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Review

De Novo Domestication Concept for Potato Germplasm Enhancement

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Abstract: Wild potato germplasm serves as a natural pool of agronomically valuable traits for potato breeding, such as resistance to pathogens and abiotic stresses, quality, and consumer-oriented traits. The introgression of these traits into cultivated potato is hampered by the different kinds of incompatibility and linkages between desirable and undesirable features in hybrid progeny. The trait donor improvement via correction of negative characteristics prior to hybridization to domestic potato can be a solution to the linkage drag problem. The de novo domestication concept for developing new crops using gene editing technologies was previously proposed and performed for tomato and physalis. In this review, we collected information about donor properties of different wild potato species and developed a strategy for potato germplasm enhancement using the de novo domestication approach. The possible modifications of several candidate genes responsible for undesirable traits in wild potato, including high steroidal glycoalkaloid content, self-incompatibility, tuberization under short day conditions, and long stolons are proposed. The current challenges and future prospects of implementing the de novo domestication strategy for potato are discussed.

Keywords: wild potato; de novo domestication; genome editing; glycoalkaloid; petota; *R*-gene

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1. Introduction

The loss of natural genetic diversity is a complex problem in modern potato breeding. According to recent estimation, during the domestication process, potato lost about 500 genes, including many *R*-genes (for resistance) involved in pathogen resistance. Wild potato species contain a high allelic diversity of *R*-genes and potential alleles for increased abiotic stress resistance, quality, and consumer-oriented traits [1–3]. Potato germplasm enhancement suggests the transfer of valuable traits from wild to cultivated potato [2]. The linkage between desirable and undesirable traits complicates this transfer and greatly restricts the donor potential of wild potato [4]. A recently proposed strategy for modern crop breeding is de novo domestication, an approach aiming to convert wild species into domesticated crops using genome editing methods [5]. The concept is based on the assumption that 'wild' alleles of domestication genes can be artificially converted into 'domestic' with the formation of a phenotype typical for the domestication syndrome. The concept was initially proposed and then experimentally proved for tomato [6,7]. Two research groups simultaneously showed successful introduction of domestication traits into wild tomato by targeted knockouts of a few key genes [7,8]. A similar experiment was also performed for physalis, creating new 'more domestic' genotypes having common features with modern tomato [9]. In the past five years, the progress in genome sequencing and gene function research has allowed the identification of key genes related to major domestication-associated traits for many crops, including potato [10].

The application of the de novo domestication concept requires appropriate gene and genotype selection. There are about 200 wild potato species [11], comprising many thousands of accessions in world genebanks. If de novo domestication is considered as a way to create new domestic crops, the selection of one or few wild potato genotypes seems a very difficult challenge. An alternative approach is to apply the de novo domestication concept as a tool for trait donor improvement. The selection of donor genotypes for valuable traits and their modification in order to eliminate or correct the most undesirable characteristics can accelerate the process of elite potato germplasm enhancement. Here, we discuss a strategy for potato de novo domestication considering the enhancement of potato germplasm as the main practical goal.

2. Pros and Cons of Wild Species for Potato Breeding

During the early years of potato breeding, the work of breeders was focused only on the domestic cultivated potato *Solanum tuberosum* L. Intraspecific crosses were not sufficient to develop cultivars resistant to widespread pathogens and pests. The first wild potato successfully crossed with *S. tuberosum* and then involved in the breeding process was the Mexican species *S. demissum* Lindl. The work with wild potato was initiated in 1908 by J. Broili and K.O. Muller, and led to development of so-called W-races of potato. In 1934, the first cultivar with introgressions of wild potato germplasm was developed. This Sandnudel cultivar contained genes of late blight resistance [12]. After the Latin American expeditions of N.I. Vavilov (1925–1927, 1932) and the foundation of the first wild potato germplasm collection, the new potato cultivars with different resistance traits transferred from wild germplasm were developed. The N.I. Vavilov All-Russian Institute of Plant Genetic Resources became the first potato genebank, providing the opportunity for phenotyping of wild potato accessions, genotype selection, and interspecific crosses [13]. Potato germplasm enhancement allows for development of new cultivars harboring resistance to viruses, late blight, potato cyst nematode, Rhizoctonia disease, etc. Some other important characteristics, such as starch content in tubers, resistance to cold sweetening, high tuber solids, or abiotic stress resistance, can also be related to introgressions from wild relatives [2,14].

Despite the progress in the development of resistant potato cultivars, the number of wild genotypes involved in potato breeding is limited. According to our estimation, about 10% of 228 wild potato species (based on the taxonomical system of J.G. Hawkes [11]) are involved in breeding [12,15,16]. Jansky et al. [14] reports on twelve of 107 wild relatives in the pedigrees of European and North American cultivars. Independent researchers acknowledge the great disparity between the large number of potential trait donors and the limited success in their actual involvement in elite potato cultivar development [14,17,18]. Many species are still not sufficiently studied, and others with confirmed valuable traits cannot be readily crossed with cultivated potato [2,19]. Other complications are the high adaptive variation and unpredictable phenotypic plasticity within species, unclear species boundaries, and, as a result, the great number of poorly described closely related accessions in germplasm collections. The use of wild potato germplasm in breeding must be preceded by phenotyping, genotyping, annotation, resistant genotype searching, and maintenance. Every wild potato genotype can be considered to be a source of certain resistance or other valuable traits, but not every genotype can be used as a trait donor [20]. The genes controlling desirable characteristics are inherited together with genes defining negative features, such as long stolons, small tubers, bitterness, photoperiod sensitivity, and short dormancy [14]. The negative characteristics of potential donors are poorly described, whereas most published research works are usually focused only on positive results. The identification and description of negative properties is an important gap to be filled in wild potato germplasm annotation. The long-term study of wild potato germplasm in the N.I. Vavilov All-Russian Institute of Plant Genetic Resources (VIR) has focused on evaluation of both positive and negative characteristics of wild potato accessions as potential trait donors. Table 1 shows the examples of wild potato species from the VIR collection, involved in

hybridization with cultivated potato and harboring a pool of agronomically important properties coupled with undesirable characteristics.

Table 1. Valuable and negative traits of wild species involved in hybridization with cultivated potato.

Species	Pathogen Resistance	Desirable Characteristics for Breeding	Undesirable Characteristics for Breeding	Reference
Series *Bulbocastana* (Rudb.) Hawkes				
S. bulbocastanum Dunal	*Synchytrium endobioticum* (Schilb.) Percival, *Phytophthora infestans* (Mont.) *Pectobacterium carotovorum* subsp. *atrosepticum* (van Hall 1902) Gardan et al., *Leptinotarsa decemlineata* Say, *Epilacha vigintioctomaculata* Motschulsky., *Globodera rostochiensis* Woll., *Meloidogyne chitwoodi* Golden, O'Bannon, Santo et Finley viruses: PVX, PVY.	High starch content in tubers (up to 37%)	Susceptible to *Oospora pustulans* M.N.Owen et Wakefield Bad tuberization under long-day conditions	[21,22]
Series *Commersoniana* Bukasov				
S. commersonii Dunal	*S. endobioticum*, *Streptomyces scabies* (R. Thaxter), *O. pustulans*, *P. atrosepticum*, *G. rostochiensis*, *G. pallida* Stone, *L. decemlineata*, *E. vigintioctomaculata*, viruses: PVY, PVA, PVM.	High starch content in tubers (up to 37%). Frost, heat, drought tolerant	Small tubers	[23]
Series *Yungasensa* Correll.				
S. chacoense Bitter	*S. endobioticum*, *G. rostochiensis*, *G. pallida*, *L. decemlineata*, *E. vigintioctomaculata*, viruses: PVY, PVA, PLRV.	No data	Susceptible to *P. infestans* and frost, long stolons	[23,24]
Series *Megistacroloba* Card.et Hawkes				
S. raphanifolium Cardenas et Hawkes	*Verticillium albo-atrum* Reinke et Berthold, *V. dahlia* Kleb.	Frost, drought tolerant.	Susceptible to *P. infestans*. Bad tuberization under long-day conditions	[23]
S. megistacrolobum sabtax *toralapanum* Cardenas et Hawkes	Viruses: PVX, PVM, PLRV.	Frost tolerant,	Susceptible to *P. infestans*.	[23]
Series *Maglia* Bitter				
S. maglia Schltdl.	*S. endobioticum*	No data	Susceptible to *P. infestans*.	[23]
Series *Tuberosa* (Rudb.) Hawkes (wild species) i				
S. verrucosum Schltdl.	*P. infestans*, *Alteraria solani* Ell. et Mart., *L. decemlineata*, *E. vigintioctomaculata*	High starch content	Small tubers.	[21]
Series Tuberosa (wild species) ii				
S. multidissectum Hawkes	*S. endobioticum*, *P. atrosepticum*, *G. rostochiensis.*	Frost tolerant	Susceptible to *P. infestans*.	[23]
Series Tuberosa (wild species) iii				
S. berthaultii Hawkes	*P. infestans*, *S. endobioticum P. atrosepticum*, *G. rostochiensis*, *L. decemlineata*	No data	No data	[22–24]
S. kurtzianum Bitt. et Wittm. ex Endl.	*G. rostochiensis*, *L. decemlineata*, *E. vigintioctomaculata*, viruses: PVX, PVY.	High starch content in tubers (up to 28%).	Susceptible to *P. infestans*. High SGA content	[22,23,25]

Table 1. *Cont.*

Species	Pathogen Resistance	Desirable Characteristics for Breeding	Undesirable Characteristics for Breeding	Reference
S. microdontum Bitter	*P. infestans*, *S. endobioticum* *Meloidogyne hapla* Chitwood, *G. rostochiensis*, *G. pallida*, *L. decemlineata*, viruses: PVY, PVA, PVS.	Drought tolerant.	Susceptible to *Clavibacter michiganensis* subsp. *sepedonicus* (Spiekermann & Kotthoff) Davis et al., black leg disease. High SGA content	[22–25]
S. vernei Bitter et Wittm.	*P. infestans*, *S. endobioticum*, *A. solani*, *Rhizoctonia solani* (Kühn), *O. pustulans*, *P. atrosepticum*, *G. rostochiensis*, *L. decemlineata*; viruses: PVX, PVY, PVA, PVS, PVM.	Frost tolerant (up to −4 °C).	Susceptible to High SGA content.	[22,23,26]
Series *Acaulia* Juz.				
S. acaule Bitter	*S. endobioticum*, *S. scabies*, *O. pustulans*, *P. atrosepticum*, virus PVX.	Frost tolerant	Bad tuberization under long-day conditions	[23]
Series *Longipedicellata* Buk.				
S. fendleri A. Gray ex Torrey syn. *S. stoloniferum* Schltdl.	*P. infestans*, *A. solani*, viruses: PVY, PVX, PLRV.	High starch content in tubers (up to 28%).	No data	[21]
S. polytrichon Rydberg syn. *S. stoloniferum* Schltdl.	*P. infestans*, *L. decemlineata*, *P. atrosepticum*, viruses: PVY, PVA.	Tuberization under long-day conditions	No data	[21]
S. × *vallis-mexici* Juzepczuk et Bukasov	*P. infestans*, *S. endobioticum*, *P. atrosepticum*	No data	Bad tuberization under long-day conditions	[21]
Series *Demissa* Bukasov.				
S. demissum Lindley	*P. infestans*, *S. scabies*	Frost, heat, drought tolerant. High starch content in tubers (up to 33%).	Small tubers	[21]

3. Agronomically Important Genes of Wild Potato

The genetic study of wild potato has mainly focused on identification of so-called *R*-loci and *R*-genes responsible for pathogen and pest resistance. Most identified *R*-loci are related to late blight resistance. Late blight caused by the oomycete *Phytophthora infestans* (Mont.) is the most harmful potato disease, and is capable of overcoming different control strategies [27,28]. Introgression or transfer of *R*-genes from wild species to cultivated potato provides field resistance to late blight and remains the most sustainable means of pathogen control [29–31]. Virus and nematode resistance associated with known *R*-genes from wild germplasm is also the focus of modern potato breeding [32,33]. Examples of *R*-genes identified in wild potato species are given in Table 2.

Table 2. Mapped and identified genes for pathogen resistance in wild diploid potato.

Species	Pathogen Resistance	Mapped *R*-Loci or Identified Genes	Reference
Series *Bulbocastana*			
S. bulbocastanum Dunal	*Phytophthora infestans* (Mont.)	*Rpi-blb1*	[34]
		Rpi-blb2	[35]
		Rpi-blb3	[36]
		Rpi-bt1	[37]
	Meloidogyne chitwoodi Golden, O'Bannon, Santo et Finley	*RMc1blb*	[38]

Table 2. *Cont.*

Species	Pathogen Resistance	Mapped *R*-Loci or Identified Genes	Reference
Series *Pinnatisecta* (Rudb.) Hawkes			
S. brachistotrichum (Bitter) Rydb	*P. infestans*	*Rpi-bst1*	[39]
S.× *michoacanum* (Bitter) Rydb.	*P. infestans*	*Rpi-mch1*	[40]
S. pinnatisectum Dunal	*P. infestans*	*Rpi-pnt1*	[41]
Series *Circaeifolia* Hawkes			
S. capsicibaccatum Cardenas	*P. infestans*	*Rpi-cap1*	[42]
Series *Yungasensa*			
S. chacoense Bitter	*P. infestans*	*Rpi-chc1*	[43]
	Virus PVY	*Ry chc*	[44]
	Viruses: PVY, PVX	*Ny chc*, *Nx chc*	[45]
Series *Megistacroloba*			
S. megistacrolobum Bitter	Virus PVM	*Rm*	[46]
Series *Piurana* Ochoa(Piu)			
S. paucissectum Bitter	*P. infestans*	*QTLpcs10*, *QTLpcs11 QTLpcs12*	[47]
Series *Tuberosa* (wild species) ii			
S. mochiquense Ochoa	*P. infestans*	*Rpi-moc1*	[48]
S. sparsipilum Bitter	*P. infestans*	*Pi_QTLspr-1*, *Pi_QTLspr-2*	[49]
	Virus PVY^{c}	*Nc spl*	[50]
	Globodera pallida Stone Pa2, Pa3	*Gpa V^{s}spl*, *Gpa XI^{s}spl*	[51]
Series *Tuberosa* (wild species) iii			
S. berthaultii Hawkes	*P. infestans*	*Rpi-ber1* *Rpi-ber2*	[52]
S. microdontum Bitter	*P. infestans*	*Rpi-mcd1*	[53]
S. spegazzinii Bitter	*P. infestans*	*Pi_QTLspg*	[49]
	G. rostochiensis Woll. Ro1-Ro5	*Gro1*,	[54]
	G. rostochiensis Ro1	*Gro1-4*	[55]
	G. rostochiensis Ro1 *G. pallida* Pa2, Pa3	*Gro1.2*, *Gro1.3*, *Gro1.4*, *Gpa3*	[56]
	G. pallida Pa2, Pa3	*GpaM1*, *GpaM2*, *GpaM3*	[57]
S. venturii Hawkes et Hjerting	*P. infestans*	*Rpi-vnt1.1*	[58]
S. vernei Bitter et Wittm.	Virus PVX	*Rx vrn*	[59]
	G. rostochiensis Ro1	*GroV1*	[60]

As mentioned above, wild species carry various beneficial properties in addition to pathogen resistance, such as resistance to abiotic stresses and quality traits, but there is not yet much information about the specific genes and alleles responsible for these properties. Few reports describe QTLs or candidate genes for quality and abiotic stress resistance. The *S. commersonii* Dunal genome sequence analysis revealed 126 cold-related genes that are lacking in *S. tuberosum*. It is hypothesized that high expression of *S. commersonii* galactinol synthase (GOLS1) in conjunction with the increased activity of the cold-associated and -inducible proteins may contribute to the frost tolerance of *S. commersonii* [61]. *S. candolleanum* Berth. genome sequence analysis revealed large differences between wild potato and *S. tuberosum*. Many genes that were lost during domestication are implicated in signal transduction pathways, such as the G-protein coupled receptor (GPCR) signaling pathway. GPCRs are involved in plant responses to a wide range of biotic and abiotic stresses [1]. Different end uses of potato cultivars require different ratios of amylose and amylopectin in starch. Analysis of potato lines with high amylose content,

which were generated by crossing with the wild potato species *S. sandemanii* Hawkes, revealed that gene encoding isoamylase-type debranching enzyme Stisa1 is a candidate for increased amylose phenotype [62]. Cold-induced sweetening resistance is an important agronomic trait that defines the quality of tuber frying products (such as chips). Analysis of the mapping population that was generated by crossing the susceptible cultivated potato clone to the highly resistant wild relative (*S. chacoense* Bitter) clone revealed two QTLs for resistance to cold-induced sweetening [63]. A high nutritional value of potato tubers is also very important for consumers. A high folate diploid clone from the wild potato relative *S. boliviense* Dunal was crossed with a low/medium folate diploid *S. tuberosum* clone. Analysis of progeny revealed SNP markers that have potential to be used in marker-assisted selection for breeding high folate potato varieties [64].

4. Candidate Genes for Correction of Undesirable Traits in Wild Potato

Obviously the most differences between wild and domestic potato belong to genes controlling domestication traits. Two major domestication traits in potato are reduction in steroidal glycoalkaloid (SGA) content and tuberization under long-day conditions. Accumulation of steroidal glycoalkaloids is one of the main disadvantages of wild potato species as trait donors. An example of an undesirable linkage between good quality and high SGA content is the story of the Lenape cultivar. Release of the Lenape cultivar bearing introgressions from *S. chacoense* was a starting point in breeding for processing quality improvement. Lenape demonstrated much better chipping characteristics than all other cultivars. However, due to high SGA content inherited from *S. chacoense*, it was removed from commerce [65]. There are about 80 different SGAs found in potato species. Two major SGA compounds found in tuber bearing Petota subsection species are alpha-chaconine and alpha-solanine. SGAs play a protective role against pests and pathogens, and are also toxic to humans [66]. The biochemical pathway leading to these compounds consists of many enzyme-catalyzed steps and is regulated by a few key transcription factors [66,67]. The knockout of the key enzymes of the SGA synthesis pathway is one of the possible strategies to reduce SGA content in wild potato. It was shown that targeted knockout of the *St16DOX* gene encoding steroid 16α-hydroxylase prevents SGA accumulation in potato hairy root culture [68], and knockout of the *StSSR2* gene results in a decrease in cholesterol and SGA, and has no effect on plant growth [69]. The EMS-induced mutations in other genes encoding enzymes of SGA synthesis (including a few *GAME* genes, for glycoalkaloid metabolism) were also associated with a decrease in SGA content [70]. Moreover, silencing of genes connected with SGA biosynthesis, such as *SGT1* and *SGT2*, that encode enzymes catalyzing glycosylation steps in SGA biosynthesis [71], *GAME4* [72], and the recently identified dioxygenase-encoding *DPS* gene [73] led to a reduction in total SGA levels. The de novo domestication approach involves modification of genes associated with domestication. The domestication-related gene controlling SGA accumulation was identified in multiple genome comparisons between wild and cultivated potato [10]. It encodes APETALA2/Ethylene Response Factor (AP2/ERF) GAME9 (glycoalkaloid metabolism 9), activating different genes controlling the SGA biosynthesis pathway [74]. Modification or knockout of the *GAME9* gene in wild potato is needed to verify the role of this transcription factor in the domestication-associated SGA decrease in potato. Another SGA regulatory region was found in QTL analysis of the F_2 population after crossing the cultured *S. tuberosum* and wild *S. chacoense* species. It revealed a *qSTF8* locus associated with SGA accumulation in the tuber flesh of wild potato. A group of transcription factors genes co-expressed with *GAME* genes was identified in the *qSTF8* locus of *S. chacoense* [75]; these can also be considered to be candidates for knockout in de novo domestication experiments.

A second trait strongly associated with domestication is tuberization in summer under long-day and warm conditions [76]. Wild potato usually produces tubers late in autumn during short days and at low temperature. The search for long-day associated genes in domestic potato revealed a key regulatory gene for tuberization time control. *StCDF1* gene encoding CYCLING DOF FACTOR family protein acts between the circadian molecular

clock and tuberization signal induction [77]. Late tuberization during a short day was associated with the intact allele of this gene, and early tuberization under a long day was associated with mutations leading to either a truncated gene product or modification at the C-terminus. The result was confirmed in an experiment where overexpression of the truncated allele caused the conversion from short-day to long-day tuberization in potato [77]. Genome comparison between wild and domestic potato also showed that most studied long-day potato varieties contain a truncated version of the *CDF1* gene [10]. The reconstruction of frameshift mutation leading to a premature stop-codon at the C-terminus of the *CDF1* gene product is the most obvious means to achieve the tuberization under long-day conditions in wild potato. Another strategy to induce early tuberization is the knockout of flowering repressor SELF-PRUNING 5G (SP5G) involved in tuberization repression under long-day conditions [78]. The changes in the *SP5G* gene regulation in domestic tomato are associated with day-length neutrality in comparison to late flowering wild genotypes. Targeted knockout of the *SP5G* gene in day-length-sensitive tomato leads to early flowering and compact plant architecture [79]. The same modification in wild potato can potentially improve both tuberization time and plant morphology.

A serious barrier for successful crosses between wild and domestic potato is different kinds of sexual incompatibility preventing either pollination or normal seed development [4,80]. The only well-described incompatibility mechanism, known at genetic and molecular levels, is self-incompatibility. Self-incompatibility is typical for many potato species and prevents self-crosses and crosses with genotypes having the same alleles of compatibility-controlling genes [4]. Self-incompatibility can be overcome using targeted genome modification. It was shown that Cas9/gRNA-mediated knockout of the *S-RNase* gene leads to generation of self-compatible potato [81,82]. The introduction of self-compatibility alleles in wild potato germplasm prior to hybridization with domestic potato will facilitate further self- and back-crosses in order to create homozygous lines or achieve desirable trait introgression.

Other traits needed to be corrected in wild potato are associated with the growth habit of stolons and tubers. Many wild potato species produce long stolons with small tubers of different shapes and sizes, whereas domesticated potato has short stolons with large uniform roundish tubers. The stolon architecture and tuber initiation are shown to be controlled by gibberellic acid (GA) and cytokinins [83]. The *GA20ox-1* gene shows signatures of selection [1] and its expression change is associated with altered stolon architecture [83–85]. *GA20ox-1* is a candidate gene for modification in order to improve the stolon architecture but, due to the pleiotropic effect of this gene, the effect of its modification is impossible to predict. Tuber dormancy is an important characteristic because the undesirable tuber sprouting or too-long dormancy period can seriously affect the potato quality. Tuber dormancy and sprouting time are known to be regulated by environmental factors and associated with different hormone signals, but key genes affecting this trait are still to be identified [86]. QTLs have been identified for tuber shape and size control [1], but key genes are not known and de novo domestication cannot yet be applied for these traits.

5. The Strategy for Trait Donor Improvement

The successful application of de novo domestication for trait donor improvement requires three basic components: (i) known target genes and a means of their modification, (ii) well-annotated wild potato genotypes with high donor potential, and (iii) a transformation platform to perform target modification. The current knowledge provides the possibility of only a few basic modifications related to domestication traits in potato. The number of known genes controlling undesirable characteristics is limited. Nevertheless, the genes responsible for major domestication traits are identified and can be artificially modified. The first step in application of the de novo domestication approach for wild potato should be the experimental validation of the candidate gene modification effects. The most phenotypically valuable target genes will form a basic set of targets for donor improvement. Genome editing methods based on RNA-guided Cas endonucleases require the

selection of a genomic target site for each precise modification. Because the potato species are phylogenetically close to each other, it should be possible to select target sites conserved across many potato species and use the same guide RNAs to modify the same genes in different genotypes. The modular gRNA set for customized improvement of selected traits can serve as a domestication toolkit enabling the correction of specific undesirable traits in the selected genotype (Figure 1a).

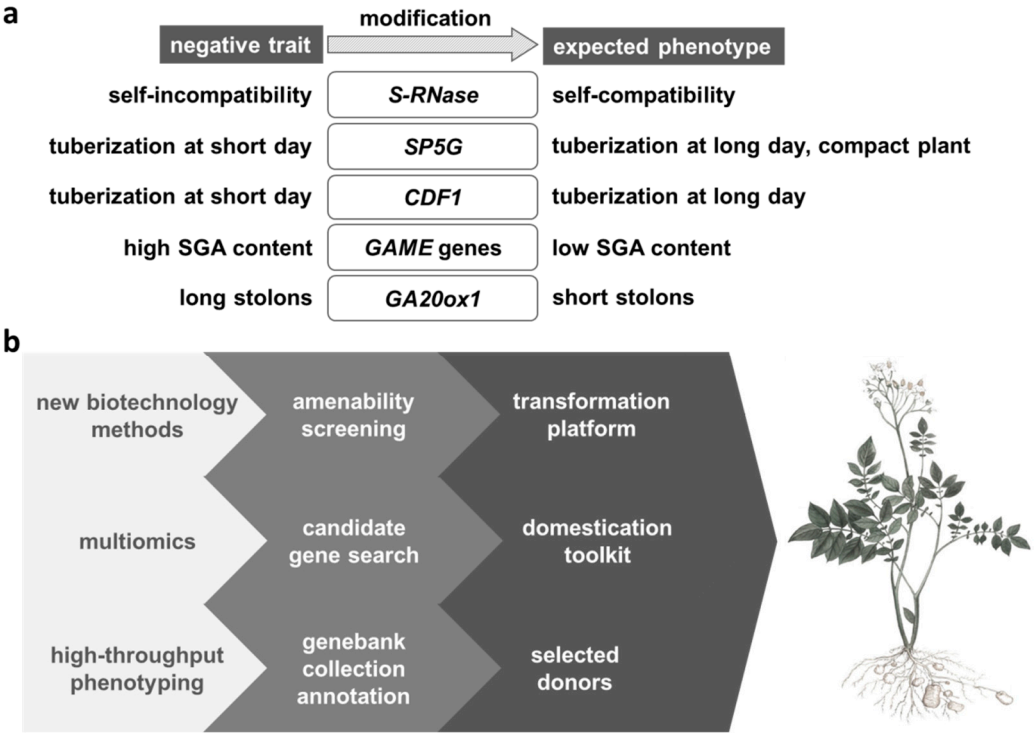

Figure 1. De novo domestication strategy for wild potato. (**a**) The candidate genes for modification and expected improved phenotypes. *S-RNase—Self-incompatibility RNase*, *GA20ox-1—Gibberellic acid 20 oxidase 1*, *SP5G—SELF-PRUNING 5G*, *CDF1—CYCLING DOF FACTOR 1*, *GAME—GLYCOALKALOID METABOLISM*; (**b**) Scheme of de novo domestication strategy from general approaches to precise experimental design.

Due to high diversity of wild potato accessions, the genotype selection is the next question to address. A wide research dataset is available for valuable traits of wild potato species, but only a small portion of genebank accessions have been tested comprehensively and, in most cases, the genetic regulation and phenotypic plasticity of studied traits remain elusive. Revision and systematization of existing data from different databases and early published work may be sufficient to reveal accessions with high donor potential. The bottleneck for scaled improvement of wild potato germplasm is in vitro regeneration and genetic transformation. Few reports of regeneration system establishment and successful genetic transformation are available for wild potato species [87–89]. It is difficult to predict the efficiency of genome modification methods for different genotypes; hence additional efforts are required to estimate the general amenability of wild potato for genetic transformation. It can be concluded that current knowledge allows only proof-of-concept experiments for potato de novo domestication. Scaled application of the approach in breeding requires the pipeline development to advance all three components of the technology (Figure 1b).

The approaches for further development of the de novo domestication concept have been discussed in a few recent reviews [5,90–92] The integration of multiomics data (transcriptomics, proteomics, and metabolomics) together with pan-genome assembly will accelerate the identification of domestication-related and trait-controlling genes. A high-throughput phenotyping pipeline based on dynamic fixation of multiple parameters and

wide application of automated imaging systems will define the best genotypes for de novo domestication. Modern imaging and image-processing technologies allow the mining of such characteristics as overall growth habit, stress resilience, rate of photosynthesis, and productivity [5]. Unfortunately, the pathogen resistance or specific biochemical constituents cannot be easily assessed by massive screenings. An even more complicated issue relates to the development of a universal transformation and regeneration platform. Most biotechnological methods related to genetic transformation or genome editing are genotype specific. The development of new approaches aiming to overcome genotype dependency is one of the main problems in modern plant biotechnology [93]. The proposed integration of different approaches for scaled potato germplasm enhancement is greatly hindered by insufficient annotation of genebank collections and low data availability. Integrated efforts of world genebanks are needed to create transparent, comprehensive, and user-friendly databases accumulating all information about genes, phenotypes, and transformation methods for wild potato germplasm. Such databases will be instrumental for practical breeders working on potato germplasm enhancement and the development of new potato cultivars.

6. Conclusions

The nature of potato as a vegetatively propagated tetraploid crop causes specific problems in breeding, such as loss of genetic diversity and accumulation of deleterious alleles. The need of new genetic material in potato germplasm is very high. Here, we propose a pre-breeding strategy for wild donors, which includes their description and analysis, followed by the selection of appropriate donors and modification of their undesirable traits with targeted genome editing. In this review, we provide information about positive and negative characteristics of wild potato species. The data were collected during a long-term study by VIR, some of which was not previously published in English. The state-of-the-art de novo domestication concept for potato wild relatives includes modification of only a few genes because there is still a lack of research data relating to both wild potato genetics and phenomics. However, we believe that application of the concept for wild relatives can greatly facilitate the process of valuable trait transfer from wild to cultivated potato. Modification of few domestication-trait-related genes may solve the linkage drag problem and improve such characteristics as high SGA content, day-length sensitivity, growth habit, and self-incompatibility. The application of de novo domestication technology for donor improvement is complicated by insufficient annotation of genebank collections. An integrated approach including multiomics, precise phenotyping, and development of biotechnological methods can provide sufficient resources for routine application of the de novo domestication concept for potato germplasm enhancement.

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