CRISPR/Cas9 and the Future of Agriculture: Innovation, Regulation and Food Security

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Agriculture faces several challenges, such as climate change, soil degradation, and food insecurity. Because traditional plant breeding methods have produced numerous improved crop varieties and continue to generate additional genetic variation for new traits via recombination, this method will remain central to crop improvement. Traditional breeding does, however, face a significant barrier to rapid response to emerging threats such as diseases, pests, and abiotic stresses due to both the time required to develop new crop varieties and linkage drag. As such, CRISPR/Cas9 has been recognized as a key complementary technology to support these efforts. In this review, the authors examine how CRISPR/Cas9 is being utilized in agricultural research, compare its potential with that of previously developed technologies, and evaluate the economic, social, and regulatory challenges that may limit or enhance the ability to use gene-edited crops responsibly and equitably.

Introduction

The contemporary global agricultural systems are under threat from climate change, soil erosion, and food insecurity[1,2]. Climate change is steadily increasing temperatures, which threatens food production and food stability, coupled with extreme weather events and pest pressure on crops[3–5]. Therefore, agricultural technologies that promote food production are necessary, especially resilient agricultural technologies[6]. Resilient agricultural technologies, like selective breeding, can increase production and improve critical crop characteristics; however, their slow, imprecise method hinders the agricultural system from keeping pace with rising climate change pressures and population growth[7,8].

The development of technological advancements, such as genome editing, specifically CRISPR/Cas9, has made plant breeding more impactful through increased specificity, efficiency, and profit[9,10]. CRISPR/Cas9 also allows for faster construction or modification of crops with improved protection against biotic stresses from pests and diseases, resistance to nonliving stresses (drought, salinity), and enhanced nutritional value of food[11,12]. These features make CRISPR/Cas9 a useful agricultural technology for improving food security and supporting more sustainable farming systems[6].

However, the introduction of CRISPR/Cas9 into society can present complications; intricate economic, ethical, and regulatory issues all serve as barriers to better technological implementation despite exciting technical possibilities[13,14]. There are varied regulations governing whether CRISPR/Cas9 crops are the same as traditional crops and GMOs, and globally, people experience this differently[15–17]. These uneven regulations create barriers for farmers, especially in developing regions, to adopt technologies such as CRISPR/Cas9 or GMOs[18,19]. Beyond regulations, there are multiple obstacles to accepting and adopting the crop technology due to the nature of consumer and market acceptance[20,21]. Added complexities regarding ethical issues around property rights, market resistance, and public acceptance factor into access surrounding the distribution of CRISPR-based agricultural innovations[13].

This paper examines the role of CRISPR/Cas9 in developing crops to address climate change pressures and food insecurity issues. It includes specific case studies related to pest resistance, drought tolerance, and nutritional improvements so that CRISPR-based genome editing can be compared in general terms to older and traditional GMO strategies. It also discusses the legal, economic, and ethical issues associated with CRISPR in agriculture. Understanding how these aspects come together is often ignored, but very important for influencing better policy and possibly assisting the next generation of farmers in agriculture in their use of CRISPR in a responsible manner within their systems to make food production systems more resilient and improve global food security.

Literature Review

Scholarship on crop improvement can be grouped into four broad categories: traditional breeding, transgenic genetic modification, pre-CRISPR genome-editing systems, and CRISPR/Cas9 editing[7,22]. Research on traditional breeding has emphasized its continued importance in developing improved crop varieties and preserving genetic diversity in

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breeding programs[23]. At the same time, many researchers have identified practical limitations associated with traditional breeding methods, including long breeding cycles and linkage drag[8]. Research on transgenic crops has documented significant advances related to reduced inputs and enhanced pest resistance; however, it has also noted substantial regulatory controversy and varying levels of public acceptance[24,25].

Prior to the widespread adoption of CRISPR/Cas9, other targeted-editing technologies, including zinc-finger nucleases and TAL effector nucleases, were developed[26,27]. These technologies demonstrated that site-specific DNA modification in plants was possible[28]. However, they often required significantly greater design complexity and cost than CRISPR/Cas9[29]. Understanding how CRISPR/Cas9 emerged from earlier efforts to improve targeting precision in plant breeding provides important context, since it shows that CRISPR/Cas9 did not appear in isolation or simply replace all previous approaches to crop improvement[30].

Recent literature on CRISPR/Cas9 focuses primarily on four areas: disease resistance, increased production efficiency, nutritional enhancement, and climate-stress tolerance[12]. Across these areas, there appears to be general agreement that CRISPR/Cas9 represents a flexible platform for making targeted edits[31]. However, reported effects vary depending on crop type, target gene, testing environment, and trial scale[32]. There is also a growing body of literature addressing regulation, intellectual property, public acceptance, and equitable access in the use of CRISPR/Cas9[33]. Collectively, this scholarship suggests that the future value of CRISPR/Cas9 will be shaped by factors beyond scientific performance alone, including governance, cost structure, and distribution[34].

Methods

The present paper was designed as a systematic review of CRISPR/Cas9 applications in agriculture. Literature searches were conducted through major academic databases, including Google Scholar, PubMed, Web of Science, and Scopus. Each search used multiple terms, including "CRISPR/Cas9 agriculture," "CRISPR crop disease resistance," "CRISPR drought-tolerant plants," "CRISPR nutritionally enhanced crops," "regulation of genome-edited crops," and "ethics of CRISPR in agriculture." Additional searches used combinations of crop-specific and trait-specific terms, such as "rice CRISPR for bacterial blight," "tomato CRISPR MLO," "cassava CRISPR for virus," and "CRISPR CKX for increased yield."

Studies were selected based on the criteria that they were peer-reviewed, directly related to CRISPR/Cas9 or other genome-editing applications in plant production systems, and provided empirical evidence relevant to the agricultural use of CRISPR/Cas9. Primary research papers were given priority for trait-specific statements, especially those providing quantifiable results. Selected review articles were retained for technical background information and broader regulatory context. Non-academic websites, blogs, and news articles were excluded from the evidence base.

During data extraction, the crop species, target gene or pathway, trait studied, study type, reported results, and author-noted limitations were recorded. In addition, for studies examining governance issues, data extraction included jurisdiction, regulatory issues, stakeholder groups, and principal conclusions. Because the studies included in this review varied widely in crop type, methodology, and outcome measures, a narrative synthesis was used instead of a meta-analysis.

A qualitative quality assessment was applied to give greater weight to peer-reviewed studies with identifiable gene targets, measurable results, and sufficient contextual detail. A PRISMA-style screening strategy was used to assist in selecting appropriate sources[35]. Titles and abstracts were initially evaluated to screen records. Duplicate records were removed before full-text evaluation to identify the final included papers.

Crop Improvement

For hundreds of years, crop improvement has been at the heart of agricultural development[23]. Traditional breeding techniques using selection across generations have produced most of the cultivated varieties in use today to support modern food systems[7]. Although traditional breeding continues to be crucial because it provides necessary genetic diversity through recombination, there are limits to this technique. The problems with traditional breeding do not arise from recombination itself, but rather from the fact that plant breeders cannot control which combinations of linked traits are passed down to offspring. As a result, desirable genes may also be inherited alongside unwanted ones, a problem known as linkage drag[8]. Additionally, breeding timelines can be long if several characteristics need to be combined in a single variety, or if repeated backcrossing, testing, and evaluation are required. This can make it particularly difficult for plant breeders to respond rapidly to new diseases or changing climate conditions[30]. Thus, while CRISPR/Cas9 technology should not replace traditional breeding techniques, it can allow for faster, more targeted modification of traits considered most beneficial[31].

From Traditional Breeding to CRISPR

The domestication of wild species into staple crops is one of modern agriculture's earliest technological achievements, dating back roughly around 10,000 years ago in the Fertile Crescent and in independent regions such as Mesoamerica and East

Asia[23]. For instance, the transformation of teosinte into modern maize is a classic example, a process that took place thousands of years ago, and repeated selection for new traits such as larger kernels, improved flavor, maturation, and developed natural resistance against local pests and diseases[36]. Later milestones showed how technology could support food security. During the mid-20th century, the Green Revolution occurred, representing a turning point that introduced the semi-dwarf wheat and rice varieties[37,38]. Yield increases from these crop varieties, together with pest-resistant innovations such as Bt maize and Bt cotton introduced in the 1990s, helped reduce famine risk in several areas of Asia and Latin America[25,39]. Over time, the breeding process was noticeably shortened with new methods of crop improvement, and this difference is crucial when conventional approaches are compared with modern genome editing tools (Figure 1).

This differentiation is important since the primary benefit of using CRISPR/Cas9 does not lie in eliminating each subsequent step of development; rather, it lies in the ability to advance the initial modification of a specific set of characteristics through the front-end of a breeding program[30]. Progress has been slow and occasionally contentious, even with Bt and other transgenic traits, underscoring the potential and limitations of pre-CRISPR biotechnology[24]. The urgency of adjusting crops to swift climate change, new pests and diseases, and more frequent extreme weather events is becoming more and more at odds with this slow pace[40,41]. Crop varieties that can be adapted in a few seasons and that provide multi-stress tolerance at both the physiological and molecular levels are essential for farmers in today's unstable agricultural environment[3].

Early Genome Editing: ZFNs and TALENs

Before the discovery of CRISPR/Cas9 technology, scientists studying plants had experimented with several earlier genome-editing techniques[29]. Meganucleases, zinc-finger nucleases (ZFNs), and transcription activator-like effector nucleases (TALENs) were among the first major attempts to move beyond the slower and less targeted process of conventional breeding in the early 2000s[26,27]. They were able to work due to the design of proteins to recognize and separate particular DNA segments, which results in double-strand breaks (DSBs)[28]. After the break, the homology-directed repair (HDR) or non-homologous end joining (NHEJ), the cell's independent repair process, will take over, allowing breeders to introduce, remove, or potentially alter genes[42].

This innovation allowed plant breeders to modify the best-performing crops directly, while still preserving their valuable genetic background[27]. It also enables precise "trait stacking," an action where multiple desired traits could be integrated without the randomness of traditional recombination[42]. Previous studies demonstrated the feasibility of this approach[26]. For example, TALEN-mediated editing of the OsBADH2 gene in rice generates new fragrance traits, while not negatively affecting crop yield[22]. But one of the technologies utilized is the maize editing employing ZFN-based technology with the target of herbicide tolerance and pest-resistant genes[43].

However, both TALENs and ZFNs also had important limitations. Picking desired protein domains was expensive and took a long time while also necessitating a high degree of specialization[29]. Editability was generally low, particularly among polypoid crops such as wheat, and off-target risks also showed technical limitations[44]. These limitations meant that although ZFNs and TALENs showed research potential, they were not widely adopted in commercial breeding programs[43].

The combination of both potential and limitations gave rise to a new system which is faster, cheaper and more easily accessible[9]. The emergence of CRISPR/Cas9 technology provided a practical method of genome editing[10].

CRISPR-Cas9: A Major Development in Genome Editing

CRISPR/Cas9 increased the practicality and accessibility of targeted genome editing for use in plant science[10,45]. Of bacterial origin as an immune system defense against infection, CRISPR/Cas9 entails the utilization of a guide RNA to locate Cas9 nuclease at a desired DNA sequence that the nuclease cleaves through a specific cut[46]. Since older tools were time-consuming and required elaborate protein engineering, the relative simplicity of CRISPR makes it significantly less expensive, quicker, and simpler[47]. Multiplex editing, which allows the simultaneous editing of multiple genes, provides a special benefit for more complicated agronomical traits like the development of drought tolerance, which involves the coordinated change of genes[48].

In plant breeding, this precision has changed the crop improvement process[45]. CRISPR/Cas9 enables precise alteration of genes controlling yield, stress tolerance, pest and disease defense, and nutritional content[49]. Editing OsSWEET genes in rice conferred resistance against bacterial blight; changing ARGOS8 in maize raised water-limiting growth stage tolerance at the farm level; and knocking out the MLO genes in tomato conferred lasting protection from powdery mildew[50–52]. Beyond resilience, scientists at the level of the banana and potato seek a cure for catastrophic tropical diseases, while other projects aim for nutritional and environmental goals, such as β-carotene-enriched rice for the elimination of vitamin A deficiency and nitrogen-use-efficient wheat for reducing dependence on fertilizers[53–55].

These developments show that the technology has become an important tool in agricultural biotechnology[9]. Success with the technology, however, hinges on more than technological success. Regulatory regimes differ immensely: the United

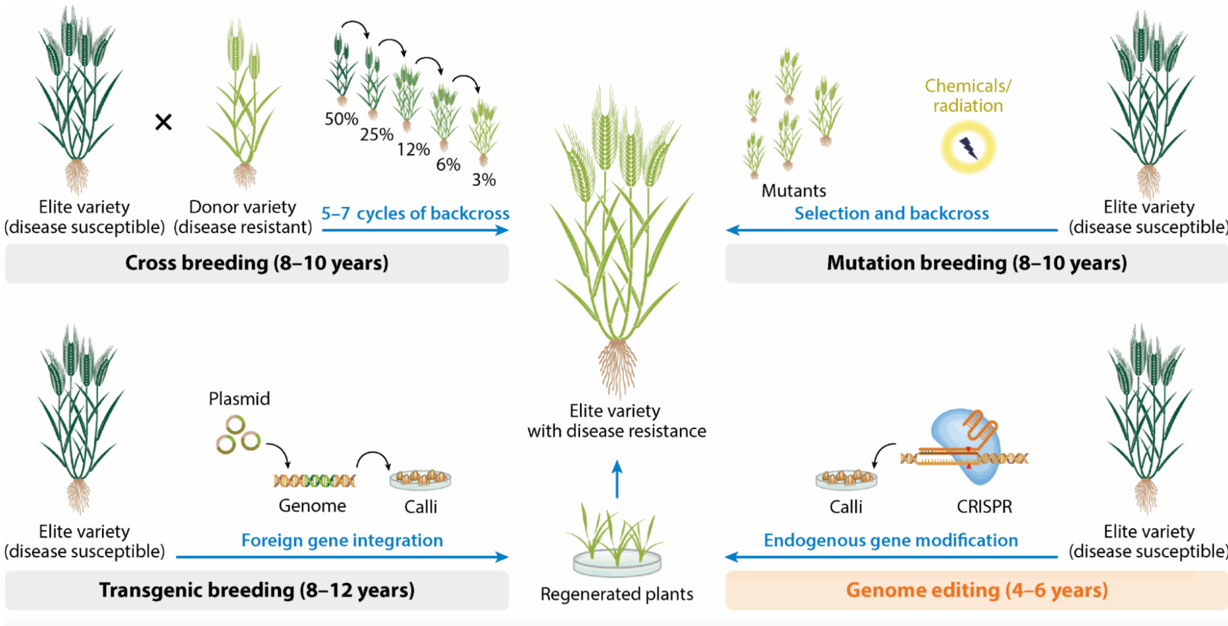

Figure. 1 Provides an approximate comparison of developmental times for different plant-breeding methods; however, a crop-specific or regionally variable timeline should not be inferred from the figure. Conventional (and associated) testing will generally take approximately 8 to 10 years in many programs. The extended timeline of 12 to 15 years includes additional periods for field evaluation, regulatory approval, seed multiplication, and expansion for commercial production. Although the "front-end" of the initial trait-development phase using CRISPR/Cas9 may expedite the targeted gene editing of specific traits, subsequent downstream validation, field testing, and regulatory assessments are also factors influencing the total time prior to agricultural use [31]

States, Argentina, and Japan exempt a few of the CRISPR-edited crops from the GMO regulatory framework, whereas the European Union uses stricter regulations [15–17]. Intellectual property conflicts introduce additional complexity, and customer acceptance hinges upon how the product appears with respect to the product's safety, naturalness, and trust [15,20]. These broader considerations of the law, ethics, and society come later.

Technique and Agricultural Applications of CRISPR/Cas9

Figure 2 provides a general overview of how CRISPR/Cas9 functions in plants, from sgRNA-guided target recognition to double-strand break repair.

The CRISPR/Cas9 system incorporates two fundamental parts: a short RNA molecule called the single-guide RNA (sgRNA), which has a specific DNA target sequence, and the Cas9 protein, a nuclease that cleaves DNA at a specific location [46]. When Cas9 induces a double-stranded cleavage at the DNA level, the plant cell repairs the cleavage through an internal process either by joining severed parts or through a template with a specific repair [42]. With the use of this, scientists can knock out undesirable genes, introduce new sequences, or introduce specific changes that enhance desirable traits [43].

Relative to established systems such as zinc-finger nucleases (ZFNs) and transcription activator-like effector nucleases (TALENs), CRISPR/Cas9 is simpler to engineer, less expensive, and able to edit hundreds of genes simultaneously (multiplex editing) [48]. Multiplex capacity becomes of specific use with complex traits such as drought tolerance or flowering time, with the action of hundreds of genes [56].

The use of CRISPR / Cas9 for cytokinin oxidase / dehydrogenase (CKX) gene editing has provided valuable information about CKX involvement in cytokinin metabolism, which is linked to tiller formation and, subsequently, grain number [57,58]. Some trials have shown an association with improved yields; however, the size of this improvement will depend on the genetic material of the crop being studied and the environmental factors associated with each trial, and therefore must be evaluated based on the specifics of their individual study settings rather than as a general or universal percent increase [59].

In addition to yield, CRISPR enhances the survival of plants under severe conditions. Researchers edited genes regulating how the plant responds to drought and salty soil, such as transcription factors DREB and ABA hormone receptors, and created more resilient crops while not compromising other valuable traits [60]. By combining CRISPR with extensive data from

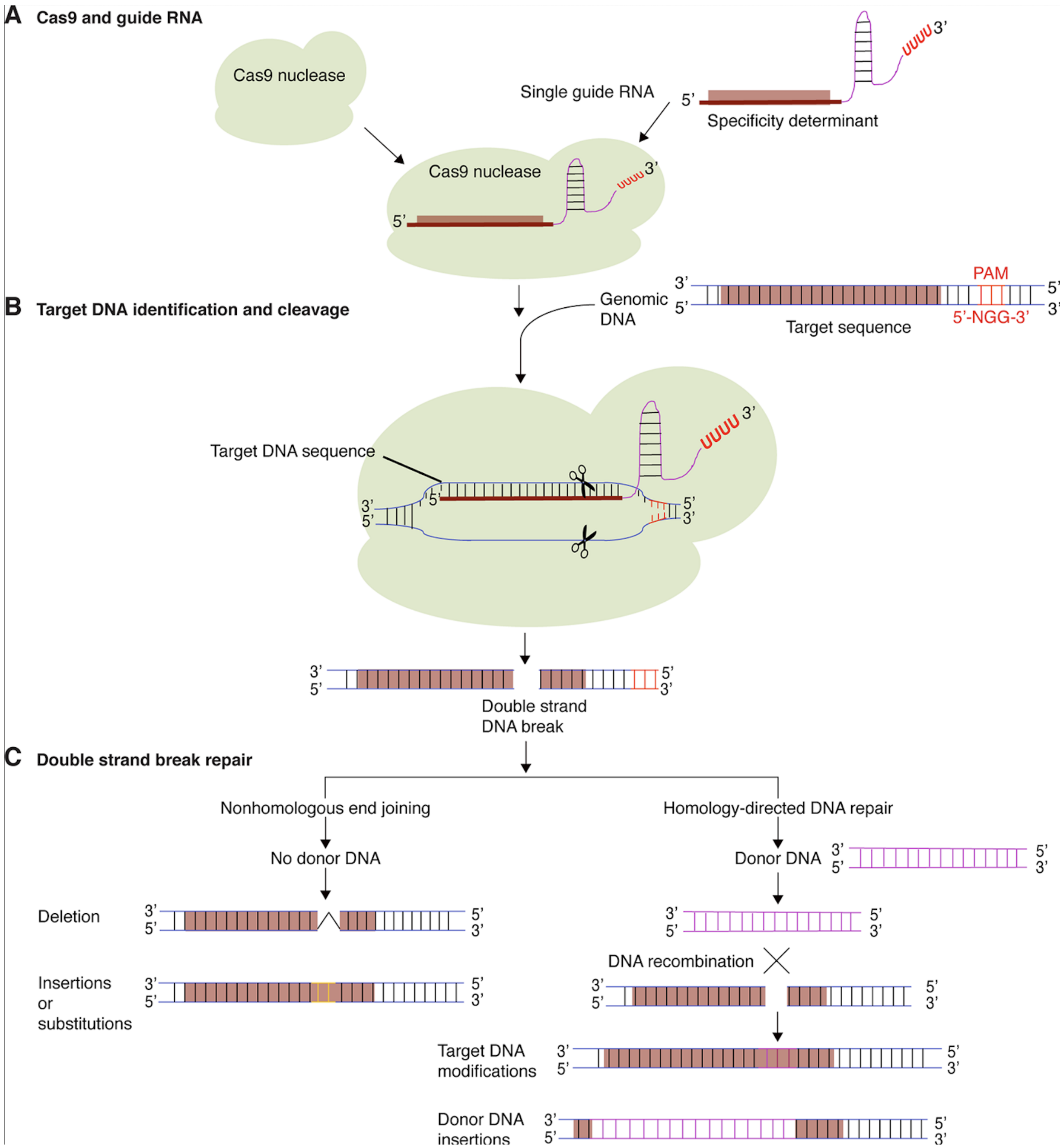

Figure. 2 Provides a general overview of how CRISPR/Cas9 functions in plants. It specifically outlines the step-by-step process of sgRNA-directed target-site identification (DNA targeting), followed by double-strand break repair[46]

plant gene expression (transcriptomics) and metabolite profiles (metabolomics), scientists are able to engineer wiser and more specific changes, and with much less undesirable outcomes and greater yields of improved edited crops[61].

Crop quality is also improved using CRISPR. For instance, high-scent rice has been produced through the disruption of the OsBADH2 gene for better flavor[22]. For soybeans, oil composition is altered through editing of fatty acid desaturase genes (FAD2), yielding oils with good shelf life and improved health benefits[62,63]. In peanuts, cyanogenic glycosides are lowered through editing of CYP79D1/D2 genes for improved safety of foods through the reduction of toxic metabolically generated compounds indigenous to the plant[64].

Examples of CRISPR-Based Resistance in Various Crops

CRISPR technology has additionally been found to be an effective tool for creating pest- and disease-resistant crops through the editing of susceptibility genes used by pathogens to infect plants[11]. Because this approach can reduce dependence on chemical pesticides, it is often viewed as less harmful to the environment; however, both chemical and genetic methods still raise concerns related to human health and beneficial insects[5].

A recent study showed that bacterial infection was reduced in rice because the pathogen could no longer hijack the plant's sugar transport system when the promoter of the SWEET genes was edited. Rice is a staple crop throughout much of Asia, and losses caused by bacterial blight amount to billions of dollars annually[50,65].

This study illustrates the value of using CRISPR to provide disease resistance by altering the route that pathogens use to infect the host plant rather than by inserting new DNA into the plant[66].

Viruses affecting crops have also been targeted using CRISPR technology. Cassava and banana are two crops that have received attention[55]. Cassava has been studied because of its susceptibility to cassava brown streak virus (CBSV), which threatens food security for millions of people in Africa each year[67]. Researchers have attempted to edit the eIF4E gene family in cassava using CRISPR to make it resistant to CBSV, resulting in no adverse effects on plant growth or yield[67]. Similar studies have also been conducted in banana, where edited varieties have demonstrated resistance to banana streak virus[53]. Because virus transmission often occurs through insect vectors, which can be difficult to control, CRISPR-based resistance may provide an important option for producers who cannot afford other means of managing these diseases[53].

Fungi that cause plant diseases have also been targeted using CRISPR technology. Researchers have successfully used CRISPR to target the MLO gene in tomato varieties and confer resistance to powdery mildew[52]. By reducing the number of fungicide applications needed by farmers, this approach can also reduce fungicide-related costs[68]. Similarly, researchers have used CRISPR to modify susceptibility genes in wheat and grapevine, including TaMLO and VvWRKY52[44,69]. These modifications resulted in decreased susceptibility to powdery mildew and gray mold, respectively[69]. The end result of this research is reduced post-harvest damage and better preservation of food quality during storage and transportation. These examples demonstrate that CRISPR technology can be used to provide disease resistance by interfering with a fungus's ability to obtain the components it needs from the plant in order to complete its life cycle[11].

Unlike conventional transgenic crops like Bt corn, which contain insecticidal proteins produced by bacteria, most CRISPR-based technologies operate by deleting or editing the plant's own genes. Because of this, many view CRISPR technology as involving less regulatory complexity and potentially higher levels of public acceptance[13],[21].

There are some limitations to consider. Just as pests develop resistance to certain pesticides and Bt proteins, they may also develop resistance to CRISPR-based protection. Additionally, large-scale monoculture production of improved varieties may create evolutionary pressures on local ecosystems and may contribute to the development of alternative forms of pathogens. To reduce these risks, CRISPR-based resistance should be used in conjunction with integrated pest management strategies such as crop rotation, natural predators or parasites, and habitat diversity. This would allow the genetic component of crop improvement to strengthen sustainable agricultural systems rather than replace them[5].

Examples of CRISPR-based resistance in various crops are listed in Table 1.

Productivity Characteristics

Sink Capacity and Grain Number

CRISPR/Cas9 was utilized to study genes which contribute to sink potential and grain yield[57]. Cytokinin dehydrogenases are a group of enzymes that regulate the degradation of cytokinins; therefore less active CKX is associated with higher levels of available cytokinin for processes like tillering and grain numbers[58]. The yield enhancements found in edited lines were generally dependent on the crop type, site of testing, trial design, and other factors such as alterations in grain size or plant morphology[59].

Plant Structure and Biomass Distribution

Other modifications targeted the genes responsible for controlling the physical attributes of the inflorescence, and how biomass is allocated throughout the plant[70]. The pathways involved in this include genes such as DEP1 and TB1[36,70]. This is relevant due to the fact that modifications in the quantity of branches, plant height or the shape/structure of the inflorescence can positively impact the efficiency at which crops are harvested and overall yield[70]. However, it is worth noting that the modification of architecture does not always result in a positive outcome. An example of this would be if an edit resulted in an increase in biomass or branching; this could potentially alter where resources are being directed resulting in

Table 1 Representative examples of CRISPR-based pest and disease resistance in crops.

Crop	Target gene/region	Disease	Mechanism	Reported outcome	Citation
Rice	OsSWEET14	Bacterial blight	Reduced pathogen-induced activation of host sugar transport	Increased resistance relative to control lines in reported trials	65
Tomato	SlMLO1	Powdery mildew	Reduced host susceptibility to fungal colonization	Lower disease susceptibility reported in edited lines	52
Wheat	TaMLO	Powdery mildew	Altered susceptibility pathway	Heritable resistance reported in edited lines	44
Cassava	eIF4E	Viral disease	Disrupted host factor associated with viral infection	Virus-resistance effects reported; field validation still needed	67

either an increased risk of lodging, unbalanced reproduction, or poor grain filling[59].

Stomatal Functionality, Water Utilization and Carbon Assimilation

CRISPR/Cas9 has also been used to modify genes that regulate stomatal functionality and stress response[71]. These edits are of value to research scientists due to the importance of stomatal function in regulating CO2 uptake and water utilization[71]. There have been instances of improvements in water usage under drought conditions; however, these improvements may occur at the expense of carbon assimilation and subsequently reduce yields when no stresses exist[72].

Root Growth and Nutrient Acquisition

Genes related to root growth have also been studied by researchers due to the belief that plants grown from genetically modified seeds will develop roots that allow them to obtain more water and nutrients from low fertility and/or arid soils[73]. It is important to note that while beneficial under ideal experimental conditions, any advantages realized through root edits may not equate to similar benefits across various soil types, irrigation practices and field conditions[74].

More broadly, these types of edits may shorten breeding time and support faster adaptation of crops to widespread stresses such as drought, salt, and heat[74,75]. When combined with genomic resources and high-throughput screening, CRISPR/Cas9 may help breeders generate more durable and higher-performing varieties[61].

Improved Nutritional Properties

In addition to improvements in yield and stress tolerance, CRISPR has been evaluated as a means of enhancing the nutritional quality of agricultural products[76]. While traditional breeding programs for nutritional traits have often been time-consuming and costly due to the complexity of these traits and their linkage to undesirable characteristics, CRISPR provides an opportunity to more rapidly and precisely increase desired nutrients, decrease harmful compounds, and improve staple crops[49]. Biofortification strategies, including provitamin A-enriched rice, represent ways that genome editing and associated technologies may help address micronutrient deficiencies[77],[54]. In these cases, biofortification targets specific carotenoid and mineral biosynthetic pathways and generally increases nutritional value under the conditions tested[76].

Gene editing of fatty acid desaturases (FAD2), such as those found in oilseed crops like soybean and canola, produces oils rich in oleic acid that may lead to better oil quality, longer shelf life, and potential nutritional benefits[62,63].

CRISPR also enables the reduction of antinutrients and toxins[64]. For example, reductions in cyanogenic glycosides may reduce cyanide risk from consumption[78]. Gene edits that reduce allergenic proteins and other toxic compounds may also broaden safe use across varieties[79].

Nutritional Enhancement: Golden Rice & Beyond

Although significant progress is being made in addressing crop stresses, hunger persists because of both insufficient caloric intake and inadequate levels of essential nutrients[2]. Supplemental nutrition is viewed by much of the scientific community as one useful method for addressing nutrient insufficiency[76]. The biofortification of staple crops, such as Golden Rice, is viewed by some as another option[77].

Most discussions surrounding Golden Rice focus on it as a model for crop biofortification, specifically concerning the enhancement of provitamin A in a staple food[54]. CRISPR technology can similarly address nutritional objectives through more refined genetic modification[80]. Because the nutritional contribution provided by a single serving can vary based on factors such as portion size, preparation, carotenoid loss during processing, and the nutritional standards used for comparison, claims regarding dietary contribution should be presented with caution[81].

Furthermore, genetic modifications that reduce toxic compounds or enhance nutrient profiles in staple crops demonstrate how gene editing may contribute to improved health outcomes, as illustrated in Table 2.

This approach may improve nutritional traits without requiring significant dietary change[81]. Nonetheless, it cannot replace balanced diets or broader efforts to alleviate poverty and improve global access to food[14]. Other researchers have cautioned that reliance on a small number of engineered staples could create dependence rather than address the systemic causes of malnutrition[82]. Therefore, CRISPR-based nutritional enhancements should be regarded as supplements to existing food-system and public-health initiatives rather than substitutes[78].

Climate Stress and CRISPR/Cas9

Climate change poses a major challenge to world agrosystems, subjecting crops to further stress through drought, heat stress, flooding, and raised soil salinity[41,83]. These stresses are already leading to decreases in yields of major staple crops such as rice, wheat, and maize, especially in developing regions that rely almost entirely on rain-fed agriculture[3,4]. Traditional breeding methods often are too slow to respond to such rapid changes; CRISPR/Cas9 technology offers a system of directly editing stress-related genes with a much shorter timeframe[75,84].

The potential for these "benefits" will come at a cost. For example, a plant that is able to conserve water more effectively during a drought event, due to an improved ability to close stomata, will likely reduce gas exchange and potentially limit growth when receiving adequate water. As such, while these plants will perform better during stress years, they will likely produce lower yields in typical growing environments. The degree to which this is a significant issue will depend upon the irrigation regime, the frequency of stress events, and the overall production goals of the farming system[71,72].

Water Management and Irrigation Context

Because of this, CRISPR-based traits that are intended to enhance water-use efficiency during drought should always be viewed within the framework of water management[40]. Therefore, the potential benefits of a drought-related trait will vary depending upon whether a system relies on rain-fed agriculture or irrigation[83]. While reducing maximum yield per acre under optimal conditions may still represent an improvement in rain-fed systems where water limitations occur repeatedly, it is unlikely to result in similar improvements in irrigated systems[41].

Similarly, changes to growth regulators of the roots encourage greater depth of roots and thus offer improved access to groundwater in dry soils[73]. Salinity tolerance has been improved through the targeting of the ion transporter genes that control the intracellular equilibrium of sodium and potassium and permit rice and tomato to survive in soils that otherwise would be too saline for agriculture[60]. Thirdly, CRISPR has also been used to alleviate flooding stress through genetic changes to ethylene-response factors and the Sub1A gene in rice that permit survival for longer under submersion, a desirable characteristic of monsoon-driven flood-prone regions[85].

Figure 3 summarizes the major effects of drought stress and the plant responses that are relevant to CRISPR-based improvement of tolerance and yield.

Heat stress, increasingly imperiling pollination and grain fill, has been addressed through heat-shock factor gene edits that allow crops to preserve fertility and yields during heat waves[83]. These innovations illustrate how CRISPR may help stabilize yields under adverse weather conditions[75]. Stabilizing yields under climatic stress also minimizes farmer risk and fortifies food chains, both particularly at risk of shock from smallholder systems[40].

However, key criticisms should be understood. Some scholars are of the view that genetic technologies such as CRISPR could target only the "symptoms" of climate change and overlook its underlying drivers, i.e., greenhouse emissions and unsustainable land use practices[2]. Others further warn that promising lab results may not always translate into reliable field performance under a wide variety of environments and therefore promote fears of a lack of scalability[32]. In this context, CRISPR should best be understood as part of a complete approach. CRISPR may increase short-term resilience through the development of stress-tolerant crop varieties; however, it cannot replace broader systems-level approaches such as emissions mitigation and sustainable farming practices[86].

CRISPR Reduces Breeding Time and Can Lower Long-Term Costs, but Initial Research and Approvals Remain Expensive

CRISPR/Cas9 represents a major technological development in agriculture because it allows highly specific genome editing for the production of crop varieties with improved environmental stress tolerance, lower chemical-input requirements, and improved nutritional quality[84]. While technologies offer high potential for long-term economic as well as social benefits, the application of CRISPR is also accompanied by high initial costs, regulatory hurdles, as well as complex ethical concerns[82,87]. Balancing potential fast breeding for sustainable agriculture against financial, legal, and ethical concerns is an essential concern for researchers, implementers of policies, as well as farmers[88].

CRISPR/Cas9 has changed plant breeding with the potential of high-efficiency and high-precision gene editing[47]. With

Table 2 CRISPR-Edited Crops For Nutritional Improvement; examples include rice that has been enhanced with beta-carotene (provitamin A), soybeans with better fatty acid content, high levels of iron and zinc in corn, and lower cyanide producing compounds in cassava.

Crop	Target Gene(s)	Nutritional Trait Improved	Health Benefit
Rice	PSY, CRTL	↑ β-carotene (provitamin A)	Reduces vitamin A deficiency (blindness, immune dysfunction)[77]
Soybean	FAD2	↑ Oleic acid, ↓ PUFA	Healthier oil, improved heart health, longer shelf life[62]
Maize	NAS, IRO2	↑ Iron & zinc	Reduces anemia and stunting in vulnerable populations[12]
Cassava	CYP79D1/D2	↓ Cyanogenic glycosides	Safer consumption lowers the risk of cyanide poisoning.[64]

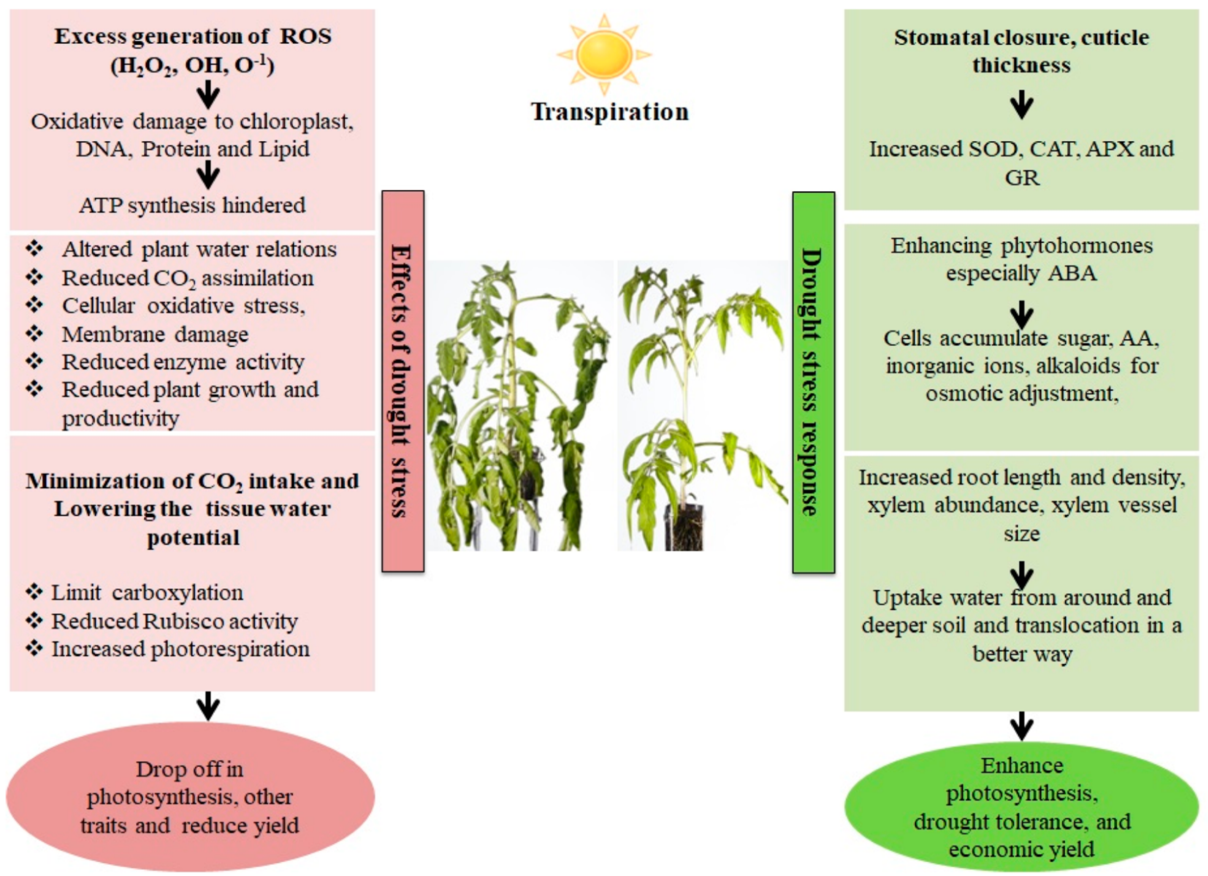

Figure. 3 Effects of drought stress (left) and plant responses (right), and CRISPR-enabled traits such as antioxidant capacity, ABA control, osmotic adjustment, and deeper rooting to improve photosynthesis, tolerance, and yield.[72]

the targeting of very minimal target genes, breeders can avoid the uncertainties of conventional techniques and realize desired characteristics at higher levels of consistency[45]. Aside from labor and resource cost savings, such advancements also enable quicker response measures to problems confronted by crops, such as climate change and pest resistance[47].

CRISPR may provide substantial long-term economic benefits. Through time savings in the creation of new crop varieties, farmers can realize faster returns on investment[88]. CRISPR-edited crops also require less chemical input, such as fertilizers and pesticides, which cost less and reduce environmental effects[68].

This notwithstanding, initial costs are high. Specialized equipment, skilled laborers, coupled with comprehensive regulatory approvals, make research and development an economically prohibitive undertaking, especially for localized farmers and enterprises within developing nations[19,87]. Further, the discrepancy of regulatory frameworks across different nations usually translates into commercialization failures as well as increased costs[89,90]. CRISPR crop development costs should be viewed with caution as laboratory editing alone does not represent all development costs[87]. As such, development costs may include target identification, transformation and regeneration, molecular validation, greenhouse testing, multi-site field trials, regulatory preparation, and eventually seed multiplication or deployment[91]. Therefore, broad estimates such as multiple million dollar development costs are more useful when they can be separated into distinct categories rather than presented as one undifferentiated figure[88].

In addition to shortening the early stages of trait development by directly modifying target genes instead of repeated crossing and backcrossing (selected breeding bottlenecks), later stages such as field validation approval and scaling remain major contributors to total time and costs[49,89]. In conclusion, while crispr-cas9 may reduce selected breeding bottleneck times, its overall economic value will depend on crop type, traits being edited, regulatory environment, and deployment model[90].

Patents and Licensing May Limit Access for Small-Scale Farmers or Developing Countries Although CRISPR technology provides important benefits for crop improvement, large-scale use is hindered by issues of intellectual property (IP)[92]. Several entities control the original CRISPR/Cas9 patents that result in compliant license requirements[34]. The IP barriers may deter use of the technology by small-scale farmers and smaller organizations who seek to use the technology in nations that do not have sufficient finances to overcome license barriers[18,55].

In addition, commercial use of crops bred with CRISPR biotechnology often involves high licensing costs that become prohibitively expensive for resource-poor areas[92]. In Latin America, for instance, the patent landscape of CRISPR in crop agriculture is continuously evolving with an explosion of applications and multiple licensing platforms that could hinder access by local farmers and researchers[19,34]. This fragmented system also creates a threat of innovation concentration by an elite few of large multinational companies, hence leaving public-sector entities and small seed enterprises at the mercy of costly contracts[93]. In practical terms, this means that the most urgently needed traits for food security, like resistance of cassava against sorghum virus, may not be developed for crops that are almost exclusively grown by poor countries because their markets are not profitable enough in the eyes of patent owners[93].

Beginning with the problems identified above, some researchers have suggested the application of humanitarian-use licenses, public funding, and/or more open licensing agreements as ways to improve access to CRISPR technology for people in developing countries[94]. The practical value of these approaches will depend on whether governments, public-sector breeders, and private patent holders adopt them in ways that reduce licensing barriers for nonprofit researchers, small seed enterprises, and resource-poor producers[92].

Reduced Need for Pesticides or Fertilizers Can Save Costs and Benefit the Environment

The economic advantages of CRISPR/Cas9 are especially notable when considering its ability to reduce costly chemical inputs[68]. Genes involved in pest or disease susceptibility can be altered so that crop varieties may exhibit resistance to threats that typically require high applications of pesticides[50]. For example, rice varieties in which the SWEET gene promoter was edited displayed good levels of resistance towards bacterial blight, which reduced the need for chemical applications[65]. Other editing that resulted in resistance similar to that of rice editing was vital for preventing crop loss (ensuring the crop existed) in wheat, maize, and potato while helping farmers with reduced inputs and competition with similar crops[39].

Opportunities to improve nutrient-use efficiencies also arise from CRISPR[73]. Editing root development genes of plants, which may enhance nitrogen metabolism, could provide an opportunity for means to supplant or reduce fertilizer headaches without reducing yield or compromising yield[95]. This represents direct savings for farmers who typically spend significant portions of their annual income on fertilizer[25]. In doing this, less fertilizer will reduce nitrogen runoff into rivers and oceans, which is one of the leading causes of eutrophication[96]. In this manner, CRISPR-developed crops may increase efficiencies while easing some environmental pressures and aligning agricultural practices curated to the goals of climate and biomes[96].

How CRISPR/Cas9 Can Benefit Economically

Beyond the opportunities for potential cost savings for farmers in the form of reduced inputs, CRISPR has broader economic possibilities[24]. For example, ”breeding” speed of improvements will mean farmers will have access to matched crop cultivars much faster than if that breeding was conducted using traditional breeding, which could take years to a decade or more, as the accessibility to the ”breeding” will always be electronic or physical amounts of satellite feeds, drone feeds, or crop sensing[33,61]. Again, the speed to breed will allow for more opportunities for farmers to develop responses to other problems with any emerging threats related to either pest, disease, or climate-related exploits to stabilize food and farm incomes[33].

Additionally, CRISPR-enabled crops may afford value-added products that may be even more competitive in any given vegetable/tuber oil-based or other markets with improved efficiency and/or reduced costs due to CRISPR-applicable nutrients[79]. Value-added products include additional nutrients available in consumer products, such as biofortified rice, commonly known as ”superfoods” or products that are related while reducing trans-fat, such as high oleic soybean oil products[79,80]. In this manner, each company will hold promise for higher profits, along with addressing each idea of public health, ”one nutrition” concern[81].

At a macro level, CRISPR can make the economics of agriculture less volatile by boosting crop resistance[84]. Crops that are resistant to drought, flood, or heat stabilize national food systems, insulating vulnerable populations from inflation in food prices due to climate-induced crop losses[4,86]. Realizing such benefits, though, hinges on overcoming obstacles like expensive R&D, contested intellectual property rights, and asymmetrical access to the technology[6,93]. If these obstacles are surmounted, CRISPR can yield extensive, long-term economic gains to both developed and developing agricultural economies[39].

Ethical Considerations

Although CRISPR/Cas9 shows substantial potential for the improvement of crops, its utilization creates ethical challenges that extend beyond the lab. The three key areas of concern are safety, equity, and public acceptability, and the extent to which CRISPR is responsibly used will depend on these issues[94].

While safety is a major issue regarding CRISPR/Cas9 technology in agricultural biotechnology, the method was developed to edit a genome at specific locations; however, “off-target” edits may occur if the guide RNA binds to DNA sequences that are very similar to the target site[97]. Unlike the risk associated with random mutations occurring during mutagenesis, off-target edits depend upon the degree of sequence similarity and therefore must be assessed on a target-by-target basis[98]. Typically, researchers investigate the likelihood of off-target editing using next-generation sequencing, molecular validation, and comparisons of edited lines against identified potential off-target sites[98]. Methods used to reduce the risk of off-target editing include improved guide RNA design, higher-fidelity versions of Cas enzymes, and downstream screening of edited lines[99]. Consequently, assertions that CRISPR/Cas9 is “no riskier” than traditional plant breeding should be qualified: while some uses of CRISPR/Cas9 do not pose significantly increased risk over traditional breeding techniques, the mechanisms of these two technologies differ, and each edited line must still be tested[100].

Equity and access are central issues, as well. Due to the expense of research, licensing agreements for the offspring of crops, and regulatory approval, CRISPR development currently predominantly impacts multi-national corporations[14]. Smallholder farmers—the groups that carry the majority of risk of being food insecure—are the groups that will likely be left behind[18]. Depending on specific arrangements, the use of CRISPR may have the ability to expand opportunities for some farmers. Some possible mechanisms to facilitate that could include humanitarian-use licenses, public-private partnerships, or government-funded marginally subsistence crop breeding programs that skip the overhead of commercial hybrids or marketable seeds[16]. Absent mechanisms like this, however, CRISPR’s promise to contribute to food security could reinforce, rather than ameliorate, food security of existing inequities on the global agricultural landscape[94].

A major ethical concern with the genetic modification of food is the potential for inconsistent consumer response. Several empirical studies have demonstrated that consumer perceptions and responses regarding genetically modified food differ across regions, food types, desired traits, and the manner in which the technology is introduced[20]. For example, a recent 2024 survey of 1,202 individuals in the United States and Switzerland showed greater willingness among consumers in the United States toward genetically modified foods than among consumers in Switzerland. This finding suggests that differences in regulatory approaches to genetically modified foods can influence consumer perceptions of risk. Additionally, this study demonstrated that acceptability is also influenced by affective considerations, beliefs about values, and social trust[101].

Research has also shown that acceptability may depend on the specific trait or traits being marketed. A 2023 national choice experiment using data from table grape consumers indicated that consumers were willing to pay slightly less per pound for CRISPR-developed grapes than for conventionally bred grapes. However, the results also indicated that consumers viewed sweetness, crispness, and flavor as significantly more important in purchase decisions than the method used to develop those characteristics[102]. Moreover, a 2023 U.S.-based study examining different forms of informational treatment found that while most consumers responded positively to gene editing after exposure to information, some retained concerns regarding the safety of genetically modified foods. Furthermore, the study suggested that consumer opinions differed based on their perception of the reliability of the sources providing that information[101].

Therefore, public acceptance should not be viewed solely through the lens of scientific literacy. Transparency, institutional trust, perceived naturalness, and the belief that genetically modified foods are subject to fair regulation of risk-benefit trade-offs also play critical roles in shaping public opinion[21]. It is therefore likely that traits perceived as reducing pesticide use, improving nutritional content, or directly benefiting consumers will be viewed more favorably than traits seen as primarily benefiting producers or corporate interests[102].

Taken together, these three areas raise a question about acceptability that needs to be raised again: CRISPR can offer great technical solutions to growing crops and increasing food production; however, together, the questions about the fairness, safety, and trust of systems supporting and governing the use of this technology, and the long-term effects of CRISPR[82].

Conclusion and Future Perspectives

The use of CRISPR/Cas9 for crop development is an important opportunity; however, its future in agriculture depends upon how responsibly it is developed and implemented[100]. Based on the information in this article, the next step in developing this technology should be to address the need for better field testing under diverse conditions, improve clarity and consistency in regulation, increase availability for smallholder producers and researchers in resource-poor countries, enhance evaluation of off-target damage and environmental risks, and develop greater public trust through increased transparency and clearer communication about both the advantages and limitations of using CRISPR/Cas9[32,90,97,101]. Therefore, rather than being viewed solely as a method for addressing food security challenges and climate-related stresses, CRISPR/Cas9 should be seen as one part of a comprehensive approach to meeting these challenges by supporting all aspects of sustainable agriculture, including sustainable production methods, equitable delivery mechanisms, and continued funding for plant breeding research[86].

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