

# A SWOT Analysis of the Implications of CRISPR/Cas9 Technology in Crop Production: A Review

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## ABSTRACT

CRISPR/Cas9 technology has become popular in modern plant science and allows crop scientists to manipulate DNA sequences and modify gene function. Gene editing using CRISPR has been used in different food crops such as potato, tomato, maize, rice, and fruits such as oranges and bananas. CRISPR technology is precise in gene targeting, efficient, and has shown positive results in domesticating beneficial traits of wild plant lines. Most studies focus more on gene editing using CRISPR in crops as well as future perspectives. However, few studies address CRISPR from a holistic view by looking at its strengths, weaknesses, opportunities, and threats. Therefore, in this review paper, we address CRISPR/Cas9 in crops from a SWOT analysis perspective. The technology is essential for crop enhancement in terms of longevity, nutrition, and palatability. Through CRISPR, crops are engineered to thrive and produce in environments with abiotic and biotic stress. However, despite the wide adaptation of CRISPR, there are scientific concerns on unintended genomic aberrations that trigger biosafety concerns to humanity and the environment. Lack of standard regulation and authorization of the technology also arise. There is low adoption due to skepticism from opposing views of some religious groups and bioethicists. Although CRISPR technology can be a focal point to crop production, there is a need to forge a common understanding of the development, use, and regulation. Informed consensus between political, economic, religious, and scientific groups is essential to examine this technology's scientific imperative critically.

**Keywords:** CRISPR/Cas9; Gene; Gene editing; Gene targeting; Biotic; Abiotic

## INTRODUCTION

Agriculture, and to be specific, crop production, is a significant beneficiary of science and technology through a gradual revolution of machinery, agrochemicals, and crop varieties. Such innovations have led to substantial economic gains. Despite milestone breakthroughs in plant breeding techniques, 21st century has come along with challenges whose solutions from previous centuries may prove futile. Such challenges include climate change and variations, and safety [1].

1 billion people face chronic malnutrition, and global agricultural systems are dying out, a factor aggravated by the decline of biodiversity and climate changes. However, new breeding techniques such as genomic editing have been devised to solve most of these challenges. However, characteristic of other biotechnology innovations related to food, people reject or adapt them according to socio-economic and political grounds. Presently, most agricultural practices emphasize a narrow range of crops, and at times, crops are produced away from their original place of domestication. Resource-exhaustive classical crop breeding, based

on natural or artificial genetic polymorphism, has increased the spectrum of crops that can thrive in new ecological zones, a critical factor in food security [2].

Furthermore, the discovery of precision breeding has changed the horizon of gene editing in crops. From an opinion based-survey on the potential benefits of new breeding techniques, Lassoued, Macall, Hessel, Philips, and Smyth (2019) found out that gene-edited crops had potential benefits than those developed through conventional breeding or gene modification. While traditional breeding techniques are lengthy, imprecise, and often complicated, gene editing techniques such as CRISPR are significantly improve the production of a crop. CRISPR/Cas9 is currently gaining prevalence in agriculture, especially in maize, potato, rice, Arabidopsis, cotton, wheat, and tomato. In plants, the successful application of targeted mutagenesis leads to developing a high-yielding crop, improved quality, and resistance to abiotic and biotic stress. Previous research has shown that the use of CRISPR technology can lead to the development of crops that are resistant to disease [3]. CRISPR technology is also applicable in resilience agriculture, such as developing climate-smart crops. This

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paper uses SWOT analysis to describe the implications of CRISPR technology on crop production. A SWOT analysis can be applied in foresight studies to categorize critical aspects that influence the phenomenon of interest.

## OVERVIEW OF CRISPR/CAS9

Genome editing ensures precise alterations at the genomic loci of an organism. CRISPR/Cas9 was born through bacteria-based immune system research. Jennifer Doudna and Emmanuel Charpentier discovered and developed CRISPR/Cas9. There are three main steps in CRISPR-mediated immunity: adaptation, RNA biogenesis, and interference [4].

Over the years, scientists have discovered a particular CRISPR system, CRISPR-Cas9, whose potential forms the basis of efficient genetic engineering technology. Genome editing for crop production can be best described in building resilience, adaptation, and end-use.

Gene editing makes use of specific nucleases (SSNs), which bind to a particular nucleic acid sequence. The SSNs make plant breeding potential because they have different ways to alter gene structure and function, including gene knock-in, stacking, translation, and targeted mutagenesis (Table 1).

## RECENT CRISPR/CAS9 DEVELOPMENTS IN PLANT SCIENCE

Gene-editing can be used differently to engineer crops. First, mutation can be induced to delete or alter the function and activity of the existing genes in a particular genome [5]. The second method is through gene insertion, whereby a section of donor DNA is introduced into the genetic information of plants.

CRISPR/Cas9 has been applied in rice, tobacco, tomato, wheat, maize, potato and others. The technology gives crop scientists an excellent platform to alter the function of genes and improve certain crop traits.

## SWOT ANALYSIS

SWOT analysis is both a descriptive and qualitative tool. Gudanowska (2014) posits that strengths, weaknesses, opportunities, and threats (SWOT) analysis makes it easier to support the assessment of a particular technology [6].

In identifying strengths, we want to point out core characteristics that back up adoption or continuation and benefits accrued by a particular technology. In addressing weaknesses, we evaluate the vulnerabilities, incapacities, and inherent problems in a given system. In categorizing opportunities, we analyze the external channels of application, further development, and expansion. In recognizing threats, we identify external dangers, pitfalls, risks, and weak links that hinder growth. SWOT analysis is easy to understand. SWOT analysis is also versatile to application areas and can be applied at different depths. The technique is highly visual, which makes it easy to communicate to stakeholders [7].

### Strengths

In this section, strengths will refer to the advantages, breakthroughs, and unique resources brought about by using the CRISPR gene-editing tool in crop production (Figure1).

### Broadening food sources through de novo domestication:

Recently, the genetic diversity of food crops has decreased, which has led to the depletion of some traits of wild species, such as tolerance to different stresses. However, CRISPR technology makes it possible to combine key domestication traits with good characteristics in wild lines. CRISPR/Cas9 technology holds the promise to broadening food sources through the creation of allele variants for domestication. Developing new crops through wild species diversifies food sources and widens the agricultural production in stressful agro ecological zones and areas of climatic extremes. For instance, CRISPR/Cas9 can domesticate the wild tomato (*Solanum pimpinellifolium*) to benefit the farmer. The wild tomato plant is usually bushy and produces small fruits.

**Table 1:** Application of CRISPR/Cas9 in crops for abiotic, biotic, and nutritional traits.

Crop	Target gene	Stress/trait	Reference
<b>Abiotic stress</b>			
Maize	ARGOS8	Increased yields in drought conditions	Shi et al., 2017
Tomato	SIMAPK3	Tolerance to drought	Wang et al., 2017
Rice	OsPRX2	Tolerance to K deficiency	Mao et al., 2018
	OsHAK-1	Low cesium accumulation	Cordones et al., 2017
<b>Biotic stress</b>			
Rice	OsERF922	Blast Resistance	Wang F. et al., 2016
Rice (IR24)	OsSWEET13	Resistance to bacterial blight disease is a	Zhou et al., 2015
Bread wheat	TaMLO-A1, TaMLO-B1, and TaMLOD1	Resistance to Powdery mildew	Wang et al., 2014
Cucumber	eIF4E	Zucchini yellow mosaic virus, Cucumber vein yellowing virus, and Papaya ring spot mosaic virus (PRSV-W)	Chandrasekaran et al., 2016
<b>Nutritional and other traits</b>			
Maize	ZmIPK1A ZmIPK and ZmMRP4	Phytic acid synthesis	Liang et al., 2014
Potato	ALS1	Herbicide resistance	Butler et al., 2016
Tomato	Rin	Fruit ripening	Ito et al., 2015
Wheat	TaVIT2	Fe content	Connorton et al., 2017
Sweet Orange	PDS	Induction of albino traits and decrease in carotenoid content	Zhang et al., 2017

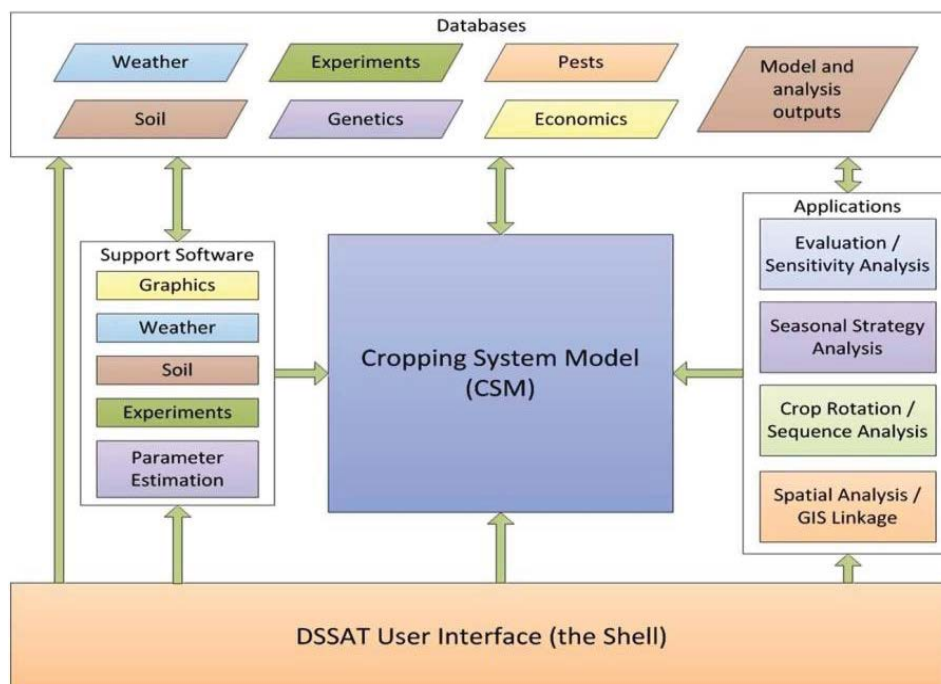


Figure 1: The DSSAT crop modeling ecosystem.

However, with CRISPR, it is possible to mutagenize its genes to obtain attractive plant architecture, increase yield, increase the size of individual fruit and improve the expression of lycopene.

De-novo domestication can also be applied to orphan crops like cowpea, yam, cassava, and other constituents of the millet group. Such 'traditional' crops are undomesticated and possess undesirable traits that make them hard to cultivate. Some of these crops, such as cassava, form an essential part of the diet in many African households. However, too much consumption of cassava can cause cassava cyanide poisoning, which leads to konzo. By using CRISPR/Cas9, it is possible to knock out the cyanogenic compound production.

**Improve shelf-life, quality, and nutrition of crops:** Extended shelf life is an essential trait for the quality of a crop, especially fruits, because it affects marketability for the consumer and the farmer. The texture of fruit is a crucial feature of emphasis in fruit farming, and therefore fruit breeders focus on altering texture traits to induce longer shelf life traits in fruits such as bananas and tomatoes. SPL gene suppression using CRISPR technology showed an improved fruit texture and shelf life without depleting the fruit's organoleptic and nutritional value. Apart from suppressing genes responsible for the collapse of the cell wall in a fruit, down regulating the production of ethylene delays the fruit softening process. Application of CRISPR/Cas9 can also serve as the ultimate answer to food allergy for people. For instance, many people are sensitive to either gliadin or glutenin proteins which make up gluten. Found that CRISPR can be used to delete most gliadin versions from wheat's genomes entirely.

**Development of beneficial biotic and abiotic traits in crops for increased yields:** As the global population increases, the available land for cultivation and water resources are dwindling, which calls for an almost 20%-70% increase in food. There is a need to revamp the classical food production systems to offset this food demand. CRISPR/Cas9 technology will lead to the development of a better crop that will safeguard food security through the following ways;

#### Disease tolerant crop varieties

Plant diseases are known to affect food security negatively, and their effects are known to escalate with climate change. Plant pathogens typically exploit plants' susceptibility (S) genes to attain their multiplication. The technology is used to induce resistance by altering a crop susceptibility (S) gene responsible for plant-pathogen interaction and, therefore, reducing pathogen fitness on the host plant.

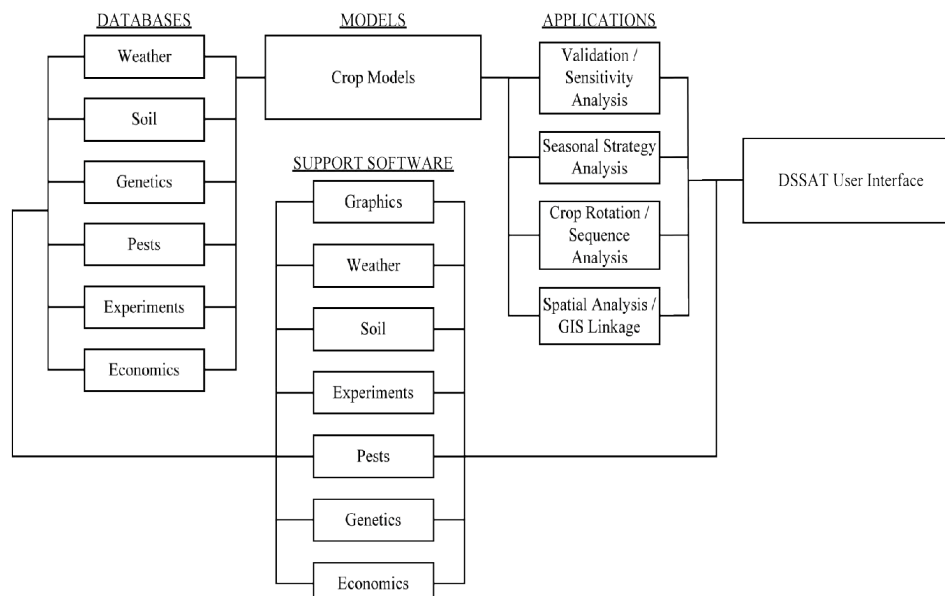
#### Increased food safety for human health

Anti-GM activists attach concerns of the human safety of GMOs on the grounds of the establishment of foreign DNA material and the insertion of transfer-DNA along with antibiotic resistance genes. CRISPR/Cas system, therefore, addresses the issue of the foreign gene because the endogenous genes are altered without any involvement of a foreign gene. However, with CRISPR technology, it is easy to achieve point mutation in genes of interest. This development enables scientists to quickly develop more transgene clean plants that bypass most strict transgenic regulations.

#### Development of crop varieties that are tolerant to drought

The physiological ability of plants to tolerate drought conditions is governed by avoidance, tolerance, escape, or recovery. Drought tolerance is the plant's ability to execute the typical plant physiological functions under drought stress by internal synchronizing responsive genes and signaling systems. Several genes can be targeted to achieve different traits for drought resistance. For example, OsSRL1 and OsSRL2 genes in rice can be targeted for leaf rolling, which reduces water loss through transpiration also note that gene ARGOS8 in maize can also be altered to achieve drought resistance by introducing the GOS2 promoter. In Arabidopsis, gene OST2 can also be targeted for stomatal response.

**Economic gains to the farmer:** The discovery of plants that clone themselves and the use of CRISPR/Cas9 will save the farmer from the exploitative' multinational seed companies. The introduction of synthetic apomixis through gene editing will lead



**Figure 2:** Diagram of database, application, and support software components and their use with crop models for applications in DSSAT v3.5: Source Jone *et al.* (2003).

to clonal seed production and increased heterosis for successive generations. These seeds that can retain their heterosis nature will significantly benefit the farmer because it would cut down the cost of adopting elite seed varieties. In addition, improved self-cloning and pest resistance will empower the farmer and make farming less expensive, practical, and efficient pursuit.

Gene editing will also pave the way to low-input agriculture. The introduction of drought and pest tolerant traits in crops will lead to farmers using fewer resources such as water, pesticides, and fertilizers and fundamentally putting fewer chemicals into the environment. Controlling undesirable biotic and abiotic stressors to crops will ultimately lead to the low cost of production and high yields.

**CRISPR technology is precise and efficient on resources:** Traditional plant breeding systems such as crossing and selection are labor and time-intensive. However, CRISPR technology resolves most challenges of classical breeding because it is faster, precise, and can be executed in many plant species (Ahmad *et al.*, 2020). Besides, only specific DNA sequences are targeted (Jaganathan, Ramasamy, Sellamuthu, Jayabalan & Venkataraman, 2018). This specificity cuts down cases of unintended gene manipulations.

### Weaknesses

Weaknesses would refer to the underlying delimitations of CRISPR technology and that which needs to be improved concerning crop production.

**Undesired genomic aberrations:** One key consideration on the use of CRISPR technology is off-target effects such as unintended gene mutation. Although methods such as SITE-seq are used to identify off-target effects, new types of mutation occur. For instance, during a Cas9 gene-editing procedure in mammalian cells, there was an unexpected massive deletion. Although such mass deletion is yet to be reported in plants, we cannot rule out its occurrence in the future, and its occurrence should be considered.

Although the CRISPR/Cas system has been successfully used for synthetic apomixis in rice to generate heterotic progenies, there was a reduction in the number of seeds with intact hybrid vigor.

There were also reported cases of tetraploid and diploid hybrids and self-fertilization.

**Possible misuse of CRISPR/Cas9:** Although biological weapons raised global concerns a long time before the advent of gene editing, we cannot refute that CRISPR can present new possibilities for biowarfare. CRISPR technology can be used to engineer biological pathogens, which opens the door for possible weaponization. Cheap available 'Do-It-Yourself' (DIY) gene-editing kits also increase fear of the potential of being misused. For instance, He Jiankui, a Chinese scientist, was imprisoned for editing the human genomes in 2018 for the very first time [8].

**Low adoption and skepticism:** CRISPR/Cas continues to face opposition from anti-play-god bioethicists and religious groups. Christianity's contention on gene editing arises from the relationship between man and his creator, the beginning of life, and the concept of co-creation. In addition, low adoption of CRISPR stems from the regulation policies, which are often based on political and socio-economic grounds. Argues that not all governments will support gene editing in crop production. For instance, USDA pointed out that it does not wish to regulate genomic editing in crops so long as no risks are intended. US-Mexico-Canada agreement also has provisions to support gene editing. However, in 2018, the European Union reiterated that any organisms altered by genetic editing would be subject to similar regulations as GMOs. Such regulations hinder cutting-edge research in genomic editing in crops.

### Opportunities

Opportunities are the turning points through which scientists can use the strengths of CRISPR technology into opportunities in a changing global food system.

**New tool for biological exploration and crop improvement:** CRISPR/Cas9 holds the key to potential scientific inventions that solve challenges in modern agriculture. CRISPR/Cas9 lays the foundation for synthetic apomixis, whereby scientists will use the technology to convert the way plants produce from sexual to apomictic modes through genetic manipulations, mutation breeding or wide-crossing with apomictic wild relatives. Although

a comprehensive understanding and mastering of the principles of apomixis is still a challenge to plant scientists, its potential remains a great interest to plant breeders in crop enhancement. CRISPR/Cas9 has massive untapped potential and has an expansive genetic toolbox for plant biologists in further research in functional genomics.

### Threats

Threats refer to what the weaknesses of CRISPR technology can expose crop production to.

**Biosafety concerns:** The biosafety for genome-edited crops is the primary concern among plant scientists. The main problems lie within the designation of guide RNA (gRNA), selection of target gene, off-target effect, and the vector transformation system. Besides, off-target gene mutations in non-targeted genome modifications in plants are a very grave concern to the biosafety of crops. There are rising fears on whether off-target effects of CRISPR that lead to undesirable phenotypes can be controlled. The biosafety concerns not only revolve around humans but also other organisms in the environment [9].

**Challenges in legal regulation:** The developments and application CRISPR/Cas9 approach in plant sciences raises serious concerns on regulations and authorization. There exist no clear national and law of nations on bioecological safety, underlying dangers, management, and abuse of CRISPR technology. In many settings, insufficient regulatory guidelines have failed to bring a legal consensus between civil society and plant scientists. Currently, there is no joint global consensus on the regulation of the CRISPR/Cas9 tool.

## CONCLUSIONS, FUTURE PERSPECTIVES, AND POLICY IMPLICATIONS

Despite biosafety concerns and lack of standard regulation, the primary finding is that gene editing using CRISPR positively impacts crop production [10].

Gene editing using CRISPR is poised to be an indispensable asset to breeders in incorporating essential traits into the genomes of crops. Previous studies have pointed out that CRISPR/Cas9 can be applied to enhance crops in various aspects to optimize crop production with few costs. However, there are also concerns about the adverse outcomes of CRISPR/Cas9 and its effects on humanity and the environment. Even with research-based evidence

on the potential and perceived benefits of CRISPR, there is still low adoption due to skepticism and a lack of clear-cut national and international policies on using and regulating the technology. Therefore, there is a need for national and international consensus with the political, economic, religious, and scientific groups coming on board to chart a clear path on the use and regulation of CRISPR/Cas9.

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