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Opinion

Accelerating the Domestication of New Crops: Feasibility and Approaches

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The domestication of new crops would promote agricultural diversity and could provide a solution to many of the problems associated with intensive agriculture. We suggest here that genome editing can be used as a new tool by breeders to accelerate the domestication of semi-domesticated or even wild plants, building a more varied foundation for the sustainable provision of food and fodder in the future. We examine the feasibility of such plants from biological, social, ethical, economic, and legal perspectives.

Development of New Crops

The green revolution of the mid-20th Century marked the beginning of a dramatic increase in agricultural yields. The revolution was fueled by high-intensity agriculture, based on high-input and high-output crops, which vastly increased crop output per area. The beginning of the 21st Century has seen an emerging discussion of the need for a second green revolution because issues with high-intensity farming, such as eutrophication and loss of biodiversity, have emerged [1–4]. This second wave of the green revolution is focused to a larger extent on environmental sustainability, low input, and increased nutritional value.

Among the >300 000 plant species currently in existence, fewer than 200 are commercially important, and only three crops – rice, wheat, and maize – account for the majority of plant-derived calories and protein consumed by humans [5–8]. One approach taken to bring about the second wave of the green revolution is to focus on increasing crop diversity in efforts to promote sustainable agricultural systems adapted to demanding environments [9–11]. This approach involves focused breeding of diverse variants of the main crops cultivated today and, more recently, the domestication of neglected, semi-domesticated, and wild plants [12].

Current breeding programs aim to include more species with desirable traits in the list of domesticated plants. Several nitrogen-fixing and neglected legumes may have the potential to be cultivated as crops that can grow on low-input and low-nutrient soils, and often have potentially high nutritional value (e.g., [13]). Compared to present-day annual crops, perennial plants typically have more-advanced root systems that not only allow them to be less dependent on fertilizer and water supply but also contribute to preserving soil quality. Thus,

Trends

A second wave of the green revolution is underway that focuses on environmental sustainability, low input, and increased nutritional value.

Of the more than 300 000 plant species that exist, less than 200 are commercially important, and three species – rice, wheat, and maize – account for the major part of the plant-derived nutrients that humans consume.

Plants with desirable traits, such as perennials with extensive root systems and nitrogen-fixing plants, are currently being domesticated as new crops.

Recent years have given rise to the use of CRISPR/Cas9 for genome editing in plants. The method allows mutations to be generated at precise locations in genes that can lead to knockout or knockdown of protein activity.

Several traits in crops that were crucial for their domestication are caused by mutations that can be reproduced by genome-editing techniques such as CRISPR/Cas9, offering the potential for accelerated domestication of new crops.

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domestication of perennials, and attempts to convert annuals into perennials, are in the breeding pipeline [14,15]. In addition, efforts to domesticate neglected or orphan crops, such as quinoa [16] or amaranth [17], have the potential to create crops that are able to thrive in environments that are suboptimal for the main crops currently cultivated.

During the process of crop domestication, humanity has for thousands of years selected plants with improved traits such as easy harvest and high yield. A variety of causative changes to the plant genomes have now been associated with these domestication events. Many of these genetic alterations are complex, but, as our understanding of domestication events expands, an increasing number of so-called **domestication genes** (see Glossary) are being associated with domestication traits. These represent single genes that have a marked effect on a domestication-associated phenotype. In the present context we define domestication genes as genes that have made domestication of a wild plant species possible. Different types of mutations have been identified. Some mutations lead to cis-regulatory changes that influence the spatiotemporal expression pattern of a gene, and others result in amino acid changes or a shortened transcript [18]. Many of these mutations result in complete or partial loss of function of the domestication genes. For example, harvest of seeds has been facilitated by neutralizing genes that promote their release from the plant (other examples are provided in Table 1).

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Table 1. Examples of Genes Important for Crop Domestication Where Mutations Creating Similar Loss of Function Could Be Achieved By Genome Editing

Crop	Gene	Function	Trait	Mutation	Refs
Barley (Hordeum vulgare)	Btr1/2	Unknown	Brittle rachis	Shortened transcript[a]	[83]
	Vrs1	Transcription factor, HD-ZIP	Inflorescence structure	Shortened transcript	[84]
Maize (Zea mays)	Tga1	Transcription factor, SBP	Inflorescence structure	Amino acid change[b]	[85]
	ZmSh1-1/1-5	Transcription factor, YABBY-like	Seed shattering	Structural change/ regulatory change[c,d]	[86]
Rice (Oryza sativa)	LABA1	Cytokinin-activating enzyme secreted peptide	Inflorescence structure	Shortened transcript	[26]
	RAE2	EPF/EPFL family	Inflorescence structure	Shortened transcript	[27]
	sh1	Transcription factor, YABBY-like	Seed shattering	Regulatory change[d]	[86]
	sh4	Transcription factor, Myb3	Seed shattering	Amino acid change[d]	[87]
	qSH1	Transcription factor, BEL1-type	Seed shattering	Regulatory change	[88]
	PROG1	Transcription factor, C2H2-type	Plant structure	Amino acid change	[89,90]
Sorghum (Sorghum bicolor)	SbSh1	Transcription factor, YABBY-like	Seed shattering	Shortened transcript/ regulatory change[d]	[86]
Tomato (Solanum lycopersicum)	Style2.1	Transcription factor, HLH	Inflorescence structure	Regulatory change	[91]

[a]Shortened transcript indicates deletion of basepair(s) that results in a premature stop codon.
[b]Amino acid change indicates single base-pair changes that have altered the coding sequence.
[c]Regulatory change indicates substitutions or deletions of bases in gene regulatory regions, and which have resulted in changes of expression levels or pattern.
[d]Convergent domestication demonstrated.

Approaches To Mimic Domestication Events

A goal of new crop domestication is to mimic the domestication events that have occurred throughout history, such as achieving shatter resistance. The knowledge gained from studying domestication events in model crops can be translated into breeding of related wild plants. This process requires detailed knowledge of the genome for both the model and target plant. The genomes of an increasing number of plant species have already been sequenced or are in process of being sequenced, including the genomes of model plants, crops, **underutilized crops**, and wild plants [19]. The more closely related species are, the easier it is to translate genetic knowledge from one plant to another [20]. Thus, as more genome sequences become available, it becomes easier to understand and use genetic information for plants currently being domesticated and to identify orthologs of known domestication genes. The genomes of several plants that are currently being domesticated, including intermediate wheatgrass (*Thinopyrum intermedium*) [21], field pennycress (*Thlaspi arvense*) [22], and apios (*Apios americana*) [13], are being sequenced with the aim of creating genomic maps for these plants to aid their domestication.

Once a gene has been shown to contribute to a domestication trait in a given plant, a few approaches can be taken to mimic domestication by targeting orthologs of this gene. Frequently, mutagens are used to create random mutations, and specific mutations in the desired domestication gene can subsequently be identified. Weeping rice grass (*Microlaena stipoides*) is an Australian wild relative of rice in which several orthologs of rice domestication genes, including *qSH1* and *sh4* (genes that contribute to the shatter-resistance trait, Table 1), have been identified [23,24]. Following mutagen treatment, mutations were identified in these genes that resulted in improved shatter resistance [24]. Using random mutagenesis, the *Btr1* gene in a wild barley accession was mutated, and this resulted in plants that resembled domesticated barley, with a non-brittle rachis [25]. Thus, a loss-of-function mutation in a single domestication gene can indeed result in a domestication phenotype.

Another approach taken is to silence genes by RNAi and thereby lower the expression of the domestication gene. In the case of an introgression line of rice with long, barbed awns, lowering the expression of the *LABA1* gene made the awns shorter and smaller to resemble the domesticated phenotype [26]. Reducing the expression of another domestication gene in rice, *RAE2*, resulted in a similar phenotype [27]. RNAi has also been used to silence genes involved in fatty acid synthesis (*FAD2* and *FAE1*) in the wild plant field cress (*Lepidium campestre*), resulting in a substantial increase in oleic acid content and improved seed oil quality [28].

Accelerating Domestication Using Genome Editing

Strategies based on the power of traditional breeding have been devised for domestication of wild plants [12,29]. Recently, **genome-editing** techniques such as **CRISPR/Cas9** have been suggested as a possible method to accelerate domestication [15,30]. Targeting genes for accelerated domestication by genome editing involves reducing or abolishing gene function based on existing knowledge of the molecular function of the target gene. This requires that the genome of the target plant is sequenced to identify genes that are orthologs of known genes controlling domestication traits in related plants. The use of CRISPR/Cas9 is currently limited to cases where a loss-of-function mutation can lead to the domestication phenotype and where a transformation protocol is available for the chosen plant [30].

CRISPR/Cas9 has successfully been used to create mutations in a large number of genes in diverse plant species, and the number of plant species with genomes that have been edited is growing rapidly [31]. Two recent examples illustrate the potential for improving current crops. In rice (*Oryza sativa*), CRISPR/Cas9 has been used to create loss-of-function mutations in the

Glossary

CRISPR/Cas9: clustered regularly interspaced short palindromic repeats/CRISPR-associated protein 9. A genome-editing tool modified from a prokaryotic immune system. Mutations occur at the genome location corresponding to the designed guide RNA, where double-strand breaks are induced by the action of Cas nuclease.

Domestication gene: a gene responsible for crop traits that are essential for the domestic use of the crop. During early domestication, mutations in these genes were selected for.

Genome editing: the insertion, deletion, or replacement of a segment of DNA in the genome of an organism by use of site-directed nucleases, which are proteins able to cause DNA strand breaks at a specific genetic sequence. Normally refers to CRISPR/Cas9, transcription activator-like effector nucleases (TALENs), and zinc-finger nucleases.

Underutilized crop: a covering term for crops that are currently not being used to their full potential for various reasons.

yield-related genes *Gn1a*, *GS3*, and *DEP1*, which resulted in more grains, larger grains, or denser and erect panicles, respectively [32]. In cucumber (*Cucumis sativus*), the technology has been used to generate virus-resistant plants by disrupting *eukaryotic translation initiation factor 4E* (*elF4E*), a host gene required for the propagation of plant RNA viruses [33]. Protocols are now being developed to edit the genomes of several plant species in the process of becoming domesticated. For example, CRISPR/Cas9 technology has recently been used on a dandelion species (*Taraxacum kok-saghyz*) with the potential to produce rubber [34].

Domestication genes in current crops provide obvious targets for the domestication of new plants. Field pennycress (*Thlaspi arvense*) is a potential oilcrop that can now be transformed [22,30]. *Arabidopsis thaliana* is closely related to pennycress, and multiple loss-of-function mutant phenotypes have been characterized in *Arabidopsis*. It is likely that desirable phenotypes can be copied by mutating the ortholog in pennycress [22,30]. Shatter-resistance genes have already served as targets for domestication of *M. stipoides* [24]. Because awnlessness is a trait of domesticated rice, directly editing newly identified genes important for awn development in rice (*LABA1* [26] and *RAE2* [27]) might further accelerate the domestication of *M. stipoides*.

Thus, genome-editing techniques promise to be a useful tool in the plant breeding toolbox when domesticating new crops. Genome editing might be used to rapidly modify undesirable traits in plants and may thus dramatically accelerate the process of domestication. For instance, this approach could be used to reduce the plant content of secondary metabolites, which are often toxic (Box 1). Even wild plants may be selected for domestication by genome editing, thus raising questions not only about the use of genome editing as such but also about wild plant domestication. We focus here on the feasibility of using genome-editing techniques to accelerate the domestication of wild plants (Figure 1) from social, ethical, economic, and legal perspectives.

Social Concerns

Using genome editing to accelerate domestication for new crops would likely test ethical and legal boundaries, and thus give rise to public concerns. These concerns are broadly likely to resemble those raised for genetically modified (GM) crops [35]. The purported benefits of accelerating domestication by genome editing, including protecting soils, improved nutritional value, and new products, must be weighed against the likely ethical concerns of consumers and civil society (*cf* Palmgren *et al.* [36] in relation to the genome-editing technique). The

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Box 1. Solving the Toxicity Problem

A major factor that could prohibit potentially nutritious wild plants from being consumed as feed or fodder is their content of toxic secondary metabolites. Different plants have developed distinct batteries of specific compounds that protect them against hostile organisms. Previously, a gene-silencing approach was used to target genes involved in the biosynthesis of a toxic metabolite [92], but genome editing could potentially provide stable elimination of toxic substances in a single generation, provided that genes in the biosynthetic pathway have been identified. However, completely eliminating toxic secondary metabolites may render plants vulnerable to herbivory [93,94] or weaken them because the metabolite may have additional roles in plant metabolism [95]. Secondary metabolites may be synthesized in one part of the plant and subsequently transported to other parts of the plant. Because specialized transport proteins are essential for the transport of secondary metabolites [96], specifically targeting the genes encoding such transporters could eliminate toxins only from the intended edible parts of the plant, and not from other tissues where they impart general protection to the plant [97]. For example, field pennycress (*Thlaspi arvense*) is high in glucosinolates, making it toxic for consumption [98]. Genes have been identified in field pennycress that are orthologs of *Arabidopsis GTR1* and *GTR2* [22,99], and these genes are known to be essential for transporting glucosinolates to the seeds [96]. Likewise, in rapeseed (*Brassica napus*), mutations in the related gene *BnGTR2* are associated with low glucosinolate content in the seed [100]. *GTR*-like genes in Brassicaceae therefore emerge as mutational targets for the production of seeds with low glucosinolate content. The legume lupin (*Lupinus muralis*) has seeds with protein levels comparable to those of soybean, but lupin domestication has been hampered by the content of toxic quinolizidine alkaloids in its seeds [101]. These alkaloids are transported from the leaves to the seeds [102], and identifying the responsible transporters would likely provide a handle for accelerating the domestication of this species.
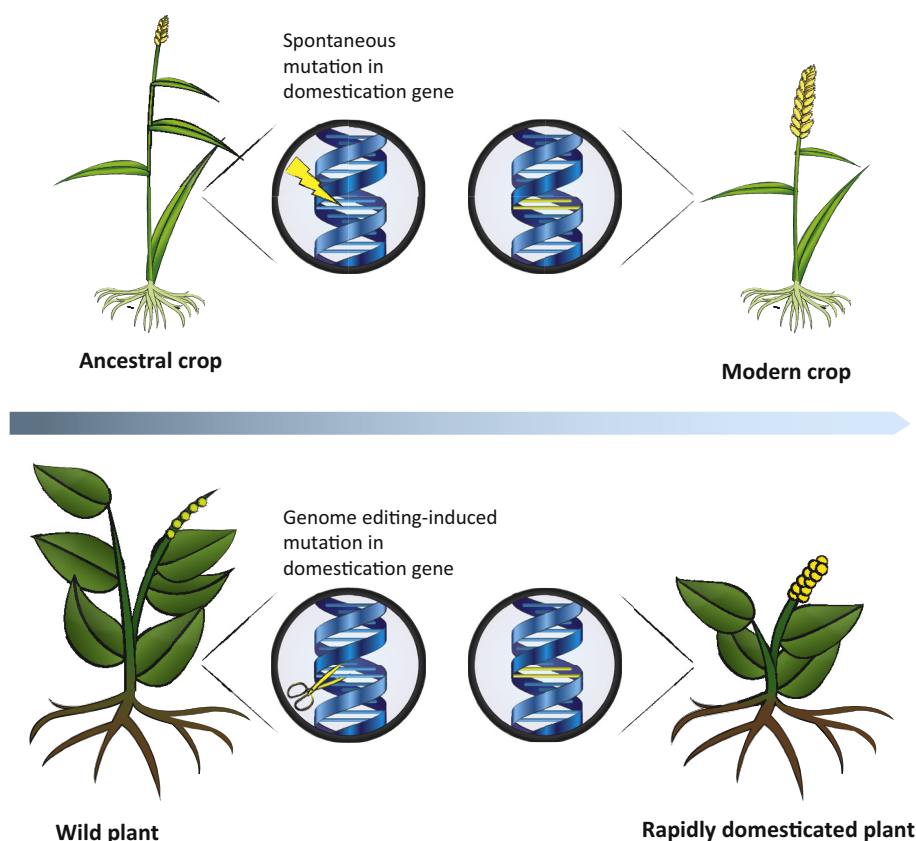
Figure 1. Accelerating the Domestication of Wild Plants. During the domestication of ancestral crops, plants carrying spontaneous mutations in domestication genes were selected for. The same genes can be targeted in wild plants by genome editing, resulting in a rapidly domesticated plant.

concerns raised in relation to GM crops include (i) harm to human health, (ii) damage to the environment, (iii) excessive dominance of specific crops owned by commercial players, (iv) negative effect on farming traditions, such as undermining farmer autonomy, and (v) the unnaturalness of technological interference [37].

When applying these concerns to domestication by genome editing, concern (i) above may be expressed in terms of the potential toxic effects of the plants developed, given the uncertainty of the outcome of gene editing. Concern (ii) may be expressed in terms of fear of potential interbreeding with wild plants and/or release into the non-cultivated environment. The relevance of (iii) and (iv) likely depends on the manner in which intellectual property rights of these newly domesticated plants are managed and on the use of benefit-sharing schemes. Concern (v) is likely to persist as long as people have different opinions about humanly instigated changes to nature, especially because naturalness is an ambiguous notion [38] and the perception of the value of naturalness varies widely [39].

Social feasibility goes beyond allaying public concerns about the harmful effects, risks and uncertainty of domesticating plant by genome-editing techniques. It also concerns issues such as autonomy at the consumer level, in the sense of freedom of consumer choice, which in turn is linked to the discussion about labeling of products and the manner in which other moral concerns, such as who bears the risks, are handled. Hence, the fundamental tension in

biotechnological debates between different concerns, for example, between autonomy and beneficence, is prone to persist in relation to newly domesticated plants.

Ethical Views

Established ethical theories, including Kantianism, contractarianism, consequentialism, and virtue ethics, all imply that promoting good consequences and avoiding harmful ones are crucial ethical concerns [40]. They also imply that the distribution of benefits and harms across humans and other sentient beings is important. Domestication is surely potentially beneficial, assuming that it does not pose significant risks to humans or animals. Derived distributional effects of introducing a new domesticated crop will depend on many factors, such as the legal framework and the capacity and willingness to invest in new technology, but domestication as such does not raise distributional concerns. If this is so, the use of genome editing for domestication is ethically feasible according to dominant ethical views. However, similar debates about GM organisms (GMOs) indicate that this argument is controversial because it ignores considerations of respect for nature and public perception of genome-editing techniques.

Biocentrism is the view that non-sentient organisms (such as plants) have an independent moral standing, in other words morally relevant interests, because they evolve for self-preservation and reproduction (see e.g., [41–43]). However, even though domestication could weaken wild plants, for example by reducing the ability of the plant to shatter its seeds, domestication might not harm them because other measures would be installed to secure seed transfer to the next generation if the plant were to be cultivated. It is therefore not clear whether domestication is harmful or damaging to the overall 'interests' of wild plants.

In contrast to a biocentric focus on individual organisms, holist ecocentrism attributes moral standing to entire ecosystems, and values the preservation of ecosystems. To oppose domestication, adherents of ecocentrism would need to explain why agricultural ecosystems featuring plants that were developed by domestication are less intrinsically valuable than are those that were not. In absence of such an explanation, holist ecocentrism supports the view that domestication is ethically feasible provided that the environmental risks are low.

According to some ecocentric views, only wild ecosystems, in other words ecosystems that lack human intervention, are considered valuable [44]. Domestic plants and animals do not contribute to the value of ecosystems, but are seen as humanity's overextension into the wild environment: 'From the perspective of the land ethic, a herd of cattle, sheep or pigs is as much or more a ruinous blight on the landscape as a fleet of four-wheel drive off-road vehicles' [45]. From this perspective, even domestication *per se* could have disvalue. Nonetheless, domestication by genome editing would only be ethically unfeasible if the relevant alternatives are less disruptive to wild ecosystems.

Whereas transgenic plants ('classical' GM plants) typically exhibit gain of function from an introduced gene, genome editing typically would involve deleting a function. This difference may be important for public perception. However, public opinion is hard to predict. If newly domesticated plants are presented as covert GMOs, and thus associated with health and environmental risks, unnaturalness, and adverse socioeconomic consequences (*cf* [46]), public opinion is likely to be negative.

It is important to stress that the ethical feasibility of domestication by genome editing is not simply a matter of favorable public perception. An influential tradition in political theory views ethical feasibility as a matter of democratic legitimacy defined as what affected parties could rationally reject. If domestication by genome editing is beneficial and non-risky, if this is at all

possible to establish and if the public perceives it as such, then following the pattern of the public GMO skepticism, the main remaining objection may be that of unnaturalness. However, as pointed out in numerous discussions, arguments related to unnaturalness are riddled with difficulty (e.g., [38,47]). Following this tradition, most theorists would therefore consider views about naturalness as private matters that could influence individual consumer choices, but do not have a bearing on ethical feasibility. Another tradition in political theory views democratic legitimacy as procedural. An outcome (a policy or institution) is legitimate if stemming from the correct procedure, typically one that includes deliberation and voting (e.g., [48]). Accordingly, domestication by genome editing would be democratically legitimate if adopted through the right procedure, although a legitimate outcome could also be the rejection.

Possibilities for Farmer and Market Acceptance

From the perspective of farmers and breeders, research into enhancing wild and underutilized species through genome editing is limited. Underutilized crops are less profitable and hence less attractive to farmers than most commonly cultivated crops. Seed companies do not develop and market underutilized crops or wild plants, and thus the dominance of highly developed crops is reinforced [8]. Moreover, there may be apprehension among producers about potentially problematic characteristics of newly domesticated crops, such as poor storability properties [49]. However, the emergence of newly domesticated plants would change this picture if these plants have enhanced properties, such as reduced sensitivity to growth conditions, optimized characteristics for local environments, or improved storage properties [50], provided that these features will induce farmers to switch crop and plant choices.

From the perspective of the consumer, in developed countries there is an increased interest in the health attributes of foods and a desire to eat more 'natural' foods, including unprocessed, organic, and traditional foods, as well as exotic crop varieties such as the yam bean (jicama – *Pachyrhizus* spp.) from Mexico [51,52] and quinoa [53], with quinoa obtaining a noticeable market share [8,51].

Nevertheless, if new properties are obtained through some form of novel technology, typically GM, some consumer resistance must be expected. Demand is likely to be affected by the legal classification of such crops [7,36,54]. The existing literature indicates that consumers prefer non-GM food to GM-based foods (e.g., [55,56]). However, studies suggest that consumers are less opposed to some varieties of GM-based products, such as those with improved functional properties, although consumers still have a preference for non-GM products [57,58]. Moreover, consumers with a positive perception of organic foods are also often those who are most opposed to applying GM technologies to food production [59–61]. Demand can be expected to vary not only between types of consumers but also between regions and countries, partly for regulatory reasons [55,56]. However, the GM-skeptical European region does not prevent more GM-friendly regions from taking advantage of these crops, which is relevant if the goal is to create or expand the market share of newly domesticated plants.

Further, some constraints may be anticipated owing to failures in markets, such as lack of information [62]. For example, familiarity and knowledge of the supply (farmers and breeders) and demand (consumer) of potential wild plants suitable for domestication by genome editing and consumption are likely to exist among farmers and consumers in limited areas, and to be embedded in local subsistence activities [50].

Potential benefits from domestication initiatives using genome editing may come in the form of so-called public goods (i.e., goods that are both non-excludable and non-rivalrous, such as environmental protection through reduced use of pesticides or fertilizer) and private goods

(i.e., goods that are excludable and rivalrous such as more tasty or storable foods). Private benefits arising for consumers will be reflected in product prices and hence provide an incentive for the market to drive domestication by genome editing. If the benefits are mainly in form of public good, public intervention to enhance domestication may be necessary because such benefits will not be reflected in the prices of the final products. Thus, to the extent that private benefits are not enough to induce innovation in domestication of plants with favorable associated public good benefits, public intervention in the form of innovation and regulatory support may also be called for.

Current Legal Status

Legally, domesticated species refer to 'species in which the evolutionary process has been influenced by humans to meet their needs' [63]. International regulations essentially promote the domestication of wild plants even if genome editing is used, but existing legal uncertainties may affect the potential of this technology. Two aspects pertaining to the legal feasibility of domesticating wild plants by genome editing need to be addressed. First, what types of wild plants should be domesticated? Second, what is the role of genome editing in the domestication process?

In terms of wild plants, several international treaties acknowledge the importance of biodiversity, with the Convention on Biological Diversity (CBD), the Nagoya Protocol (NP) and the Treaty on Plant Genetic Resources for Food and Agriculture ('Plant Treaty') being of relevance here (Box 2). The CBD recognizes the sovereign rights of States over their genetic resources within their territories, and the Plant Treaty provides a specific focus on conservation and sustainable use of plant genetic resources for food and agriculture. Several major plant species, for example *Oryza sativa* (rice), *Triticum aestivum* (wheat), *Hordeum vulgare* (barley), and *Manihot esculenta* (cassava), are within the scope of the Plant Treaty. Nevertheless, only 35 food crops and 29 forage crops are listed in Annex I of the Plant Treaty, and wild relatives of the major species are not covered [64]. However, because the CBD and the NP have a broader scope, it is reasonable to believe that the majority of wild plants, excluding those covered by the Plant Treaty, may fall under the scope of these treaties [65].

Both the NP and the Plant Treaty provide access and benefit-sharing (ABS) regimes to facilitate access and fair and equitable sharing of the benefits of genetic resources. Clear and enforceable assignment of property rights is crucial for developing new crop varieties based on domestication, as implied by the ABS rules [66]. However, lack of legal clarity might undermine the potential of domestication of wild plants. For instance, the domesticated wild plant species that were introduced before the enactment of the NP are arguably not subject to the compliance rules of the ABS regime. The Vienna Convention, which interprets international treaties, states that an international treaty 'does not have retroactive effect unless the parties agree otherwise' [67]. Regarding those species that have already been collected or stored in gene banks or botanical gardens, but have been found to be of potential value after the NP was enacted in 2014, it is an open question if domestication of such species will be subject to the current ABS regime. The answer will depend on clarifying what constitutes 'true access' and when 'true access' happens [68].

With regard to the role of genome editing in the domestication process in the EU, it should be noted that both the International Convention for the Protection of New Plant Varieties (UPOV Convention [69]) and EU Regulation {Council Regulation (EC) No 2100/94 [70]} provide for exemptions to breeder's rights. The breeder's exemption enables breeders to use plant varieties for the subsequent breeding of new plant varieties, and the breeders are broadly defined to include farmers, researchers, public institutes, and private companies. Furthermore, the UPOV Convention makes no restriction on the techniques used to breed a new plant

Box 2. Domestication of Wild Plants and Relevant International Treaties

Convention on Biological Diversity (CBD) and Nagoya Protocol (NP)

The CBD (adopted in 1992, 196 Parties [63]) is an international agreement with three objectives, including the conservation and sustainable use of biodiversity, as well as fair and equitable sharing of the benefits. The NP (adopted in 2010, 73 Parties [103]) is a supplementary international agreement to CBD to provide a legal framework for the access and benefit-sharing regime (ABS) of genetic resources.

The International Treaty on Plant Genetic Resources for Food and Agriculture ('Plant Treaty')

The Plant Treaty (approved in 2001, 141 Parties [104]) is an international agreement to provide a multilateral system of ABS that covers the plant genetic resources for food and agriculture that are listed in its Annex I.

International Convention for the Protection of New Plant Varieties (UPOV Convention)

The UPOV Convention (adopted in 1961, latest revision in 1991, 74 Parties [69]) is an international agreement that grants breeders exclusive control of a new plant variety as a protected variety. However, it also states that the breeder's exemption allows subsequent use of a protected variety by other breeders for developing new varieties.

Relationship between International Agreements

The UPOV Convention provides for breeder's exemption, which does not necessarily oppose the ABS rule introduced by the NP because the NP does not prohibit the breeder's exemption but instead renders utilization of a plant variety subject to the ABS rules. Thus, compatibility between the UPOV Convention and the NP can be achieved.

The NP does not necessarily affect the specialized international ABS regimes. Therefore, the Plant Treaty as a *lex specialis* to the NP shall apply to the plant genetic resource covered by its Annex I. The comparison (Table I) shows that the Plant Treaty provides more legal certainty, less documentation, and lower transaction cost [76].

Table I. Comparison of ABS rules between the Plant Treaty and the Nagoya Protocol

	Plant Treaty ABS Rule	Nagoya Protocol ABS Rule
Type of system	Multilateral system of multiple providers and users	Bilateral system of individual provider and user
Type of agreement	Standard material transfer agreement	Individual case-by-case agreement
Mandate	Specific mandate on plant species in Annex I	Broader mandate on genetic resources
Authority	Unique governing body of the Plant Treaty	Individual national focal points
Transaction cost	Low cost for user and provider	High cost for user and provider
Documentation	Less documentation	More documentation

variety, and thus genome editing should not *per* se be excluded. In fact, it seems that the breeder's exemption can potentially benefit domestication by genome editing, although it may arguably not apply to a new variety essentially derived from another variety.

The breeder's exemption was claimed by the European plant breeders [71,72] to challenge the NP and EU Regulation 511/2014 [73] before the European Court of Justice in 2014. The compatibility issue between the UPOV Convention and the NP could arguably be solved and the use of wild species for breeding can be undertaken under bilateral agreements between providers and users according to the ABS regime [74]. However, the difficulties of identifying any new plant variety and the origin of its genetic resources require extensive documentation and the high transaction costs of compliance with ABS rules under the NP. These burdensome factors may undermine the 'open resource' system for plant breeding in the EU, although these issues seem to be better addressed by the Plant Treaty (Box 2) [75,76].

Moreover, as a technique used in conventional breeding process, mutation of plant genes is excluded from GMO regulation by a derogation provided by Annex IB of the Directive 2001/18/EC [77]. Similarly, breeding by genome editing results in mutations but does not create any new combination. However, it arguably involves the use of recombinant nucleic acid molecules. For this reason, it is uncertain whether the use of genome editing for domestication will be excluded from the current EU GMO legal framework [54].

Concluding Remarks and Future Perspectives

As described in this review, the domestication of new crops offers the prospect of expanding crop diversity and generating increased environmental sustainability, and this process is likely to be accelerated by employing genome-editing techniques. The growth of the crops we presently depend on for food is also limited by environmental stresses and hostile organisms, hazards that are only likely to be aggravated by predicted climate changes [78–80]. Nonetheless, natural biodiversity is vast, and different plant species have developed tolerance to a range of challenging environments, including the desert, seawater, and tundra, and to the myriad of animals and microbes that threaten to consume them. One could ask why we do not take better advantage of this diversity [81]. For example, if the climate is too cold for wheat to grow, why do we not cultivate a cold-tolerant relative of wheat instead? Indeed, the grains of the cold- and salt-tolerant lyme-grass (*Elymus arenarius*) were previously collected as a food source in Iceland, where the climate does not allow cultivation of conventional cereal crops, but the plant has never been domesticated [82]. Introducing cereal domestication traits into lyme-grass and other stress-tolerant grasses offers the possibility of accelerating their domestication and producing crops that can be grown on soil that is marginal.

The process of accelerating domestication by genome editing, however, is limited by our existing genetic knowledge of domestication. As future research in the field of domestication expands our knowledge, the potential for genome editing will likely grow accordingly (see also Outstanding Questions). Socially, there are good reasons for these plants to be considered acceptable, but the technology would likely face public resistance if the resulting plants are viewed as GMOs. Ethically, accelerated domestication of wild plants using genome editing would be democratically legitimate if adopted through carefully adapted procedures. Economically, this approach could well be positively viewed by farmers and consumers, provided that it offers tangible benefits. However, the legal frameworks regulating plants rapidly domesticated in this fashion are inconsistent because of the lack of clarity regarding the legal status of rapidly domesticated plants. To avoid missing obvious opportunities, decision makers are urged to clarify the legal status of such rapidly domesticated plants.

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Outstanding Questions

Which domestication genes are specific for particular plant groups, and which are general across the plant kingdom?

How far are we from having identified the full complement of domestication genes in a model crop?

What are the limits for translating such knowledge to the domestication of related plants that have not been domesticated so far?

Will a newly domesticated crop be able to penetrate the market? How will consumers and farmers perceive and receive a new crop?

How will the public receive plants that are rapidly transformed in traits and appearance – and will this be less or more acceptable than modifying already domesticated plants?

How will property rights for a domesticated plant be allocated? Will the rights fall to the country in which the wild plant originated, or will the new crop be free to use?

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