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Genetic engineering at the heart of agroecology

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Abstract

We discuss whether genetic engineering and agroecology are compatible. For this, we investigated three cases of genetically engineered crops and considered agroecology as scientific discipline as well as a social movement. One case was the use of cisgenic modifications to make potato durably resistant to late blight, the second was the use of CRISPR/Cas to make rice resistant to bacterial blight and as a third case, we evaluated experiences with cultivating transgenic Bt crops. These cases demonstrated that genetic engineering offers opportunities to grow crops in novel integrated pest management (IPM) systems with, as direct benefit, a decrease in the use of chemical crop protection agents, and as indirect effect that the role of predators and biological control agents can become more important than in present conventional systems based on pesticides. We used a framework based on four concerns (both cons and pros) that were gathered from an extensive societal interaction organized around the Dutch research project DuRPh, which produced a proof-of-concept of a cisgenic late blight-resistant potato. We concluded that genetic engineering and agroecology certainly have synergy in the context of agroecology as science, when applied to making crops less vulnerable to pests and diseases and when combined with cultivation using IPM. By contrast, within the movement context, genetically engineered varieties may be welcomed if they include traits that contribute to successful IPM schemes and are socially benign. Whether they would actually be deemed desirable or acceptable will, however, vary depending on the norms and values of the social movements. We propose that some concerns may be reconcilable in a dialogue. Deontological arguments such as naturalness are more difficult to reconcile, as they relate to deeply felt ethical or cultural values. A step forward would be when also for these arguments everyone can make an informed choice and when these choices can coexist in a respectful manner.

Keywords
Agroecosystems, genetic modification, gene editing, CRISPR/Cas, ecology, IPM

Introduction

The term ‘agroecology’ has no universally agreed meaning. Scientists who want to apply the discipline of ecology within their research on agricultural production systems have been using this term since the 1930s. Martin and Sauerborn (2013) defined this as: ‘the science of the relationships of organisms in an environment purposely transformed by man for crop or livestock production’. From this basic definition, the use of the term agroecology has evolved, among others to a ‘normative’ or ‘prescriptive’ use by incorporating ideas about a more environmentally and socially sensitive approach to be addressed for a sustainable and fair food system (Hecht, 2018; HLPE, 2019; Wezel et al., 2009). This has often taken the form of a social movement, and the term is currently commonly used in this context.

A major objective of agroecology as science is the development of integrated pest management (IPM). IPM involves an integrated approach for the prevention and/or suppression of organisms (pests, diseases, weeds) harmful to plants through the use of all available information, tools and methods. IPM emphasizes the growth of a healthy crop with the least possible disruption to agroecosystems and encourages natural pest control mechanisms (http://www.fao.org/agriculture/crops/thematic-sitemap/theme/pests/ipm/en/).

With genetically engineered crops, we refer to crops improved by a series of techniques ranging from transgenesis through gene transfer by means of the bacterium *Agrobacterium tumefaciens* or biolistics to new plant breeding techniques (NPBTs), the most prominent presently being gene editing using CRISPR/Cas technology (Modrzejewski

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et al., 2019; Schaart et al., 2016; van de Wiel et al., 2017; Zhang et al., 2019). A variety made with NPBTs is one in which genetic engineering has been employed in some steps of the breeding process. Meta-reviews, for example, National Academies of Science, Engineering and Medicine in the United States (2016) and European Academies Science Advisory Council (2013), on transgenic crops addressed issues in societal debates and generally denoted benefits to farmers and product market chains, provided that implementation encompasses good agricultural practice (GAP) and the presence of optimal institutional contexts. In that sense, the situation is not different from other agricultural innovations, and case-wise analyses based on the trait at hand are required (Franke et al., 2011). This will not be different for crops produced with NPBTs, for which, being a more recent development, comprehensive meta-reviews are still scarce and preliminary (e.g. Hickey et al., 2019; Pixley et al., 2019; Tyczewska et al., 2018).

An important question is whether and to what extent genetic engineering and agroecology are compatible (Altieri et al., 2018; Bonny, 2017; Giller et al., 2017; Lotz et al., 2014; Mugwanya, 2019). In this perspective paper, we discuss this question focusing on genetically engineered crops in the context of agroecology used both as a scientific discipline and as a ‘social movement’. Looking for answers to this question, we follow a case-wise approach.

The late blight-resistant potato case

We will start from the outcomes of a publicly funded, 10-year lasting Dutch research programme, entitled ‘Durable resistance against *Phytophthora infestans* (potato late blight) by cisgenic modification’ (DuRPh) (Haverkort et al., 2016). This programme studied the employment of multiple resistance genes from wild potato species in well-established potato varieties via genetic modification. The genetically engineered plants would only contain resistance genes derived from cross-compatible potato species and thus can be referred to as cisgenes (Schouten et al., 2006). These resistance genes from crossable wild potato species could also have been transferred by traditional breeding, but this would take considerably more years and, because of the outbreeding nature of potato, it is impossible to stack them in existing varieties with traditional techniques of crossing and selecting. The DuRPh project resulted in a clear proof-of-concept that existing potato varieties could be made durably resistant with this approach in combination with the specifically developed resistance management strategy based on IPM principles (Kessel et al., 2018). In the long term, by growing these cisgenic potatoes, a reduction of fungicides use of more than 80% compared to current practice may be achieved. More than 50% of fungicide usage in the Netherlands is aimed at controlling potato late blight, involving a total amount of 1424 Mg of active ingredient on 165,000 ha (10–16 sprays per growing season) and amounting to 10% of the potato production costs (Haverkort et al., 2009). The management system proposed by Kessel et al. (2018) encompasses low-fungicide input to protect resistances from being overcome by the pathogen and is based on monitoring of potato cultivation and genetic or phenotypic characterization of the *Phytophthora* population. The fact that using genetic engineering different resistance genes can be stacked in a single variety, and that the composition of these stacks can be adapted or proactively alternated over years to delay resistance development in evolving populations of *P. infestans*, is considered to be a key factor in resistance management in an IPM context (Haverkort et al., 2016; Kessel et al., 2018).

This research increased insight in the position and functioning of *Phytophthora* resistance genes within the potato gene pool and related ecological interactions. Molecular markers were made available for several resistance genes based on these new insights, which make breeding of disease-resistant potato varieties more precise and efficient. These insight and tools were acknowledged by potato breeders to be valuable for an organic breeding programme (Ronald Hutten, personal communication, 27 January 2020).

In the United States, the potato breeding company Simplot has introduced resistance (R) cisgenes in their innate cultivars starting with one gene, *Rpi-Vnt1* (http://www.isaaa.org/gmapprovaldatabase/advsearch/default.asp?CropID=16&TraitTypeID=3&DeveloperID=61&CountryID=Any&ApprovalTypeID=Any). Ghislain et al. (2019) used genetic modification to successfully transfer late blight resistance genes from wild potato species into smallholder farmers’ preferred potato varieties in sub-Saharan Africa. The results demonstrate that by cultivating these late blight-resistant potatoes within their current cropping systems and under their local conditions, smallholder farmers can increase their yields threefold to fourfold over the national average and so also realize a considerable increase in income.

The case of rice and Xoo

Recently, an IPM-based toolkit ready for use in practice was published, aimed at controlling bacterial blight in rice caused by *Xanthomonas oryzae* pv. *oryzae* (Xoo). There are hardly any effective crop protection agents against bacterial diseases. For that reason, bacterial blight can be disastrous for the rice crop of smallholder farmers in Southeast Asia and, increasingly, in Africa. The toolkit was based on the fairly recently developed concept of knocking out susceptibility (S) genes to create resistance against pathogens (Pavan et al., 2010; Sun et al., 2016). In this example, S genes were knocked out in a precise way using CRISPR/Cas9, that is, three SWEET genes encoding sucrose transporters that are being manipulated by Xoo for their own nutrition. Very small deletions of a couple of nucleotides in size, exactly at sites in the promoter regions of these genes that were targeted by bacterial effectors, resulted in disease resistance without hampering the functioning of the SWEET genes for the rice plants themselves. Such precise changes would be virtually impossible to achieve through classical mutagenesis. Spontaneous variants have been found in germ plasm and are helpful in identifying recessive resistances, but these resistances can more efficiently be stacked using gene editing. Various combinations of the targeted mutations were made in the background of two major rice varieties, each of which are cultivated on more than 10 million hectares. The lines with different combinations are thus adapted to confer resistance to different strains of the Xoo bacterium. In addition, tools were developed to monitor bacterial populations in the field, enabling to implement regionally adapted resistance combinations (Eom et al., 2019; Oliva et al., 2019; Varshney et al., 2019). This strategy is similar to that was proposed for the cisgenic late blight-resistant potato discussed earlier. In both cases, it is intended to ensure that the resistance traits remain available for IPM as long as possible.

The case of Bt crops

One of the earliest commercially successful types of transgenic crops provides resistance to insects by producing Cry proteins from *Bacillus thuringiensis* (Bt); they have become a major option for controlling important lepidopteran and coleopteran pests in maize, cotton and soybean. Bt's effectiveness depends on its insecticidal action, which is targeted to a specific, limited set of insect groups. This is in contrast to most chemical counterparts, which are broad-spectrum insecticides. Careful experimental research has shown that as a result of its narrow spectrum of action, insect predators and parasitoids are not harmed by Bt. At most, they are indirectly affected by lower prey quality due to the Bt action on the pest insect (Romeis et al., 2019). This would be comparable to the effects of disease resistance genes in the crop through R or S genes, as these also will impact pathogen populations. Regional suppression of pest populations has been indicated as contributing to Bt's effectiveness, which extends to growers not using Bt crops. The decreased use of broad-spectrum insecticides when growing Bt crops results in an increase in natural enemies in general, and it increases opportunities of applying biological control for other pests, as extensively reviewed by Romeis et al. (2019). In addition, a special strategy for delaying pest resistance was developed in the form of the high-dose refuge system (Carrière et al., 2016). More recently, a second option for resistance management has become available in the form stacking of different variants of Bt.

Thus, we conclude that faster introduction of combinations of resistances against plant diseases and pests offers opportunities to grow crops in novel IPM systems, with as direct benefit a lower input of chemical crop protection agents, and as indirect effect that the role of predators and biological control agents can become more important or that new cropping systems can be successfully implemented based on better insights in plant – pathogen or plant – pests – predator interactions. Such new cropping systems are also urgently needed, as pesticides are progressively being banned because of their negative environmental impacts.

Are genetic engineering and agroecology compatible?

We will answer the question whether genetic engineering and agroecology are compatible, based on a framework of four concerns (con and pro) that were brought forward in an extensive stakeholder-interaction and public debate that was organized around the DuRPh project on the cisgenic late blight-resistant potato (Haverkort et al., 2016).

First concern: novel hazards – In its Scientific Opinion of 2012, the EFSA Panel on Genetically Modified Organisms concluded that similar hazards can be associated with cisgenesis as with conventional breeding and that such hazards need to be assessed case-wise (EFSA Panel on GMO, 2012). In the case of late blight-resistant potato varieties, genetic engineering is applied within the gene pool that is used by classical breeding. A comparative approach, which considers whether similar results could be obtained by conventional breeding, has been to various extents accepted for simplifying regulation in several parts of the world, including the United States, South America, Japan and Australia. In the European Union (EU), still a strict regulation is in place, for which the European Court of Justice judged that it is applicable to genome editing as well. At present, the EU is calling for a study to gain clarity on problems in implementing its GMO Directive 2001/18/EC with regard to gene editing (http://eu-policies.com/news/eu-calls-study-justify-2018-gene-editing-legislation/). For now, given the current unpredictably lengthy and costly EU registration process of risk analyses, no breeding companies in Europe have started potato breeding programmes which include transferring resistance (cis)genes into their potato breeding programmes by means of genetic modification. For several African countries, it is unclear to what extent they will be able to develop the required legislation for growing GM crops, including potatoes with resistance genes from wild potato species (Ghislain et al., 2019).

The view of distinguishing genetic engineering within the gene pool from transgenesis also appears to be accepted among several interest groups and policymakers in Dutch society. In addition, it is the viewpoint of the present Dutch government (VVD, CDA, D66 en ChristenUnie, 2017) to facilitate the use of NPBTs such as CRISPR/Cas9, when these techniques are used within the classical breeding gene pool.

However, this may not solve all issues resulting from the problematic practical effects of regulation in the EU, as illustrated by the Bt example. At the moment, the potential IPM benefits of Bt are only possible in Spain and Portugal, as they grow varieties with the single event in maize (MON810) allowed for cultivation in the EU, even though Bt crops are widely cultivated elsewhere in the world.

Second concern: power issues – This concern hinges on the large investments needed for genetic engineering. These lend themselves to relatively strict intellectual property policies in the form of patents, instead of plant breeders' rights. Patents may prevent small breeding companies from access of the technology for improving varieties and to the use of such varieties by farmers. Patents have not prohibited economic success of the currently widely grown transgenic crops, as generally the higher technology costs were linked to increased revenues.

High investment costs and regulatory issues appear to have been a factor in limiting transgenic applications to two main traits, herbicide tolerance and Bt pest resistance, and initially only in major arable crops. However, more recently, applications have been brought on the market in smaller crops, such as a Bt vegetable crop, eggplant (brinjal) in Asia (Shelton et al., 2019). In the case of Bt brinjal, the technology was donated to a public–private partnership with the Indian company Mahyco under a USAID programme (Choudhary et al., 2014). In the DuRPh cisgenic potato example, the patent question has been addressed by providing non-exclusive licences. Wageningen University & Research has formulated the strategy that as many parties as possible should have access to the protected knowledge. In order to contribute to food supply and food security, a so-called Humanitarian Use License may be supplied as well. Under such license, developing countries may get access to available resistance genes to introduce into local varieties (https://www.wur.nl/en/Research-Results/Research-Institutes/plant-research/DuRPh/Approach-and-Background.htm).

In the case of gene editing, access to the technology is not yet clear. For CRISPR, basic patents are still disputed among two main inventors, UC Berkeley and Broad Institute, each of which have combined patents from other groups. The outcome of the dispute may actually be different between the United States and the EU. Major plant biotechnology companies and companies active in breeding of field crops have arranged for a non-exclusive license for agricultural crop. As the developments in this technology are very fast, the situation may change quickly, though. For instance, in October 2019, Anzalone et al. (2019) published their invention of ‘Prime editing’. They make all tools needed for this method freely available for research and non-profit applications through a website for DNA constructs, Addgene. Non-exclusive licenses are available for companies, including companies that aim to produce and sell reagents and kits to perform the method in any crop of interest. Thus, broad access to the technology may become a selling point when inventions in gene editing are brought to the market.

Third concern: an agroecological frame is missing – One comment on the DuRPh approach was that genetic modification can be seen as a continuation of the trend towards further industrialization of agriculture (Struik, 2014), suggesting that for this reason alone this application of cisgenesis does not fit together with agroecological principles. Giller et al. (2017) observed that industrialization was often not well defined and simply framed as a complete antithesis of smallholder agriculture and agroecology. Yet, this dichotomy will often not hold true. We interpret the term industrialization here as implying large-scale cultivations more depending on routine chemical inputs than on IPM. This concern relates closely to the question to be answered whether genetically engineered crops and agroecology will be compatible.

We will first address the concern in the context of agroecology as science. In general, applications of any technology, old or new, will not warrant sustainable farming if their products are not used within a GAP (Bonny, 2017; Lotz et al., 2018). Therefore, when a new technology such as genetic engineering produces innovative varieties, these should be combined with agroecology and grown under GAP as far as possible.

The currently grown transgenic crops can be perceived as fitting in industrialized settings, in the sense of large-scale cultivations more depending on routine chemical inputs than on IPM. This is, however, not a consequence of the technology of transgenesis but of how the cultivation of such varieties has been implemented. Indeed, examples of agroecological implementations exist as well. For instance, with regard to controlling the pink bollworm in cotton in the United States, Bt has been successfully combined with an approach of releasing sterile males (Tabashnik et al., 2010). Bt cotton was for the most part taken up successfully within small-scale farming in India and China, though this has been much debated. Sometimes results were mixed in smallholder agriculture. Important preconditions for successful introduction and particularly sustained success gathered from such cases are as follows: good quality seeds affordable through pricing or reliable credit facilities, optimal markets and logistics for harvests, availability of the trait in varieties suited to local conditions (water availability often an overriding problem in cotton cultivation) and access to extension for knowledge on cultivation according to good practice and IPM (Franke et al., 2011; National Academy of Sciences, Engineering, and Medicine, 2016). The same will be the case with Bt brinjal in Bangladesh. When discussing compatibility of particular technologies in local agronomies (including small-scale farming systems), not only economic but obviously also local biophysical conditions and social, institutional, political and cultural contexts should never be lost out of sight (Giller et al., 2017).

Above we have described examples in potato and rice in which gene editing was used to produce a set of disease-resistant varieties plus the tools to employ them in a refined form of IPM. Within the context of agroecology as science, we therefore conjecture that disease-resistant varieties generated using genetic engineering can fit very well in agrosystems in which GAP is pursued.

Discussing this question in the context of agroecology as social movement: As a social movement, agroecology is difficult to define. There is a lot of variation between countries with regard to how agroecology developed as a movement. For example, in the United States, agroecology was first established as science, then was used to address environmental problems from intensive agriculture and then a knowledge basis was developed including traditional practices that laid a foundation for movements to promote environmental and social sustainability. In Brazil, the movement started from traditional practice to address problems with modernization and rural poverty, and later on, agroecological science became involved by taking up participatory approaches and education programmes. In Brazil, agroecology was recognized under the umbrella of organic farming in a law, but one of the movements preferred local partnerships with consumers above formal organic certification and markets (Wezel et al., 2009). In a comparison between organic agriculture and agroecology, Migliorini and Wezel (2017) showed many similarities, with the most obvious difference being the strict observance of rules (stronger institutionalization) in organic agriculture, which includes the rejection of the use of mineral fertilizers and GM crops. The HLPE report concluded that most agroecological proponents perceive GM as not in line with their ecological principles, democratic governance and sociocultural diversity. Yet some see possibilities to address issues case-by-case, while the HLPE report also calls for better connections between local agroecological knowledge and formal science for bridging gaps with developing and transferring technology (HLPE, 2019). Thus, the question of whether agroecology that incorporates crop varieties made with genetic engineering while optimally applying ecological principles in farming, could work for movements, will depend on how the members of an agroecological movement consider all aspects of sustainability, as discussed earlier, and to what extent they see themselves as connected to the community of organic farmers that produce products according to IFOAM rules, which exclude applications of genetic engineering (IFOAM EU Group, 2015). At the moment, most farmers are looking for ways to make their practices more environmentally friendly, but only a minority does so under organic rules.

The DuRPh cisgenic late blight-resistant potato can be taken as a good example of the diversity in response from stakeholders. The researchers intensively interacted with the public at large and specific groups such as students, with policymakers, political parties, farmers and other stakeholders in the product market chain, as well as the scientific community during the research programme. Field trials were open to the public on yearly open days, during which various public discussions and debates were held about environmental and socio-economic effects. Dutch organic farmers discussed at the start of the research programme whether cisgenic late blight-resistant potato varieties would fit into their production systems. It was concluded that worldwide standards of organic agriculture do not allow genetic engineering or products derived from genetic engineering. In this context, probably the most pronounced argument, formulated in an ethical value-frame, is that breeding at DNA-level, instead of a whole-plant level, violates 'integrity of life' as described in the concept of naturalness (Nuijten et al., 2017; Struik, 2014). With regard to naturalness, Andersen et al. (2015) suggest that a lack of a shared understanding of the terms integrity and naturalness has contributed to the current impasse in the debate about using technologies that could narrow the yield gap between organic and conventional farming practices. A better shared understanding of such terms may also be helpful for the community of agroecological movements. However, as there are many ethically (deontological) loaded aspects attached to these terms, it is difficult to envisage a reconciliation. Biotechnologists, for example, may see genetic engineering as putting to use natural processes, such as *Agrobacterium* infection or CRISPR-enabled targeted mutations that can also occur naturally, in other words cooperating with nature to regain natural traits from wild ancestors of crops providing disease resistance, whereas some organic organizations may perceive the resulting varieties as a product of manipulating nature and so utterly unnatural compared to putting to use ecological principles to avoid plant disease.

The (official) organic movement has also put forward other values that are also important for agroecological movements, such as the precautionary principle (related to the aforementioned first concern) and socially sensitive approaches (Lammerts van Bueren et al., 2008; Nuijten et al., 2017), related to the second concern. Greenpeace acknowledged the DuRPh-project because of the advantage of the newly developed molecular markers for resistance genes in potato to be used in organic and conventional breeding (personal communication by Herman van Bekkem, Greenpeace campaigner for sustainable agriculture in The Netherlands, 4 September 2015). In their official communication, however, Greenpeace only stresses that this type of research should not leave the laboratory because of the precautionary principle (https://www.greenpeace.org/nl/landbouw/). On the other hand, several other environmental groups, farmers' organizations and political parties reacted in general positively or with a positive criticism. The Dutch green political party GroenLinks stated in its election programme that cisgenic crops should be allowed to be grown under strict conditions (GroenLinks, 2017). Forerunner farmers linked to the Dutch foundation 'Skylark' ('Veldleeuwerik' in Dutch strive to realize a future-proof and healthy food production, using innovation and knowledge sharing and centring on stewardship and a responsible approach of nature, soil, air, water and habitat (https://veldleeuwerik.nl/en/). In this approach, a breeding toolbox should also contain NPBTs including CRISPR/Cas to activate, insert and combine resistances against diseases in crop varieties (personal communication, Hedwig Boerrigter, director Foundation Skylark, 15 April 2019).

Fourth concern: The costs of abandoning new technology in agriculture – Already, during the 10-year programme, many Dutch potato farmers indicated and still today indicate their great interest in growing cisgenic late blight-resistant potato varieties in their crop rotation to be able to significantly reduce fungicide inputs. The Dutch farmer organization LTO Nederland considers new breeding technology as an essential tool for systems approaches based on IPM to make arable farming less dependent on chemical crop protection (LTO Nederland, 2019). Economists have calculated that the costs of refraining from genetic engineering applications can be considerable. For instance, China has approved Bt rice in 2009 but has not started to cultivate Bt rice varieties since then; this delay was estimated as coming with a cost of 12 billion US dollar (Jin et al., 2019). In the case of controlling the western corn rootworm in maize, several options exist that vary in profitability with local circumstances, including crop rotation, but Bt would be one of the best contributions to a management system for European farmers (Dillen et al., 2010). Next to this view based on costs, there is also an ethical side to abandoning technology when it is available. The Danish Council on Ethics (2019) evaluated the ethical arguments and came to the conclusion that gene technology and agriculture are compatible and, moreover, considering the serious threats for agriculture, that it would be unethical to turn down the use of technology, unless there are good reasons for doing so.

Conclusion

Various scientific disciplines, including agronomy, classical breeding, plant science and socio-economics can be considered as being in the heart of agroecology. We conclude that genetic engineering and agroecology can certainly be compatible in the context of agroecology as science, when applied to make crops less vulnerable to pests and diseases, and when the cultivation practices of varieties produced with this technology, are optimized to be combined with IPM practices. In cases like the DuRPh late blight-resistant potato and bacterial blight-resistant rice where genetically engineered varieties are even essential for successful implementation of IPM, genetic engineering and agroecology will become interdependent, placing genetic engineered varieties at the heart of agroecology.

Within the social movement context, genetically engineered varieties may also fit in or be welcomed if they include traits that contribute to successful IPM schemes and are socially benign. Whether they actually fit together will, however, vary across movements, as for instance shown in the potato DuRPh case. Many movements and actors are concerned with the sustainability of agriculture and are working, each in their own way, to stimulate a transition to a sustainable agriculture. It will depend on the various angles prioritized by movements whether specific genetically engineered traits may be found acceptable. We propose that some may be considered reconcilable as a result of a respectful discussion. For instance, power issues around technology may be difficult to resolve as they are part of a complex societal debate on distribution of revenues between all stakeholders (breeders, farmers, retail, consumers) and relate to discussions about monopolies as well. However, institutional arrangements may be put in place to address power issues and competition laws exist that can prevent or break up undesirable monopolies. Arrangements can be developed in discussion between stakeholders, as in the case of Bt brinjal. There may always remain cases, for example, for local or traditional varieties, for which a technology may not be feasible if only because costs may be too high.

The DuRPh potato case clearly demonstrates a range of different deontological angles with respect to ‘naturalness’ and ‘integrity of living organisms’ with the NPBT cisgenesis among groups of stakeholders. Deontological arguments such as naturalness appear more difficult to reconcile, as they relate to deeply felt ethical or cultural concepts. In the end, not everyone may choose to welcome genetically engineered varieties, but a step forward will be when everyone can make an informed choice and when these choices could coexist together in a respectful manner.

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