created compliance costs and trade barriers, encouraging commercial biotech investment to shift toward North American and Asian markets (Guerra, 2022).

In response to climate-driven agricultural challenges, the European Commission proposed a legislative overhaul in July 2023 for New Genomic Techniques (NGTs). The proposed framework introduces a two-tiered classification:

- **Category 1 NGT (NGT1)**: Plants containing targeted edits comparable to natural variation or traditional mutagenesis (defined by specific thresholds, such as a maximum of 20 insertions or

deletions) are treated as equivalent to conventional breeding and exempted from GMO regulatory burdens (Koller, 2025).

- **Category 2 NGT (NGT2)**: Plants carrying broader modifications or transgenic insertions (SDN-3) remain subject to standard GMO risk assessment procedures.

China maintains a tiered hybrid regulatory framework under its Safety Evaluation Guidelines, providing a fast-tracked approval pathway for gene-edited plants that contain no foreign transgenic elements (Grantina-Ievina & Rostoks, 2026).

Table 2. International regulatory oversight models and legal classifications for gene-edited crops.

Country / Region	Primary Regulatory Basis	SDN-1 & SDN-2 Legal Status (Foreign DNA-Free)	Key Exemption / Regulatory Thresholds
United States	Product-based (USDA Coordinated Framework / SEC Rule)	Exempt from GMO oversight	Evaluated on trait risk; exempt if achievable via traditional breeding
European Union	Process-based (Directive 2001/18/EC; NGT Proposal 2023)	Historically regulated as GMO; NGT1 proposal aims for exemption	Moving toward exemption for Category 1 NGTs (<20 edits)
United Kingdom	Product-based (Genetic Technology Act 2023)	Exempt from GMO oversight	Exemption granted for Precision Bred Organisms (PBOs)
China	Tiered / Hybrid (Safety Evaluation Guidelines 2022)	Fast-tracked evaluation pathway	Simplified Tier 1 management for non-transgenic edits
India	Product-based (MoEF&CC Revised Guidelines 2022)	Exempt from GMO oversight	Group 1 (SDN-1) and Group 2 (SDN-2) exempt from GEAC assessment
Brazil	Product-based (CTNBio Normative Resolution No. 16)	Exempt on a case-by-case basis	Non-GM status assigned if final product lacks recombinant DNA
Japan	Product-based (Genome-Edited Food Guidelines 2019)	Exempt from GMO oversight	Mandatory notification; exempt if foreign genetic material is absent

6. Technical Bottlenecks and Future Perspectives

Despite rapid technological progress, several technical, biological, and economic bottlenecks continue to impact the application of CRISPR-Cas platforms in crop improvement:

1. **Tissue Culture and Transformation Efficiency**: Broad adoption remains constrained by tissue culture limitations. Many commercial elite crop inbreds are recalcitrant to *Agrobacterium*-mediated transformation or plant regeneration. While co-expressing developmental morphogenic regulators (such as *Baby boom*, *Wuschel2*, or *GRF-GIF* chimeras) improves transformation efficiency in monocots, developing tissue-culture-free delivery mechanisms remains a research priority. Direct viral vector delivery, nanoparticle-mediated complexes, and floral-dip transformations offer potential solutions (Mookkan et al., 2017).
2. **Off-Target Mutations**: Unintended cleavage at non-target genomic sites with sequence similarity to the sgRNA remains a technical concern. However, off-target rates in plant systems are lower than in mammalian cells. In addition, unintended mutations introduced during initial editing can typically be segregated out through backcrossing with parental lines. Engineered

high-fidelity Cas variants (such as SpCas9-HF1 or HypaCas9) and base editing platforms further minimize off-target risks (Basit & Zheng, 2026).

3. **Complex Polygenic Trait Engineering**: While single-gene knockouts (*S*-genes, yield suppressors) are straightforward, complex traits like drought tolerance and nitrogen-use efficiency are governed by intricate polygenic networks. Advanced multiplex CRISPR platforms using Cas12a crRNA arrays or multiple pol III promoters allow simultaneous targeting of multiple loci across interconnected metabolic pathways (Helliwell & Yang, 2012).
4. **Integration with Pangenomics and Speed Breeding**: Combining pangenomics with high-throughput CRISPR editing enables the identification and targeted introduction of beneficial stress alleles into commercial crop varieties. Integrating these technologies with speed breeding protocols which use controlled growth environments to achieve up to six generations per year can significantly shorten the development cycle for climate-resilient cultivars (Ghorbanzadeh et al., 2025).

7. CONCLUSION

CRISPR-Cas genome editing has fundamentally transformed plant biotechnology, establishing a powerful and precise platform for developing climate-resilient, high-yielding crop varieties essential for global food security. This review demonstrates that CRISPR-Cas systems, through their diverse molecular toolkits spanning nucleases, base editors, prime editors, and epigenome modifiers, enable targeted modifications ranging from single nucleotide substitutions to complex multiplex gene disruptions. The documented successes including maize *ARGOS8* promoter engineering for drought tolerance, *EDR1* and *SlMLO1* knockouts for powdery mildew resistance, and multiplex editing for synthetic apomixis validate CRISPR's capacity to address both abiotic and biotic stresses while optimizing yield architecture. The evolving global regulatory landscape presents both opportunities and challenges. Product-based frameworks in the United States, Brazil, and Japan increasingly exempt transgene-free SDN-1 and SDN-2 edits from GMO oversight, facilitating commercial deployment, while the European Union's proposed NGT categorization signals a potential shift toward science-based, trait-focused regulation. However, technical bottlenecks in transformation efficiency, off-target effects, and complex polygenic trait engineering persist as significant hurdles. Future progress will depend on integrating CRISPR with emerging technologies pangenomics, speed breeding, and advanced delivery systems to accelerate breeding cycles and expand crop improvement to underutilized orphan crops with inherent stress tolerance. Ultimately, realizing CRISPR's full potential requires continued innovation in molecular tools, regulatory harmonization, and public engagement to ensure equitable access to climate-smart crop varieties for farmers worldwide.

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