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Current Opinion in Plant Biology

CRISPR/Cas9-based genome editing of banana for disease resistance

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Banana production is severely constrained by many pathogens and pests, particularly where a number of them are co-existing. The use of disease-resistant banana varieties is one of the most effective ways to mitigate the negative impacts of pathogens on banana production. Recent advances in new breeding techniques have the potential to accelerate breeding of banana for disease resistance. The CRISPR/Cas9 based genome editing has emerged as the most powerful tool for crop improvement due to its capability of creating precise alterations in plant genome and trait stacking through multiplexing. Recently, the robust CRISPR/Cas9-based genome editing of banana has been established, which can be applied for developing disease-resistant varieties. This article presents a synopsis of recent advancements and perspectives on the application of genome editing for generating disease-resistant banana varieties. It also summarizes the current status of regulatory requirements for the release of genome-edited crop varieties among different countries.

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Current Opinion in Plant Biology 2020, **56**:118–126

This review comes from a themed issue on **Biotic interactions**

Edited by **Ksenia Krasileva** and **Benjamin Schwessinger**

https://doi.org/10.1016/j.pbi.2020.05.003

Introduction

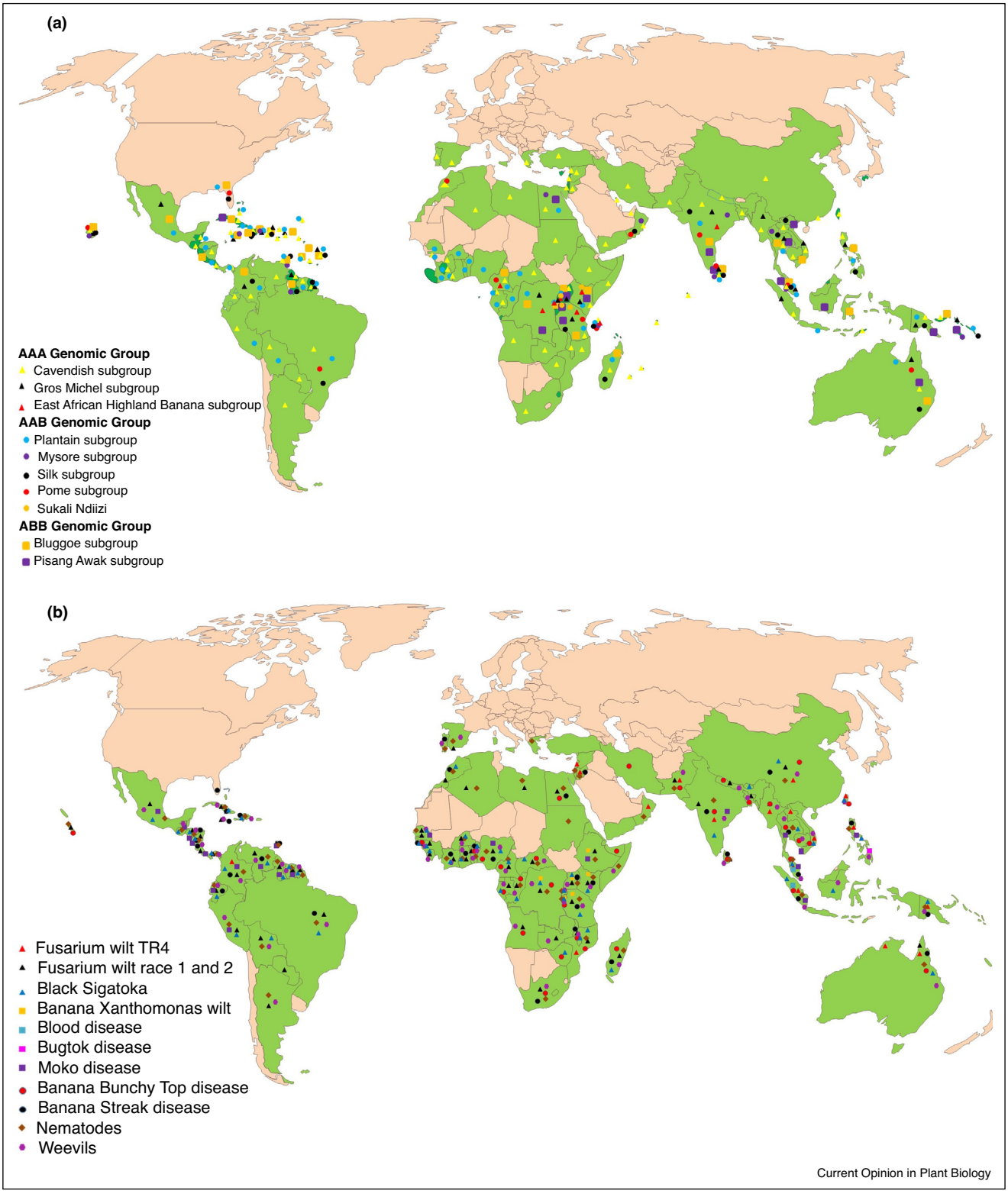
Plant pathogens and pests pose a serious threat to food security as they are estimated to cause around 20–40% losses of food production worldwide [1]. Currently, they are creating an even higher risk to food security due to climate change and increasing global trade. Several catastrophic plant pathogens affect banana (*Musa* spp.), which is one of the major staple food crops in 136 countries grown on 11 million hectares of land (Figure 1) [2••]. Its global production is approximately 153 million tons annually, supplying food to more than 400 million people [2••]. Bananas are mainly cultivated by smallholder farmers for household consumption and local or regional markets; only approximately 15% of production enters international markets. Besides contributing to food security as a staple crop, it generates income as a cash crop, particularly in tropical and sub-tropical countries. Africa supplies one-third of the world's banana production, with East Africa being the largest banana-growing region accounting for about 40% of the aggregate production in Africa. Banana provides 30–60% of the daily per capita calorie intake in some East African countries such as Burundi, Rwanda, and Uganda, with the highest consumption at 0.5 kg per person per day in Uganda [3].

Several different types of banana are grown globally (Figure 1a); however, large-scale farmers grow mainly the Cavendish type of dessert banana for local and international markets. Other types of dessert banana varieties such as Gros Michel, Sukali Ndiizi, Mysore, Silk, and Pome are also grown at a low level. Besides, cooking types such as the East African Highland Banana and bluggoe, the roasting type plantain, and the brewing type such as Pisang Awak are also grown mainly in Africa.

The biggest challenge in agriculture is to feed the growing human population, which is projected to reach 9.7 billion in 2050 and 10.8 billion by 2100 compared to 7.7 billion in 2019 [4•]. Therefore, there is an urgency to close the yield gap in staple crops and enhance food production to feed the world. In Africa, the emphasis should be on banana rather than on cereals, unlike other parts of the world, as it is one of the main crops used for staple food and generation of income. Investment in the genetic improvement of banana holds great prospects for improving food security as it feeds more people per unit area of production than other staple crops [5••].

To fulfill the increasing demand for food with limited resources, better and efficient ways to produce food are required. The development of banana resistant to diseases by conventional breeding is a significant challenge because of inter-specific hybridization barriers, which prevent the transfer of desirable agronomic traits into the genus. The major problems in traditional crossing are polyploidy, lengthy production cycle, sterility of the majority of cultivars, and low genetic variability in *Musa* germplasm [3]. Moreover, the introduction of multiple fungal, bacterial, and virus-resistant genes into the crop may cause considerable yield reduction or intensify other agriculturally undesirable traits because of genetic linkage. Modern biotechnological tools such as genetic modification (GM) and genome editing (GE) offer

Figure 1



The world map highlighting banana-producing countries as well as the distribution of different types of banana and major pathogens and pests globally. **(a)**: World map showing the distribution of different types of banana in significant banana-producing countries. The map was created based on the information on ProMusa Diversity of Banana Cultivars Portal [http://www.promusa.org/Diversity+of+banana+cultivars+portal],

cost-effective strategies for developing improved varieties of banana resistant to multiple diseases. Currently, serious efforts are underway to develop GM varieties of banana resistant to diseases and pests [3,5••]. However, the commercialization of GM crops faces hurdles due to complicated regulatory approval processes. A recent development in GE has the ability to accelerate breeding by making efficient and precise changes in the plant genome to develop new traits such as disease resistance. This article presents an overview of recent progress and perspectives to explore the application of CRISPR-Cas9-based GE for developing improved banana with resistance to diseases.

Banana diseases

Banana production is severely constrained by several diseases and pests, particularly in regions where various pests and pathogens co-exist (Figure 1b). Prominent among these diseases are banana Xanthomonas wilt (BXW) caused by *Xanthomonas campestris* pv. *musacearum*, black Sigatoka caused by *Pseudocercospora fijiensis*, Fusarium wilt, commonly known as Panama disease, caused by *Fusarium oxysporum* f. sp. *cubense* (Foc), banana bunchy top disease, and banana streak disease and pests such as nematodes and weevils (Figure 2) [3,5••].

BXW disease is considered one of the most significant production constraints for the banana in Central and East Africa [6•]. The disease affects the cultivation of all types of banana, and its impacts are severe and fast, as it has wiped out entire plantations in many of the affected areas. Overall, economic losses from BXW were estimated at US $2 to 8 billion over a decade [7]. BXW disease has negatively affected the food security and income of smallholder farmers, who depend on the banana for their livelihood.

New plant diseases potentially threaten staple crops around the world. For example, severe risks to global production of banana are currently posed by *Fusarium oxysporum* f. sp. *cubense* tropical race 4 (TR4) [8••]. In the 1950s, the first outbreak of Fusarium wilt race 1 wiped out the main commercial banana 'Gros Michel' and was replaced by Cavendish varieties, which currently cover about 90% of export markets [9]. Now, a new outburst of TR4 is threatening the production of Cavendish and other varieties of banana [8••]. For more than 20 years, TR4 has been contained in the Northern Territory of Australia and the East and parts of Southeast Asia; however, since 2010, the disease has spread to additional countries in Southeast and South Asia and the Middle East and Mozambique in Africa [8••]. Recently, TR4 has also been reported in Colombia, which is the biggest banana exporter in the world [10•]. The emergence of this new threat to banana production has created an urgency to develop disease-resistant varieties using new breeding tools such as GE [8••].

Advances and prospects of genome editing for disease resistance

To attain global food security, the application of new breeding methods for agricultural productivity is of key interest [11••]. Advances have been reported for the manipulation of desired plant genes in crops using various site-directed nucleases (SDN) such as zinc-finger nucleases (ZFNs), meganucleases (MNs), transcription activator-like effector nucleases (TALENs), and clustered regularly interspaced short palindromic repeats/CRISPR-associated protein 9 (CRISPR/Cas9) [11••]. The CRISPR/Cas9 system has emerged as the most potent tool for targeted GE, including gene knockouts, base replacement, multiplex gene editing, and regulation of gene transcription in plants [11••]. It is becoming the most popular technique for crop improvement due to its simplicity, design flexibility, and high efficiency [5••,11••]. The CRISPR/Cas9 tool is based on the induction of double-stranded breaks (DSB) at a target site and repair of the break, either through homology-directed repair (HDR) or non-homologous end joining (NHEJ). It creates user-desired mutations ranging from targeted point mutation to large deletions or insertions of exogenous DNA at the target site in the genome. There are four different types of editing—SDN1, SDN2, SDN3, and base editing [12•]. SDN1 is a highly efficient, error-prone repair of a targeted DSB through NHEJ, leading to a mutation causing gene silencing, gene knockout, or a change in the function of a gene. SDN2 is less efficient and high fidelity, generated by HDR consisting of a template-guided repair of a targeted DSB using a repair template with one or several small mutations flanked by two sequences matching both ends of the DSB. This type of repair allows the introduction of the mutation(s) at the target site. SDN3 is also less efficient, and high fidelity generated by HDR and involves the insertion of the entire gene or genetic element(s) at the target site using a donor sequence through a template-guided repair of a targeted DSB. The SDN1 and SDN2 are similar to mutations obtained through chemical mutagenesis, irradiation, or spontaneous natural mutations. Base editing generates precise single-nucleotide changes in genomic DNA or cellular RNA without causing DSBs, needing a DNA donor template, or depending on HDR. As base editing does not require a DNA donor template, thus it might be considered as SDN-1 [12•].

(Figure 1 Legend Continued) ProMusa Banana Cultivar Checklist [http://www.promusa.org/Banana+cultivar+checklist], and FAOSTAT data for banana and plantain [http://www.fao.org/faostat/en/#data/QC]. **(b)**: Distribution of major pathogens and pests globally. The world map showing the presence of various pathogens and pests co-existing in the same country. This map was created using the information on pathogen distribution from CABI [https://www.cabi.org/isc].

Figure 2

Pictures of banana plants showing symptoms of major diseases and pests. **(a)**: Banana Xanthomonas wilt, **(b)**: Fusarium wilt, **(c)**: Black Sigatoka, **(d)**: Banana bunchy top, **(e)**: Banana streak and **(f)**: Toppling of plant due to nematode infestation.

The availability of a well-annotated, whole-genome sequence of banana (http://banana-genome-hub.southgreen.fr) coupled with established genetic transformation and regeneration protocols makes the banana a strong candidate for GE. Recently, CRISPR/Cas9-based genome editing has been reported for banana [13••,14••,15•,16•]. The robust GE protocol developed for banana (AAA group) and plantain (AAB group) could provide an operational framework for single or multiple knockouts, opening up avenues for efficient and targeted genome manipulations for disease resistance [13••]. Single and multiple knockouts are also possible through classical GM technology using RNAi approach. However, RNAi does not always result in a complete knockout; therefore genome-editing could potentially be used to simultaneously knocking out genes and probably without the integration of any foreign DNA. This is a significant development as banana is polyploid and challenging to improve through conventional breeding approaches.

The use of disease-resistant banana varieties is one of the most effective solutions to mitigate the adverse effects of pathogens on banana production. CRISPR technology has been successfully applied to explore the development of crop varieties with disease resistance (Table 1, 14••,17•,18•,19,20–26,27•,28•,29•,30). GE can be used to disrupt the function of disease-causing susceptibility ('S') genes, the transcription factor, and sugar transporters as a strategy to develop resistance against bacterial and fungal pathogens [11••,17•]. For example, simultaneous mutations (insertions, deletions, and substitutions) in the effector binding elements (EBE) in the promoters of three SWEET (Sugars Will Eventually be Exported Transporters) genes (*OsSWEET11*, *OsSWEET13*, and *OsSWEET14*) by CRISPR/Cas9 conferred resistance to bacterial blight [17•]. Knockout mutations were created in the promoters of all three *SWEET* genes simultaneously using a multiplex CRISPR/Cas editing approach, where the plasmid containing multiple guide RNA (gRNA) and *Cas*9 gene were introduced using *Agrobacterium*-mediated transformation in rice. The edited lines grew normally, without yield suppression, and were resistant to different strains of bacterial blight under greenhouse trials.

The disruption of the coding region of both alleles of the S gene, LATERAL ORGAN BOUNDARIES (*CsLOB1*), conferred a high level of resistance to citrus canker [20]. The edited lines were generated through *Agrobacterium*-mediated transformation using the plasmid containing Cas9/gRNA targeting the *CsLOB1* coding region. The edited lines with frameshift mutations (deletion and insertion) showed enhanced resistance to citrus canker in the glasshouse experiments. No phenotypic changes were observed in these plants in comparison to wild type

Table 1

Advances in crop improvement for disease resistance using genome editing

Crop	Editing system	Target gene	Editing type	Repair mechanism	Delivery method	Trait	Reference
Bacterial diseases							
Apple	CRISPR/Cas9	*DIPM1*, *DIPM2*, *DIPM4*	Knockout	NHEJ	*Agrobacterium*-mediated transformation	Resistance to fire blight disease	[19]
Citrus	CRISPR/Cas9	*CsLOB1*	Knockout	NHEJ	*Agrobacterium*-mediated transformation	Resistance to citrus canker	[20]
Rice	CRISPR/Cas9	*OsSWEET11, OsSWEET13, OsSWEET14*	Knockout	NHEJ	*Agrobacterium*-mediated transformation	Resistance to bacterial blight disease	[17•]
Rice	CRISPR/Cas9	*Os8N3*	Knockout	NHEJ	*Agrobacterium*-mediated transformation	Enhanced resistance to *Xanthomonas oryzae* pv. oryzae	[18•]
Tomato	CRISPR/Cas9	*SiDMR6*	Knockout	NHEJ	*Agrobacterium*-mediated transformation	Resistance to *Pseudomonas syringae*, and *Xanthomonas* spp.	[21]
Tomato	CRISPR/Cas9	*SiJAZ2*	Knockout	NHEJ	*Agrobacterium*-mediated transformation	Resistance to *Pseudomonas syringae*	[27•]
Fungal diseases							
Cocoa	CRISPR/Cas9	*TcNPR3*	Knockout	NHEJ	*Agrobacterium*-mediated transformation (transient expression)	Increased resistance to *Phytophthora tropicalis*	[29•]
Cotton	CRISPR/Cas9	*Gh14-3-3d*	Knockout	NHEJ	*Agrobacterium*-mediated transformation	Resistance to *Verticillium dahlia*	[28•]
Grapes	CRISPR/Cas9	*MLO7*	Knockout	NHEJ	Polyethylene glycol (PEG) mediated Protoplast transformation	Resistance to powdery mildew	[19]
Grape vine	CRISPR/Cas9	*VvWRKY52*	Knockout	NHEJ	*Agrobacterium*-mediated transformation	Resistance to *Botrytis cinereal*	[26]
Rice	CRISPR/Cas9	*OsERF922*	Knockout	NHEJ	*Agrobacterium*-mediated transformation	Resistance to *Magnaporthe oryzae*	[25]
Rice	CRISPR/Cas9	*OsSEC3A*	Knockout	NHEJ	*Agrobacterium*-mediated transformation	Enhanced resistance to *Magnaporthe oryzae*	[30]
Tomato	CRISPR/Cas9	*SiDMR6*	Knockout	NHEJ	*Agrobacterium*-mediated transformation	Resistance to *Phytophthora capsica*	[21]
Tomato	CRISPR/Cas9	*SiMLO1*	Knockout	NHEJ	*Agrobacterium*-mediated transformation	Resistance to powdery mildew	[23]
Wheat	TALEN and CRISPR/Cas9	*TaMLO-A1, TaMLO-B1, TaMLO-D1*	Knockout	NHEJ	Protoplast transformation/ Biolistic transformation	Enhanced resistance to powdery mildew	[22]
Wheat	CRISPR/Cas9	*TaEDR1*	Knockout	NHEJ	Biolistic transformation	Resistance to powdery mildew	[24]
Viral diseases							
Banana	CRISPR/Cas9	Viral genome	Knockout	NHEJ	*Agrobacterium*-mediated transformation	Inactivation of *eBSV*	[14••]
Cassava	CRISPR/Cas9	*eIF4E* isoforms *nCBP-1, nCBP-2*	Knockout	NHEJ	*Agrobacterium*-mediated transformation	Partial resistance to CBSD	[38•]
Cucumber	CRISPR/Cas9	*eIF4E*	Knockout	NHEJ	*Agrobacterium*-mediated transformation	Resistance to *Cucumber vein yellowing virus*, *Zucchini yellow mosaic virus*, and *Papaya ringspot virus*-type W	[39]
Potato	CRISPR/Cas9	*Coilin*	Knockout	NHEJ	Biolistic transformation	Increased resistance to *Potato virus Y*	[40•]
Rice	CRISPR/Cas9	*eIF4G*	Knockout	NHEJ	*Agrobacterium*-mediated transformation	Resistance to *Tungro spherical virus*	[37•]
Tobacco	CRISPR/Cas9	Viral genome IR, CP, RCR	Knockout	NHEJ	*Agrobacterium*-mediated transformation	Resistance to *Tomato yellow mosaic virus*	[36]
Tobacco, Tomato	CRISPR/Cas9	IR, CP, Rep	Knockout	NHEJ	*Agrobacterium*-mediated transformation	Resistance to *Tomato yellow leaf curl virus*	[34•]
Tobacco	CRISPR/Cas9	IR, CI coding regions	Knockout	NHEJ	*Agrobacterium*-mediated transformation	Complete resistance to *Cottonleafcurlmultan virus*	[35•]

plants. Likewise, disruption of the *downy mildew resistance 6* allele of tomato (*SiDMR6-1*) gene showed disease resistance to several pathogens such as *Pseudomonas syringae*, *Phytophthora capsici*, and *Xanthomonas spp.* [21]. Similarly, knockout of the *SiMLO1* gene in tomato and *TaMLO* and *TaEDR1* in wheat enhanced resistance to powdery mildew disease [22–24].

The edited rice plants with knockout mutations in the transcription factor ethylene-responsive (*OsERF922*) gene, a negative regulator of the blast resistance, conferred increased resistance to *Magnaporthe oryzae* [25]. This study demonstrated that CRISPR/Cas9 plasmid targeting *OsERF922* induced insertion or deletion mutations at the target site leading to the frameshifts in the *OsERF922* gene. The rice mutants with the knockout of *OsERF922* showed enhanced resistance to *M. oryzae* without altering the agronomic traits. The results exhibited that all allelic mutations in the T_0 mutants were transmitted to the T_1 generation plants. The study also indicated that the mutagenic frequency could be increased by targeting multiple sites within one gene. Likewise, the knockout of transcription factor *VvWRKY52* in *Vitis vinifera* showed enhanced resistance against *Botrytis cinereal* [26]. Similarly, knockout of *SiJAZ2* showed resistance against *Pseudomonas syringae* in tomato [27•]. Zhang *et al.* [28•] demonstrated that manipulating *Gh14-3-3d* gene, the negative regulator of disease resistance, in *Gossypium hirsutum* conferred resistance to *Verticillium dahlia*.

Similar approaches of manipulating endogenous 'S' genes, sugar transporters, and the negative regulator of disease resistance can be applied in banana to enhance resistance against bacterial and fungal pathogens [31•]. The target genes in a banana for resistance to bacterial disease have been identified through the comparative transcriptomics of the resistant wild type banana *Musa balbisiana* and susceptible banana Pisang Awak [32•]. The knockout of single or multiple susceptibility genes (such as *MLO*13, *DMR6)*, transporter genes (like *SWEET14),* and the negative regulators (e.g. E3 ubiquitin ligases) can provide resistance to BXW disease. In addition, endogenous *Musa* defense genes such as disease resistance (R gene), the pathogenesis-related gene (PR), receptor kinases, and antimicrobial protein can be activated using CRISPR activation (CRISPRa) technology [32•,33•].

GE has been applied to develop resistance against geminiviruses (ssDNA) such as *tomato yellow leaf curl virus*, *tomato yellow mosaic virus*, *cotton leaf curl multan viru*s, and single-stranded RNA (ssRNA) viruses such as *rice tungro spherical virus*, *cassava brown streak virus*, *turnip mosaic virus*, and *potato virus Y* [34•,35•,36,37•,38•,39,40•]. The editing of the eukaryotic translation initiation factor (*eIF*) gene family, including *eIF4E,* its paralogue *eIF(iso)4E* and *eIF4E* isoforms *nCBP-1*and *nCBP-2* and *eIF4G*, has provided resistance to several viruses including *cucumber vein yellowing virus*, *zucchini yellow mosaic virus*, *papaya ringspot virus*-type W, *cassava brown streak virus* and *rice tungro spherical virus* [37•,38•,39]. The editing of the *eIF* gene family in banana can provide resistance to BBTV, which is an ssDNA babuvirus.

Recently, CRISPR/Cas9-based editing was applied to inactivate the integrated endogenous *banana streak virus* (eBSV), dsDNA badnavirus, integrated into the B genome of plantain (AAB), overcoming a major challenge in breeding and the dissemination of hybrids [14••]. The GE plantain 'Gonja Manjaya' were generated with mutations in the targeted sites of integrated eBSV sequences in the host genome. Sequencing and phenotyping of the edited events showed targeted mutations and confirmed the inactivation of eBSV for its ability to be converted into infectious viral particles.

Challenges of genome editing of asexually propagated and polypoid crops

Generation of disease-resistant GE banana by plasmid-based delivery of CRISPR reagents (gRNA and Cas9) may be considered as GM because the plasmid usually contains marker genes and are delivered by *Agrobacterium* into the plant cells, resulting in random integration of foreign genes in the plant genome. Even though the integrated foreign gene can be removed by genetic segregation in sexually propagated crops, this is not feasible in asexually propagated crops [41•]. The GE plants generated through *Agrobacterium*-mediated transformation may face similar hurdles to GM crops. To overcome the regulatory hurdles, considerable efforts have been made in banana and other asexually propogated crops to directly deliver the preassembled Cas9 protein-gRNA ribonucleoproteins (RNP) into the plant cells [5••,41•]. The RNPs mutate the target sites immediately upon delivery and then get rapidly degraded by endogenous proteases leaving no traces of foreign DNA elements. In banana, preassembled RNPs targeting different traits for disease resistance could be coated on gold particles and delivered to banana cell suspension cultures or protoplasts [5••]. The plant cells can then be regenerated to full plants. The foreign DNA-free approach could be useful in the production of banana for resistance to diseases. The foreign DNA-free GE plants might not require strict regulatory approval in several countries that will make the commercialization of these types of edited plants easier [11••].

Another challenge of editing of polyploid heterozygous crops such as banana is simultaneously targeting multiple alleles. A large number of transformants should be screened to recover an edited line with multiallelic mutations [41•].

Table 2

Summary of regulatory approaches in different countries for genome edited products

Country	Current regulatory approach	References
Argentina	GE crops with no foreign gene are not subjected to GMO regulation. Allows for a case-by-case assessment to determine the regulatory status of a crop.	[42•]
Brazil	Regulate GE products on a case-by-case basis and exempt crops from regulation when there is no transgene insertion.	[43•]
Chile	Regulate GE products on a case-by-case basis and exempt GE crops from regulation when there is no transgene insertion.	[43•]
Australia	Australian Office of the Gene Technology Regulator (OGTR) has proposed technical amendments to the existing definitions of the GMO regulations to better address new breeding techniques applications. According to the proposed amendment GE crops with no foreign gene integration (SDN1) are not be regulated in the same way as GMOs. The edited products, where a repair template (i.e. SDN2 and SDN3) is used to guide genome editing, are treated as GMOs.	[44•]
Canada	Canada's regulatory process is based on novelty. Their approach to GE technologies is no different from the technologies that have preceded it. If the technology creates a novel product, then it requires additional regulatory oversight.	[45]
European Union	On 25 July 2018, the European Court of Justice ruled that organisms developed using GE technology fall under the obligations of Directive 2001/18/EC; which means that GE products are considered to be GMOs.	[46•,47•]
India	India has not issued and formal guidance for regulating GE products. Current proposal is that India does not consider products developed through GE to be GMO and thus will not be reviewed under the national GMO legislation. GE products will be reviewed at a State level.	[43•]
Japan	Japan considers varieties developed using GE with no new DNA as non-GMO. Regulators recommends regulating only GMOs that have had foreign genes permanently introduced into their genomes and not those whose endogenous genes have been edited.	[48•]
Kenya	Guidelines for regulation of GE products are under development.	[49•]
Nigeria	Biosafety agency is drafting guidelines on GE.	[50•]
United States of America	No biosafety oversight of GE applications, if no genetic elements from pathogenic species or pesticidal traits are introduced	[11••]

GE, Genome editing; GMO, Genetically modified organism; SDN, Site directed nucleases.

Regulatory approaches for edited products

GE has shown immense potential for crop improvement, but the regulation of GE products is still in its early stages. There are differences among the countries regarding the regulation of GE crop varieties. The GE varieties with no foreign gene integration, particularly SDN1, are not regulated in several countries such as Argentina, Australia, Brazil, Chile, Canada, Japan, and the USA (Table 2). These countries have issued legal interpretations of various exceptions in regulatory rules and exempted GE crops from the stringent regulations similar to GMOs [11••]. GE is treated similarly to conventional breeding in Canada, and the regulation of improved plant varieties is based on novelty. In the USA, no regulatory oversight of GE applications is required if no genetic elements from pathogenic species or pesticidal traits are introduced. The world's first regulation for GE crops was reported for Argentina [42•]. Later on, Brazil and Chile adopted the same policies. Currently, many countries do not have a clear regulatory framework for GE crops. However, several countries like Kenya, Nigeria, and India are in the process of developing the regulatory guidelines for the application of genome editing.

Conclusion

GE crops can play a pivotal role in agriculture for enhancing nutrition, food safety, and security. It has emerged as a powerful biotechnological tool, which can precisely introduce new traits to crops for better yield and enhanced nutrition. Over a decade, a lot of progress has been made for creating improved crop varieties. The advances in GE have the potential to develop disease-resistant varieties of banana, which will contribute to food security, particularly in Africa. However, the commercialization of GE products has some challenges due to the regulation of genome-edited products in various countries. The usage of genome editing in crop improvement programs of banana will be boosted by developing science-based guidelines, which will treat the GE varieties similar to those generated through conventional breeding, particularly where no foreign gene is inserted. It will enhance the adoption of disease-resistant GE varieties, hence contributing to food security.

Author contributions

LT is responsible for the original concept and all authors contributed in writing and reviewing of the manuscript. JNT prepared all the figures.

Declaration of conflict of interest

The authors declare no conflict of interest.

Acknowledgement

Authors wish to thank CGIAR Research Program on Roots, Tubers and Banana (CRP-RTB) for financial support.

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