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Abstract

In the context of the global challenge of climate change, mitigation strategies are needed to adapt crops to novel environments. The main goal to address this is an understanding of the genetic basis of crop adaptation to different agro-ecological conditions. The movement of crops during the Colombian Exchange that started with the travels of Columbus in 1492 is an example of rapid adaptation to novel environments. Many diversification-related traits have been characterised in multiple crop species, and association-mapping analyses have identified loci involved in these. Here, we present an overview of current knowledge regarding the molecular basis related to the complex patterns of crop adaptation and dissemination, particularly outside their centres of origin. Investigation of the genomic basis of crop expansion offers a powerful contribution to the development of tools to identify and exploit valuable genetic diversity and to improve and design novel resilient crop varieties.

Introduction

Environmental change will result in strong ecological and genetic effects on gene and allele frequencies in many plant populations, as well as altering several aspects of agricultural systems, such as plant physiology and phenology, water availability, soil fertility, pathogen spread and host susceptibility. Many crops have evolved in response to climate change under increasingly stressful conditions in which their extinction is highly possible. However, there is more evidence for climate-driven range expansion than for range contraction [1]. This suggests that plants can cope with climate change through adaptive mechanisms, such as phenotypic plasticity and microevolution [2].

Genetic diversity represents the raw material on which adaptive selection acts, and as such, it has a fundamental role in both evolutionary history and future evolutionary pathways of a species [3]. Thus, persistent fluctuations in biotic and abiotic environmental factors provide a background of changing selection pressures to which species must respond, and in this way, genetic diversity is maintained within populations. Identification of the molecular basis of plant adaptation is needed to drive plant breeding into the development of novel varieties that can adapt to climate changes. Analysis of genetic diversity through population genomics and genotype–phenotype association approaches can be very useful tools to reach this aim [4], especially with the novel opportunities offered by the more recent advances in genomics and DNA sequencing technologies. The success of such studies critically depends on the type of plant material adopted. Moreover, if the search for the signature of selection is the objective, the populations must have an ancient and strong link with their growing environments, which must have variable agro-ecological conditions.

Populations of wild plants and wild crop relatives can easily meet these prerequisites. There are several examples in the literature that have focused on wild germplasm to detect adaptive genetic control, along with studies on model species such as *Arabidopsis thaliana* [5•], with other examples available for crop species. Fustier et al. [6] investigated adaptation in 11 populations of teosinte, the wild progenitor of maize, along two elevation gradients in Mexico that showed continuous environmental changes over a short geographic scale. They evaluated 1,664 individuals for 18 phenotypic traits and genotyped them for 38 microsatellite markers and 171 outlier single nucleotide polymorphisms (SNPs). These significantly differentiated between lowland and highland populations and/or correlated with environmental variables. They showed that >50% of the traits were differentiated due to local selection. A recent landscape genomics study of Rodriguez et al. [7•] reported on an

analysis of correlations between molecular markers and ecological variables at a continental scale. They analysed a sample of 310 wild common bean georeferenced accessions that they genetically characterised at 131 SNPs. Geographic and environmental data were combined with genetic diversity data to separate the effects of geography from those of ecology, and they reported a total of 26 loci (19.9%) that were putatively under selection for adaptation. Among these, different loci were shown to have compatible functions with adaptation features, such as chilling susceptibility, cold acclimation, and mechanisms related to drought stress [7•]. Recently, Mier y Teran et al. [8] characterised 112 wild common bean accessions that were representative of the geographic distribution of the Mesoamerican gene pool. This was applied at the molecular level (11,447 SNP markers) and the phenotypic level (root trait evaluation, comparison of control and drought stress), and considered environmental variables from the geographic coordinates of the origin of each accession. They defined genomic regions that were associated with productivity and drought adaptation in the wild germplasm.

Within the cultivated gene pools, the above-mentioned prerequisites for such studies are satisfied only by populations of landraces (or, if available, by experimental populations, as composite crosses specifically developed over multiple generations of experimental evolution). Landraces offer unique opportunities for integration of association mapping and signatures of selection analyses. Indeed, landraces are the product of an evolutionary interaction with the agro-ecosystem, and consequently, their genetic composition is determined by both stochastic and human-mediated or natural selection over decades of evolution, which means that they have maintained a considerable amount of genetic variability. Moreover, when multiple landrace populations grown in contrasting agroecological environments are compared, it is possible to tag the signatures of divergent selection [9-12]. This makes it possible to investigate the genes that are responsible for the ‘genomic architecture’ of the local adaptation of plants. After domestication, food crops spread widely between different geographic and cultural areas at different levels and to different extents, and this process ultimately contributes to the diversification of local agricultural subsistence.

Among cereals, barley and maize are examples of crops that have achieved adaptive success worldwide (**Figure 1**). Barley is one of the primary plants that originated and was domesticated in the ‘Fertile Crescent’ about 11,000 years ago, and was later disseminated worldwide over a wide range of agro-climatic conditions [13]. Some of these conditions were particularly extreme, such as in Tibet, Nepal, Ethiopia and the Andes, where farmers

cultivated barley on mountain slopes at altitudes higher than those for any other cereals [14]. Maize also has one of the broadest worldwide dissemination ranges. It was domesticated once in the Balsas region in the valley of Mexico about 9,000 years ago, and it subsequently spread to geographically and ecologically diverse environments, from Canada to Chile [15]. Similarly, among legumes, the common bean can be considered as a crop that is now successfully widespread [16]. The post-domestication phase of crops outside their centres of origin (i.e., at regional, continental, worldwide levels) towards a wide range of agro-ecosystems has led to phenotypic and genetic divergence between domesticated forms. This process can be considered a fascinating model for the study of the adaptive evolution of crops, and it offers the possibility to discover new interesting genetic variants that have potential use in a climate alarm context, like that which we are currently in.

Diversification traits

Meyer and Purugganan [17•] reported on several observed traits in crops that accompanied their domestication and diversification, and their improvement phase. It is not particularly easy to clearly distinguish between genes that underlie domestication and those that control diversification traits. This is the case even if the genetic basis of adaptation might be more related to diversification traits that are related to post-domestication stages, such as for pigments, variations in size and chemical composition of edible parts, changes to the mating system (promoting allogamy or autogamy), resistance or tolerance to abiotic and biotic stresses, reduced vernalisation and photoperiod sensitivity, and changes to flowering time, the life cycle and dwarfism [17•]. It is important to consider that these traits can vary among crop species, considering also that they relate to crops that have adapted to specific agro-ecological conditions and cultures. In this regard, several examples can be found in the literature where the function of genes defined as putatively under selection during domestication of crops can be ascribed to diversification traits, thus traits upon which both natural and human selection have acted during crop expansion.

In common bean (*Phaseolus vulgaris*), Bitocchi et al. [18] compared selection analysis data obtained for the same genes in different studies of varying sizes, data types and methodologies. To study the effects of domestication at the genome level, they analysed nucleotide diversity at 49 gene fragments on a sample of 39 wild and domesticated Mesoamerican accessions of *P. vulgaris*. By applying population genomics approaches, they identified several genes that showed footprints of selection. At the same time, they used the SNP data of Rodriguez et al. [7•] to perform selection tests on a wider sample, which included 417 and 160 wild and domesticated accessions, respectively, of common bean. Finally, data were included from two further studies that focused on investigation of the domestication process in common bean [19,20•]. The final comparison of the data from these four studies provided independent evidence of selection for four genes: *AN-Pv33, AN-DNAJ, Leg223, AN-Pv69*. Gene-function investigations revealed that all of these genes are involved in plant resistance/ tolerance to abiotic stresses, such as heat, drought and salinity. In this regard, adaptation of plants to abiotic stresses is of crucial importance, because they are among the major environmental factors that affect plant productivity. By accessing the *Arabidopsis thaliana* stress-responsive gene database (http://srgdb.bicpu.edu.in/) [21], we have identified a list of genes that were detected as functionally involved in abiotic stress responses in *Arabidopsis*. The OrthoFinder algorithm [22] and the 2.1 version of the *P. vulgaris* reference genome (https://phytozome.jgi.doe.gov/pz/portal.html) were then used to

identify orthologous genes in common bean. A total of 770 common bean genes were found to be orthologous to *Arabidopsis* genes involved in abiotic stress responses (**Table S1**), 126 of which showed signature of selection during domestication in Bellucci et al. [20] and/or Schmutz et al. [19] **(Figure 2; Table S1**). Among these genes, a very interesting candidate is a homologue of *K^+ uptake transporter6 (KUP6)*. The *KUP6* gene has been shown to be a key factor in osmotic adjustment, through the balancing of potassium homeostasis in cell growth and drought stress responses in *A. thaliana* [23]. Its function is directly mediated by abscisic acid signalling, and under water-deficit stress this involves inhibition of cell expansion in both roots and guard cells, which is driven by decreased turgor. In Bellucci et al. [20], *KUP6* was also among the small fraction of outlier genes for which selection has increased the nucleotide diversity in the domesticated pool compared to the wild pool, which suggests selection due to crop expansion into the new environments with unexpected biotic and abiotic stresses (i.e., diversifying selection).

Meyer et al. [24] reported an example of geographic and environmental divergent adaptation between four populations of African rice (*Oryza glaberrima* Steud.). They sequenced the genomes of 93 landraces that spanned from west to central sub-Saharan Africa, to investigate the African rice post-domestication spread, its subsequent adaptation to local environments, and the genes that were involved in these processes. They focused on salinity tolerance, as one of the major traits associated with geographic adaptation of African rice. The accessions were phenotyped for various salinity-associated fitness traits, and they found a significative loss of salinity tolerance in the southwest inland population. This adaptive phenotype was thus suggested to arise from the costs of maintaining tolerance in a geographic area associated with greater precipitation and decreased soil salinity. In contrast, no significant differences were seen for the northwest, northeast and southeast subpopulations. Genome-wide association studies allowed them to identify 11 loci that contained several genes that were putatively involved in salt-stress tolerance. Among the most significant of these was an orthologue of the *O. sativa HAK5* gene. HAK5 has been shown to be a key component in the acquisition and transport of potassium, to improve salt resistance in potassium-deficient rice plants [25], and it might have had a crucial role in *O. glaberrima* adaptation along the western Atlantic coast.

The timing of important developmental stages (e.g., flowering time) is another main diversification trait that defines adaptation of plant populations to different environments. In maize, numerous studies have focused on identification of the genetic control of flowering time and on genetic variations at identified genes in different materials from diverse

environments. Buckler et al. [26•] used a nested association mapping population of 200 recombinant inbred lines from 25 crosses, which resulted in a total of 5,000 lines for identification of genes or genomic regions associated with flowering time. These lines were phenotyped in four locations over 2 years. Quantitative trait locus (QTL) mapping showed that the differences in flowering time were not caused by a few genes that had large effects, but rather by the cumulative effects of numerous QTLs (i.e., <100), each of which had only a small impact on this trait [26•]. However, to date, although a large body of mapping information on the QTLs that control maize flowering time is available [27,28], the molecular basis of these QTLs remains almost totally unknown, with the exception of four genes that have been demonstrated to be involved in flowering time: *Dwarf8* [29]; *ZmCCT* [30-32]; *Vgt1* [33]; and *ZCN8* [34].

The *Dwarf8* gene has been shown to be an orthologue of the gibberellic acid insensitive (*GAI*) gene, which is a transcription factor that negatively regulates gibberellin responses in *A. thaliana*. Association analysis has identified several interesting polymorphisms in maize *Dwarf8*. One of these is a 6-bp deletion in the C-terminal region of the open reading frame, and this showed strong association with flowering time [29]. With the aim to evaluate the contribution of *Dwarf8* to maize adaptation to temperate climates, Camus-Kulandaivelu et al. [35] analysed a wide collection of traditional landraces (144 from America, 131 from Europe) for indel polymorphisms in the *Dwarf8* gene. They reported a variation in the frequency of the *Dwarf8* deletion associated with altitude and latitude, which demonstrated that these features have an important role in driving local maize adaptation [15,35]. In particular, for American landraces, they showed that the frequency of the *Dwarf8* deletion was higher in northern Flint maize (83%) compared to maize groups from the tropical Caribbean (2%) and Mexican (4%). Instead, the Andean group that was represented by populations that originated from high altitudes (on average, 2,200 m a.s.l.) showed a frequency of *Dwarf8* deletion of 58%. Similarly, in Europe, *Dwarf8* deletion has prevailed in landraces from northern Europe.

Vgt1 is also one of the major maize flowering-time QTLs, and a miniature transposon that is located ~70 kb upstream of *ZMRap2.7* was shown to be the causative variant of *Vgt1* that contributes to maize adaptation to temperate regions [33,36,37]. Ducrocq et al. [36] carried out an association mapping study on 375 maize inbred lines, which included inbred lines representative of the American and European diversity, with a wide range of flowering times. They reported that the *Vgt1* early allele showed higher frequency in the tropical materials. Moreover, the frequency of *Vgt1* alleles among the tropical populations varied

with the altitude of the collection site, while the early allele was rare at low altitudes. These data support the hypothesis that adaptive selection followed domestication of maize, with early and late materials adapted to high altitude and low altitude cultivation systems, respectively.

Yang et al. [31] showed that a CACTA-like transposon insertion within the *ZmCCT10* promoter repressed *ZmCCT10* expression, which makes maize insensitive to long days. Likewise, Huang et al. [32] identified a Harbinger-like transposable element at ~57 kb upstream of *ZmCCT9* that functions as a *cis*-acting repressor of *ZmCCT9*, to enhance maize adaptation to higher latitudes. Comparisons of the gene sequence from teosinte and tropical and temperate maize revealed that both the adaptive insertions were completely absent in teosinte, and so they are likely to be *de-novo* mutations that occurred after the initial maize domestication [30-32].

Recently, Guo et al. [34] reported that two natural *cis*-variants in the promoter of *ZCN8* were gradually targeted by selection during the spread of maize from its tropical origin to northern North America, which led to earlier flowering plants that were adapted to the temperate growing regions. In more detail, *ZCN8* was proposed to be homologous to *A. thaliana* FLOWERING LOCUS (FT), and they considered it to be the maize florigen gene [38,39].

Another interesting example was the study of Vigouroux et al. [40••] on pearl millet. They analysed a total of 192 landraces that had been collected during two different periods (i.e., 1976, 2003) throughout Niger, in the Sahel, which is one of the driest agro-ecosystems in Africa. This geographic area had undergone recurrent drought during this interval of 25 years. Along with the analysis of the phenological and morphological changes in the two samples evaluated in field experiments, they also investigated the genetic diversity across these two samples. In particular, they analysed the change in allele frequency at the *PHYC* flowering time locus [41], and showed that the allele that conferred earliness increased from 9.9% to 18.3% over this time frame. This study is an example of the strong adaptation of plants to changing environmental conditions even over relatively short evolutionary timescales. It also suggested that exploitation of genetic variability within landrace populations represents a strategy in response to future climate changes. However, they recommended the consideration of the mating system of the crop species, as they indicated that this strategy might be successful for allogamous species, such as pearl millet, but that further studies would be needed for autogamous species [40••].

SNPs are the markers of choice in different population genomics studies because they are the most abundant bi-allelic and co-dominant markers that are characterised by simple mutational patterns and by high-throughput and low-cost detection. Despite this, many other examples exist in literature that are based on structural variations, which refers to genomic changes in DNA segments of >1 kbp, such as insertions, deletions, inversions, or copy-number variations. It is highly possible that genes responsible for acclimatizing and adaptation to different agro-ecological conditions and stress resistances will be identified in such genomic changes [42••]. As an example, Zhou et al. [43] reported the duplication and evolutionary history of the *COR15* gene that is involved in cold-stress defence, which was previously detected in two copies in several species of *Brassicaceae*. They cloned the homologous *COR15* sequences of 10 species of *Brassicaceae*, and when they performed evolutionary analyses they found significant inter-lineage differences in the evolutionary rates between the original and the duplicated genes. The most interesting data were perhaps observed for the analysis of the *COR15* genes of the *Draba* species, which contrary to the other lineages, is mainly present in cold-temperature, highly arid regions. Three important lines of evidence were observed: (i) the estimated non-synonymous and synonymous substitution ratio appeared to be higher among the duplicated genes; (ii) positive selection was detected for the duplicate *COR15* gene; and (iii) functional divergence was shown between the two groups of the proteins. Overall, these observations indicated that the functional differences in the *Draba* lineage between *COR15a*, as the original gene, and *COR15b*, as the duplicated gene, have been driven by adaptive evolution. This allowed its spread to cold locations during the Quaternary climatic oscillations, and subsequently its expansion to arid alpine and arctic regions. Similarly, De Bolt [44] examined whether *Arabidopsis* plants grown under different temperatures for several generations showed any differences in copy number variations relative to the control situation of growth under normal conditions. They showed that high temperatures promoted chromosomal segmental duplications.

Recent studies have also suggested that polyploids might have greater phenotypic flexibility for gene expression in response to environmental differences [45]. Ceccarelli et al. [46] showed that chromosome endoreduplication in *Sorghum bicolor* is a fundamental part of the adaptive response of plant genomes to salt stress. Their results showed that when exposed to salt-induced treatments, only competent genotypes underwent endopolyploidy of the root cortex cells, which allowed them to grow under sublethal salinity concentrations. The wide variability obtained as a result of polyploidy events was thus directly correlated

with the tolerance increase of *S. bicolor* to salinity, which highlighted the important role of this mechanism in adaptive responses to different abiotic conditions. Similarly, Saleh et al. [47] reported that citrus tetraploid rootstock is more tolerant to salt stress than their corresponding diploid.

Selection for adaptation

Local adaptation occurs when populations that grow under heterogeneous environmental conditions evolve different phenotypic traits that provide a fitness advantage in their specific environment [48]. Selection acts on sequence variation, which can derive from the standing variation that has a long history of segregation within a crop before the advent of selection, or *de-novo* mutations that originate in populations (i.e., wild forms or landraces), or from hybridisation. Knowing the sources of variation on which selection for adaptation can act is important for several reasons, such as, for example, to understand how rapidly populations can adapt [3]. Exhaustive evidence that shows the relative role of standing variation or *de-novo* mutations after changes in the environment is still lacking. Adaptation is likely to be slower if selection acts on *de-novo* mutations, compared to what would be expected when it acts on standing variation, where beneficial alleles might already be available at higher frequencies [49]. Moreover, on average, adaptation from standing variation appears to occur through the fixing of more alleles with small effects [3,50], and can have greater potential for adaptation if the rate of environmental change is fast, rather than slow, by traversing larger distances in the phenotype space.

Along with useful standing variation and *de-novo* mutations, selection for adaptation can also act on new genotypic variations due to recombination after hybridisation [51,52]. In common bean, Bellucci et al. [20•] analysed RNA sequencing data from a set of Mesoamerican wild and domesticated accessions, and they showed that most of the genes detected as under selection during domestication showed reduced diversity in their domesticated compared to their wild forms, as expected under positive selection from standing variation. However, 2.8% of the outlier genes showed no diversity in the wild form, and polymorphism in the domesticated form. This thus suggested that in some cases the selection increased the nucleotide diversity of domesticated materials at target loci, the function of which was associated with adaptation traits, such as abiotic stress responses and flowering time [20•]. Interestingly, in the same species, Bitocchi et al. [18] analysed nucleotide data of 49 gene fragments in a sample of Mesoamerican wild and domesticated accessions, and they detected an excess of nonsynonymous mutations in the domesticated forms, particularly in the coding regions, compared to the non-coding regions. These mutations appeared to be recently derived mutations, and the investigations into the functions of their relative genes (responses to biotic and abiotic stresses) support a scenario where new functional mutations were selected for adaptation during diversification.

In maize, Guo et al. [34] asked whether the *ZCN8* gene can affect natural variations in flowering time. They performed association analysis by sequencing *ZCN8* and its upstream and downstream regions in segregant populations derived from a cross between W22, a temperate *Zea mays* ssp. *mays* inbred line, and 8759, a *Z. mays* ssp. *parviglumis* accession. They found a SNP in the promoter region of *ZCN8* (i.e., SNP-1245) that coincided precisely with the allelic differences in flowering time between all of the parents of the teosinte–maize populations used in their study. They also sequenced the *ZCN8* gene in a panel of 513 maize inbred lines and 45 teosinte lines (including lines of *Z. mays* ssp. *parviglumis*, the maize progenitor, and lines of its close relative species *Z. mays* ssp. *mexicana*). These data revealed that the early flowering allele of SNP-1245 was present in ~24% of the teosinte accessions, which suggested that this polymorphism was a standing variant in the maize wild progenitor selected during the early domestication of maize. Guo et al. [34] also detected a three-base-pair deletion variant (i.e., Indel-2339) about 1,000 bases from SNP-1245 that was associated with flowering time and showed higher expression of *ZCN8*. Moreover, they did not find this allelic variant in the maize progenitor, although it was present in *Z. mays* ssp. *mexicana*, from which gene flow resulted in its introgression into maize [53]. Furthermore, low frequency of Indel-2339 (5%) was shown for South America germplasm (i.e., tropical maize), while it was selected at a higher frequency in northern United States accessions (30%; temperate maize). Overall, these data suggested that two independent associated mutations (i.e., *cis*-regulatory variants) in the promoter region of *ZCN8* arose in a stepwise manner: SNP-1245 during the early domestication of maize, and subsequently Indel-2339 during maize diversification into the Mexican highlands. The discovery that *ZCN8* has more than one functional mutation that segregates indicated that genes associated with crop domestication and diversification are subject to recurrent mutations that might be selective targets at different times during evolution.

Identification of adaptive introgression can be relatively easy when materials collected at different times are available, such as with historical collections. A recent example was seen by the study of Bitocchi et al. [11], where the effects were evaluated for hybridisation of modern maize and landraces over a relatively short period of 50 years. Bitocchi et al. [11] analysed and compared the genetic diversity of two samples of maize landraces from central Italy that were collected at two different times: an old collection that was carried out before the introduction of hybrid varieties, and a recent collection that had evolved in co-existence with modern maize. Population structure analysis allowed the

352 detection of introgression from modern maize. Coupled to the data of selection analyses
353 (i.e., detection of outlier loci in comparisons between historical and recent maize collections),
354 these data indicated that selection pressures for adaptation have favoured new alleles that
355 were introduced by migration from hybrids over the last 50 years. These data showed the
356 crucial role of migration in the evolution of landrace populations grown on farms.
357

The Columbian Exchange: adaptation of crops from American homelands into Europe

The introduction of New World crops into Europe after the Columbus 1492 voyage was one of the most important evolutionary events related to agriculture, adaptation and biological changes, and more generally, to human society. In 1972, the historian Alfred Crosby coined the term 'Columbian Exchange', to designate the process of the biological diffusion triggered by the colonisation of the Americas by Europe. The benefits of the New World crops have resulted in their adoption in all parts of the world, which demonstrated that as the basis of this process, the plants underwent significant adaptation to the various agro-ecological conditions [54]. The growing knowledge about the adaptation of crops to new environments through the study of their introduction and expansion into Europe (i.e., a historically well-defined event of recent introduction and rapid adaptation) will be of great use for future major environmental and socio-economic changes, such as increases in temperature, variability of rainfall, and new consumer preferences. Several crops were introduced into Europe from the Americas (e.g., tomato, maize, beans, squash, potato, tobacco). This dissemination process occurred during the same historical period for several species, and it was characterised by diverse features (e.g., different mating systems and ploidy) that can be exploited to investigate their effects on genome diversity and to highlight the genetic control of adaptation. There are numerous studies in the literature for different crops that have highlighted the changes that occurred in their genomes due to colonisation of new agro-ecosystems. Here, we present some examples for three crops that were involved in the Columbian Exchange, and which have been among the most important: potato, maize and common bean.

Following long debate during which most studies have suggested multiple domestications for *Solanum tuberosum L* (potato), Spooner et al. [55] demonstrated the monophyletic origin of cultivated potatoes through phylogenetic analysis and cladistic data. These showed that landraces of potato originated in the Andes of southern Peru, and subsequently became widespread throughout Chile, thus assuming the present-day distributions of the original cultivars. Potato was not brought to Europe by Columbus or others soon after the discovery of the New World in 1492; potato arrived later. The reason for this is that potato is a cool temperate crop of the high Andes of South America and was not discovered by the Spaniards until 1532 [56]. Potato cultivation in Europe spread rapidly, and also reached locations with significative growth and climate differences. For potato, the most important adaptation trait to European conditions – and a key event in its history – was to overcome the short-day dependency for tuberisation, due to the equatorial origin of

potatoes [57-59••]. Indeed, when introduced into temperate zones, wild material forms tubers only during the shorter autumnal day lengths. The gradual arrival of winter, which is characterised by freezing temperatures, stops the correct maturation of the tubers, consequently killing the plant. In the *A. thaliana* model system, the pathway that controls flowering time is very complex, and the complexity of this regulation involves four intricate networks of signalling pathways (i.e., photoperiod, vernalisation, autonomous, gibberellins) [60] (**Figure 3A**). Among the proteins involved in this complex pathway, cycling Dof (DNA-binding with one finger) factors (CDFs) are a group of plant-specific transcription factors that repress flowering by down-regulation of the expression of the *CONSTANS* (*CO*) gene, a central regulator of the photoperiod pathway [61]. In potato, the plant maturity phenotype has been reported as a major effect QTL that maps to chromosome 5, and this phenotype is a measure of several important secondary traits. These include development of the canopy, vegetative growth, onset of tuberisation, leaf senescence, life-cycle length and pathogen resistance [62]. Kloosterman et al. [57] used ultra-dense amplified fragment length polymorphism markers and two diploid segregant potato populations derived from crosses between wild and domesticated genotypes. In this way, they narrowed down the locus responsible for the plant maturity phenotype to a region of around 110 kb on chromosome 5. Screening for putative candidate genes, they identified the potato homologue of *CDF1* in this QTL region (*StCDF1*, *Solanum tuberosum CDF* gene 1). They sequenced *StCDF1* in the progenies of the mapping populations, which allowed identification of three *StCDF1* allelic variants: *StCDF1.1*, which was characteristic of short-day-dependent tuberisation descendants, and two insertion variants, *StCDF1.2* and *StCDF1.3*, that were typical of the early maturing/ tuberising descendants. Kloosterman et al. [57] established that *StCDF* conserves its repressive function on the two potato *CONSTANS* genes (*StCO1/2*) that repress tuber formation during long days [63]. They also suggested that due to the loss of their C-terminal end, the *StCDF* Andean variants (i.e., *StCDF1.2*, *StCDF1.3*) led to accumulation of *StCO1/2* repressors. This interaction indirectly induced expression of *StSP6A*, the potato homologue of *FLOWERING TIME* (*FT*), which resulted in induction of tuber development under long days (**Figure 3B**). The absence of post-translational regulation of *StCDF1.2* and *StCDF1.3* allowed them to remain constant throughout the day, which formed the basis of potato diversification at different latitudes. A recent investigation explored haplotype diversity at the potato maturity locus *StCDF1* using a panel of 58 samples [58]. These included South American wild species, South American landraces, and North American cultivars derived from modern breeding programmes. Here, Hardigan et al.

[58] reported 55 haplotypes for *StCDF1* that encoded 27 peptide variants. Four haplotype groups contained conserved deletions that affected the structure of the StCDF1 peptide. The DNA phylogeny of haplotypes at the *StCDF1* locus revealed that almost all long-day landraces/ cultivars contained alleles that encoded shortened *StCDF1* proteins that were derived from introgression from wild species. This suggested a key role for the extant natural populations as essential sources of untapped adaptive potential. In the case of potato, *StCDF1* allele introgression from the wild species allowed potato cultivation in North America, and, probably, also subsequently in Europe. A very interesting study that focused on the origins and adaptation of European potatoes was carried out by Gutaker et al. [59••]. The strength of their work was the investigation of historical samples that spanned 350 years of potato evolution in Europe. Their materials included 29 historical herbarium specimens that they obtained from different European museums, which included three Chilean and 26 European historical samples. They also analysed 43 South American modern samples, and 16 European modern samples. An array-based targeted re-sequencing approach was used that allowed them to target the whole chloroplast genome and ~4.3 Mb of the nuclear genome, including *StCDF1* [57]. Analysis of these genetic data initially allowed Gutaker et al. [59••] to highlight the very complex scenario related to the introduction and wide spread of potatoes in Europe. These data indicated that the oldest European materials (i.e., collected between 1650 and 1750) derived from an ancestor of the Andean landraces, while in the subsequent 100 years there was introgression from newly introduced Chilean potatoes. The scenario is more complex considering that twentieth century European potatoes did not descend from their nineteenth century admixed predecessors, but are the result of introgression from wild potato species, as they were used in twentieth-century breeding programmes to introduce pathogen resistance [64]. It is also interesting that Gutaker et al. [59••] highlighted the re-introduction of European potatoes into America, and that this impacted upon the Andean and Chilean potato diversity; indeed, European ancestry was detected in potatoes in the South American modern-day sample. Gutaker et al. [59••] also investigated the origins of the long-day adaptive alleles in the *StCDF1* gene. They reported the appearance of *StCDF1.2* and *StCDF1.3* adaptive alleles in Europe starting from 1810 only, with none of these insertion variants present in the oldest European samples of Andean descent (1650-1750), nor in the Andean landraces. For this reason, they excluded (with high confidence) the possibility that adaptation to long-day tuberisation had arisen from the Andean landraces standing variations. They showed the appearance of the adaptive alleles in Europe in correspondence with admixture with the newly introduced Chilean

potatoes. However, there was no evidence of direct correlations between the adaptive variants and the historical samples from the lowlands of Chile. Gutaker et al. [59••] thus hypothesised that the adaptive insertions in the *StCDF1* gene originated *de novo* in Europe, and then became rapidly fixed due to their dominant inheritance and breeding advantage. However, they also stated that this hypothesis needs to be further confirmed, as their sampling of historical Chilean specimens is not particularly representative, and thus it did not allow clear rejection of the possibility of a Chilean origin of these adaptive insertions.

Another very important crop that became widespread in Europe during the Columbian exchange was *P. vulgaris* (common bean). This species originated in Mesoamerica, and wild forms became widespread by subsequent migration into South America; domestication took place independently in two geographically distant areas, Mesoamerica and the Andes, which represented the two main gene pools of the species [16]. The Mesoamerican common bean appears to have arrived in Europe through Spain and Portugal in 1506, following the first voyage of Columbus; then in 1528, the exploration of Peru by Pizarro opened the possibility of the introduction of the Andean common bean. *P. vulgaris* spread into the Old World over a very short time, and many common bean landraces rapidly evolved in Europe as a result of its adaptation to new agro-ecological growth conditions. The dissemination of common bean into and across Europe followed very complex pathways, which involved different introductions from the Americas, and at the same time, direct exchanges among countries within Europe, and between European and other Mediterranean countries [16]. To investigate the evolutionary patterns of the common bean far from the Americas, Angioi et al. [54] analysed a wide sample of *P. vulgaris* accessions, as 94 from the Americas, and 307 from Europe. They included chloroplast simple sequence repeats (SSRs), and nuclear data (i.e., phaseolins, three indel-spanning markers of the PvSHATTERPROOF1, Pv*SHP1*, gene) and morphological data (i.e., coat pattern, seed size, colour and shape). In this way, Angioi et al. [65] showed that both the Mesoamerican and Andean gene pools were present in Europe and that the European germplasm was more prevalent as the Andean origin (67%). The trend was maintained at a smaller scale (i.e., a country level), whereby the Mesoamerican proportion was higher in the eastern parts of Europe, with a maximum of 46% in Greece, while the Andean type was most frequently found in three European macro areas: the Iberian Peninsula, Italy and central-northern Europe. Interestingly, and contrary to expectations, the European common bean did not show any strong reduction in genetic diversity due to the introduction bottlenecks and selection for adaptation to these new agro ecosystems and consumer preferences; indeed, Angioi et al. [54] and previous studies have

494 shown very low reductions in diversity in common bean from Europe. These findings
495 indicated a high level of gene flow among the different European geographic regions.
496 Furthermore, they highlighted the role of the breakdown of the spatial isolation between the
497 Mesoamerican and Andean accessions in Europe, with promotion of hybridisation, which
498 had a significant impact on the maintenance of genetic diversity. By combining these
499 chloroplast and nuclear data, they were able to identify hybridisation events, and they
500 estimated that 44.2% of the European landraces derived from at least one hybridisation
501 event between the Mesoamerican and Andean forms. Gioia et al. [66] complemented the
502 dataset of Angioi et al. [65] with nuclear SSRs, and analysed a set of 89 American and 256
503 European landraces. Gioia et al. [66] combined the data from the recombination of the gene-
504 pool-specific chloroplast SSRs, phaseolin and *PvSHP1* markers and the Bayesian
505 assignments and admixture analysis based on nuclear SSRs, through which they were able
506 to identify hybrids and distinguish them as 'pure' Mesoamerican and Andean genotypes.
507 Novel combinations of genes/ genomic regions thus arose in Europe after the common bean
508 introduction and during its dissemination, on which adaptive selection acted (i.e., adaptive
509 introgression). The new '-omics' technologies can help to fine-tune the molecular basis of
510 these adaptations of the common bean in Europe, an aspect that is ongoing in the
511 BEAN_ADAPT project (funded through the 2nd ERA-CAPS call, ERA-NET for Coordinating
512 Action in Plant Sciences). This project is based on a multidisciplinary approach (i.e.,
513 genomics, population/ quantitative genetics, biochemistry, plant physiology), with the aim
514 being to dissect out the genetic basis and phenotypic consequences of the adaptation of *P.*
515 *vulgaris* and its sister species *P. coccineus* from their centres of origin in the Americas into
516 Europe and the new European agro-ecological environments.
517 Maize is probably the most important New World crop that was involved in the
518 Columbian Exchange. Rebourg et al. [67] characterised a set of 131 European maize
519 landraces according to morphological and genetic data (i.e., restriction fragment length
520 polymorphism), and classified them into genetic groups that showed clear differentiation
521 according to latitude. Six main European races were detected based on morphological and
522 genetic differences: 'German flint', which included landraces mainly grown in Germany or
523 the Alsace; 'north-eastern European flint', which included landraces mainly from France,
524 and also Spain, Portugal and several eastern European countries; 'southern European flint',
525 which was characterised by landraces from various countries which were mainly in southern
526 Europe; 'Italian orange flint', as Italian landraces, with some others from southern Spain;
527 'Czechoslovakian type'; and 'Pyrenees-Galicia flint', which was characterised by two

528 homogeneous subgroups, as the landraces from Galicia, and those from the Pyrenees and
529 other regions of France. Then Rebourg et al. [68] included genetic data of 88 American
530 landraces that were representative of the main American races in their previous dataset [56],
531 to infer the genetic relationships among American and European maize populations. They
532 showed signatures for the introduction of a bottleneck (European landraces retained overall
533 75% of the genetic diversity of those from America), and identified various types of American
534 maize that were introduced into Europe at different times or in different places, which gave
535 rise to distinctive European races [69]. Beyond confirming the importance of Caribbean
536 germplasm, which was the first maize type to be introduced into Europe, they highlighted
537 the close relationship between southern Spain and Caribbean populations, whereby the data
538 revealed that introductions of North American flint populations had a key role in the
539 adaptation of maize to the European climate. In particular, the data supported the hypothesis
540 that present-day northern and eastern European flint germplasm was directly derived from
541 North American flint populations. Northern flint populations were relatively insensitive to day
542 length, and they had low temperature requirements for flowering. Earliness was a key factor
543 for adaptation to the more temperate climates. Brandenburg et al. [70•] sequenced 67
544 genomes from both continents that covered 11 major groups, as representative of all of the
545 American and European diversity. They used several population genomics and association
546 mapping approaches to trace the origins of the European maize, and to investigate its
547 demographic and selective history. One of the main outcomes of this study was the detection
548 of admixture in the European maize materials. In particular, they reported the admixed
549 origins of the Italian flints from two contributions, the European flint and the southern
550 European populations. This excluded the possibility of a third independent introduction, as
551 had previously been suggested by Rebourg et al. [68], and instead emphasised the pivotal
552 role of admixture in environmental maize adaptation. Moreover, the data of Brandenburg et
553 al. [70•] highlighted the admixed origins of the European flints from the northern European
554 flints and the tropical landraces. Interestingly, they also investigated the footprints of
555 selection for adaptation to a wide range of climatic and ecological conditions, and they
556 showed that numerous genes/ gene networks were involved in flowering time, drought and
557 cold tolerance, and in plant defence and starch properties. An example of the candidate
558 genes for adaptation that were detected by associations between latitude and allele
559 frequency was defined at GRMZM2G095955, a gene that is located in the vicinity of the
560 maize floral activator, *ZCN8* [39]. They reported that in the *ZCN8* region there was a
561 haplotype that was common to all temperate materials, and they showed segregation of this

562 ‘temperate’ haplotype with a ‘tropical’ haplotype within the tropics, and to a lesser extent
563 within the corn belt dents. Along with the previously characterised genes, they also revealed
564 new candidates, including *ZCN5* (also known as *zen1* and *pebp5*), a gene from the same
565 family as *ZCN8* that was recently reported to be associated with flowering time variations
566 [71]. They also defined genes associated with plant responses to biotic and abiotic stresses,
567 such as the *ZmASR2* gene (abscisic acid-, stress-, and ripening induced protein 2), which
568 was shown to have increased expression at the transcript and protein level under water-
569 deficit conditions [72], and the *TPS23* gene that is involved in the control of the synthesis of
570 a volatile sesquiterpene that attracts natural enemies of herbivores upon release [73].
571

Conclusions

Deeper understanding of the evolutionary processes and complex genetics mechanisms that form the basis of adaptation of plants to different environmental conditions is a very ambitious goal for evolutionary biologists, breeders and geneticists. It also has strong implications for overcoming the current challenges that agriculture has to face, such as to guarantee food security and quality, to adapt crops to marked variations in climate, and to protect and improve the environment. In this context, the identification of the genetic architecture both at genotype and population level, that contribute to adaptive changes, can strongly influence breeding targets and strategies. The potential applications are nearly infinite for the constitution of novel varieties in breeding programmes, but it will be crucial also for biodiversity conservation, to provide help in the implementation of the appropriate strategies. We have now in-hand novel tools and approaches that allow us to face this challenge through exploiting the unprecedented experimental power available. These include:

(i) Particularly advanced techniques that offer unique opportunities to scan a genome, not only to obtain genotypic information, but also to analyse the molecular phenotype of the whole genome, through analysis of the transcriptome, the metabolome, and the proteome [20, 74-76].

(ii) We can count on improvements to the tools and approaches to analyse these data, which have also evolved to catch the complexity of these biological processes. Population genomics approaches allow the identification of candidate loci for adaptation using genotypic data without any prior information about phenotypes. Along with classical approaches aimed at detection of ‘selective sweeps’ [77], new methods and integrated approaches can be applied that take into account the concept that genes do not often actually operate as sole effectors, as they have roles in complex interactive systems, or gene networks, that ultimately lead to a phenotype [78]. As an example of the impact that gene interactions can have on the determination of the phenotype, an *A. thaliana* genome-wide association analysis reported that for root length, epistatic effects can be so strong that they overcome the additive genetic variance [79•]. In soybean, Fang et al. [80] carried out a comprehensive genome-wide association studies that enabled identification of the underlying genetic loci, loci interaction, and genetic networks across important traits.

(iii) Multidisciplinary approaches can be applied and integrated to decipher the complexity of the genetic basis of adaptation. These can combine evidence from the signatures of selection analyses with association mapping to increase the power for the detection of regions that influence complex traits, while also reducing the number of false-positive signals [81,82]. Moreover, recently, different approaches have been developed based on the use of environmental variables that are treated as quantitative traits, and their association with molecular traits can be exploited as a tool to identify the loci that underlie local adaptation [12,83]. Similarly, network analyses can be used to investigate the roles of interactions between genes in local adaptation [84], using information on linkage disequilibrium shared between genome-wide multiple loci to perform linkage disequilibrium network analyses.

(iv) Landrace populations of crops are the 'perfect' model to apply all of these approaches to investigate adaptation features in the plant genome. They also allow the possibility to compare the effects of the same evolutionary process on the genome when this occurs as the following: independently on different populations of the same species (e.g., domestication in common bean occurred independently in Mesoamerica and the Andes) [18,19]; among different crop species within the same genus (e.g., different domesticated *Phaseolus* species) [16]; and/ or among species of different genera (i.e., shattering trait in cereals) [85] that are characterised by different features (e.g., diverse mating systems, diverse ploidy levels). These aspects offer great opportunities to go deeply into the molecular and developmental mechanisms at the basis of adaptation.

In this scenario, the Columbian Exchange represents a pivotal model. It offers a great opportunity to exploit all of these available tools and approaches, along with the plant genetic resources, to finally dissect out the genetic basis and phenotypic consequences of plant adaptation to new environments. This can now come through the study of their introduction from their respective centres of domestication in the Americas, and their expansion through Europe as a recent and historically well-defined event of rapid adaptation. Numerous crop species have been protagonists of these processes and have experienced adaptation in a relatively short period of time in the same geographic range (i.e., with the same environmental changes). What we need to do now is to investigate this process more deeply in different crops, and to compare and integrate the information obtained. A better understanding of variation in landscape structure across species and environments is also necessary to understand and predict how populations will adapt [86]. Moreover, advances in statistics and increased computing power already provide the possibility to develop predictive approaches, as demonstrated by Exposito-Alonso et al. [87••] who were able to

build genome-wide environmental selection models to predict how evolutionary pressures on species will work in inaccessible environments, or even under future hypothetical climates.

Figure legends

Figure 1. Geographic distribution of barley (top), maize (middle) and common bean (bottom) landraces from their centres of domestication.

The centres of domestication are represented by white dots with black borders. The distributions of the landraces/ traditional cultivar accessions were obtained by plotting the geographic coordinates for where the seeds were collected. Data were extracted from the database of the Genesys platform (https://www.genesys-pgr.org/), which includes information from several genebanks.

Figure 2. Physical map of the 11 common bean chromosomes and genomic locations of genes putatively involved in abiotic stress responses and with selection signatures in common bean.

Common bean genes were identified based on orthology with those involved in abiotic stress responses in *Arabidopsis thaliana*, according to *The Arabidopsis Stress Responsive Gene Database* [21] and using the OrthoFinder algorithm [22]. The orthologous protein to the *A. thaliana* KUP6 is also shown in chromosome Pv03. For the map representation, we selected a subset of 126 common bean orthologues (see **Table S1** for the full list) that show selection signatures according to Schmutz et al. [19] and/or Bellucci et al. [20]. Genes potentially associated to different stress responses based on the orthology with *A. thaliana* genes are highlighted according to the legend. The physical distances in the scale are reported in megabases (Mb).

Figure 3. Schematic representation of *CDF* gene function and interactions in the photoperiod pathway.

During long days, in the *A. thailana* model system **(A)**, the interaction between GIGANTEA (*GI*) and FLAVIN-BINDING KELCH REPEAT F-BOX 1 protein (*FKF1*) induces degradation of CYCLING DOF FACTOR (*CDF*), which is a repressor of CONSTANS (*CO*). *CO* promotes flowering by initiating transcription of the FLOWERING TIME (*FT*) gene. In *S. tuberosum L.* **(B)**, the *CDF* adaptive variant does not interact with the GI-FKF1 complex, which leads to repression of *CO1/2*. In contrast to *A. thaliana*, *CO1/2* act as repressors of *SP6A*, which is

the potato homologue of *FT*. Repression of *CO1/2* allows expression of *SP6A* and promotion of potato tuberisation under long days, which forms the basis of potato diversification at different latitudes. Arrow, promotion of gene expression; truncated arrow, repression of gene expression; truncated dotted arrow, lack of repression due to pathway interruption.

Supplementary

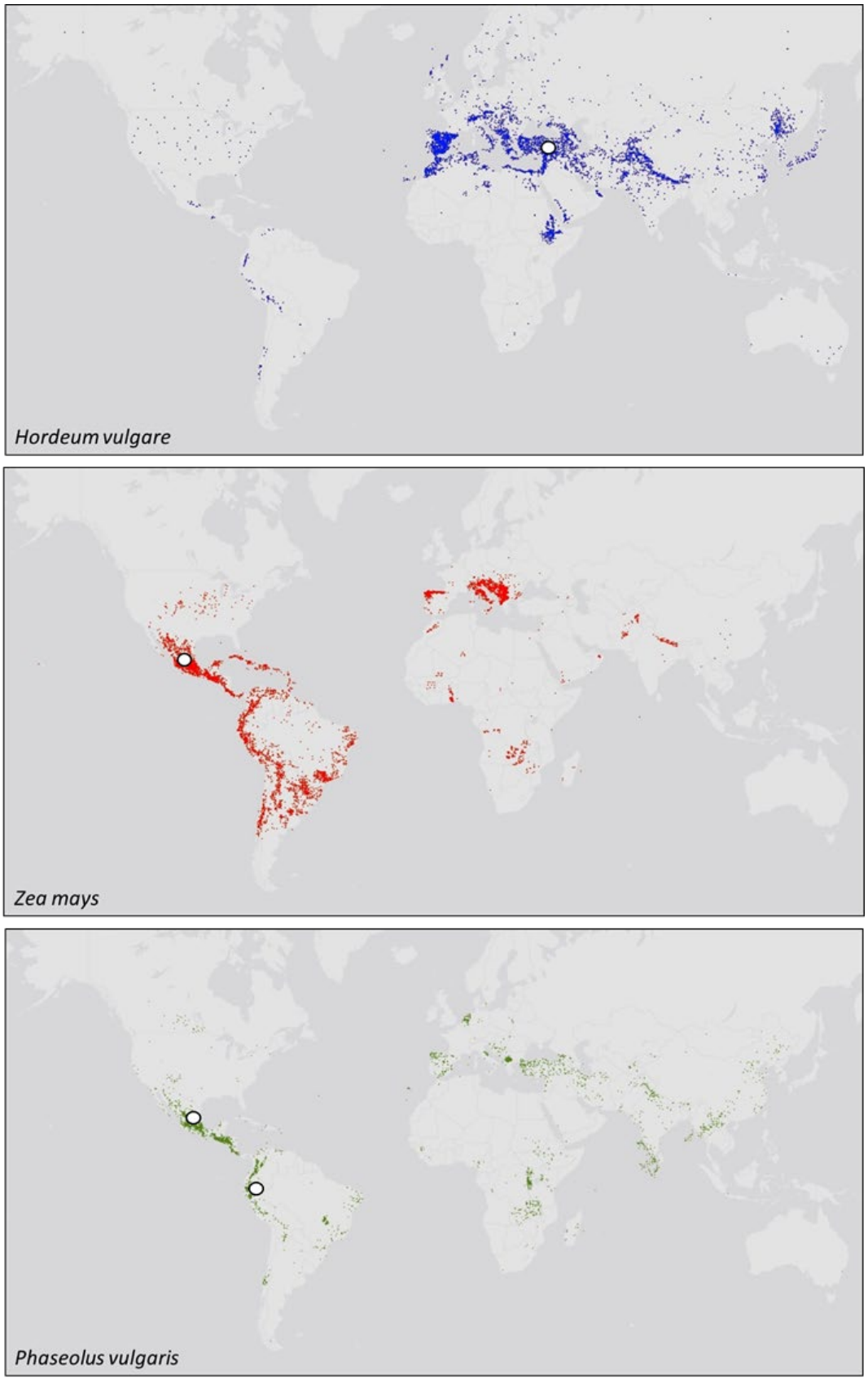
Table S1. Genes putatively involved in abiotic stress responses in common bean.

Genes were identified based on the orthology relationships (OrthoFinder algorithm) [22] with *A. thaliana* genes listed in *The Arabidopsis Stress Responsive Gene Database* [21], and with the KUP6 protein sequence. The orthogroup (i.e., cluster of orthologous genes across *A. thaliana* and common bean), the type of stress response of the orthogroup genes, the common bean gene name, its genomic location and description based on Phytozome, and the presence of selection signatures [19;20] are reported for each common bean gene.

PN; putatively neutral gene.

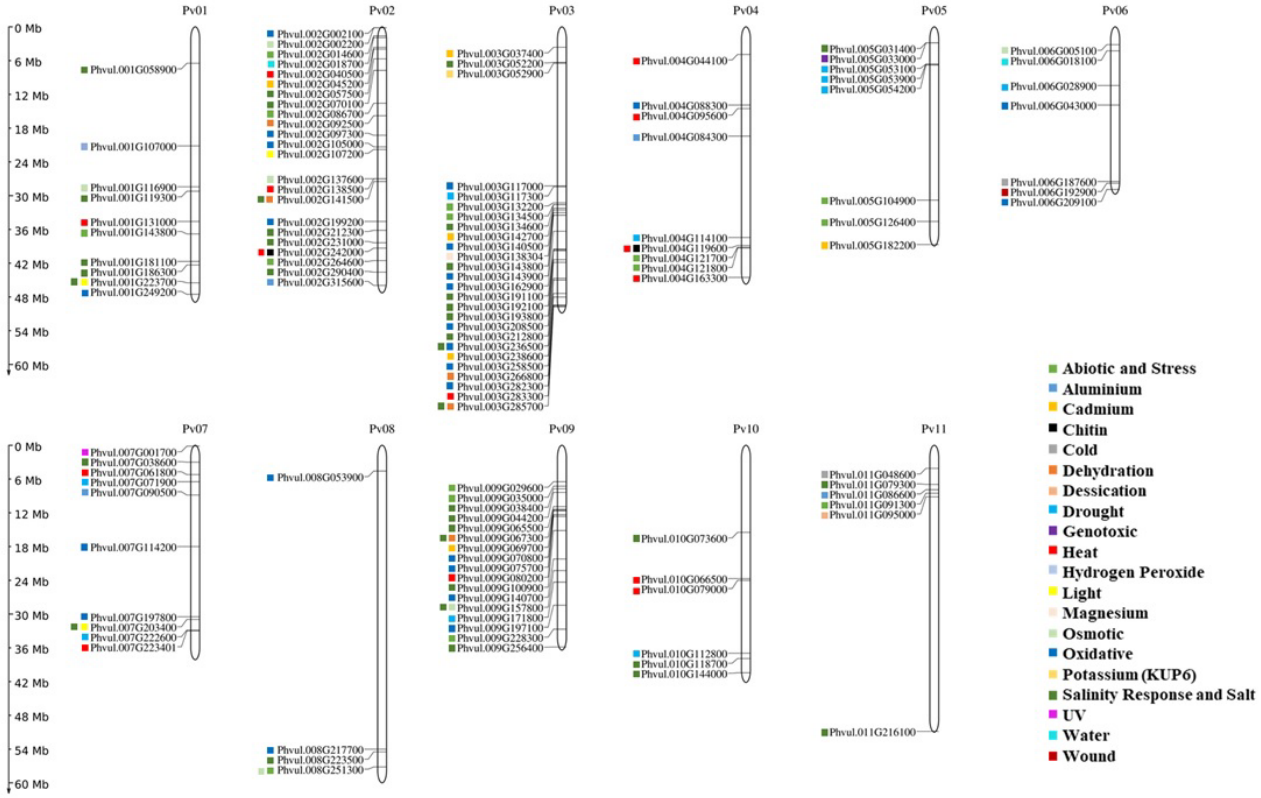
n.m; no homologous contigs from Bellucci et al. (2014) have been identified

* in the column K, according to the data of Bellucci et al. (2014), the PS (putative under selection) contig that mapped on the gene showed polymorphisms for the nucleotide sequence across domesticated accessions and was fixed monomorphic in the wild pool of genotypes.



690

691 **Figure 1**



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693 **Figure 2**

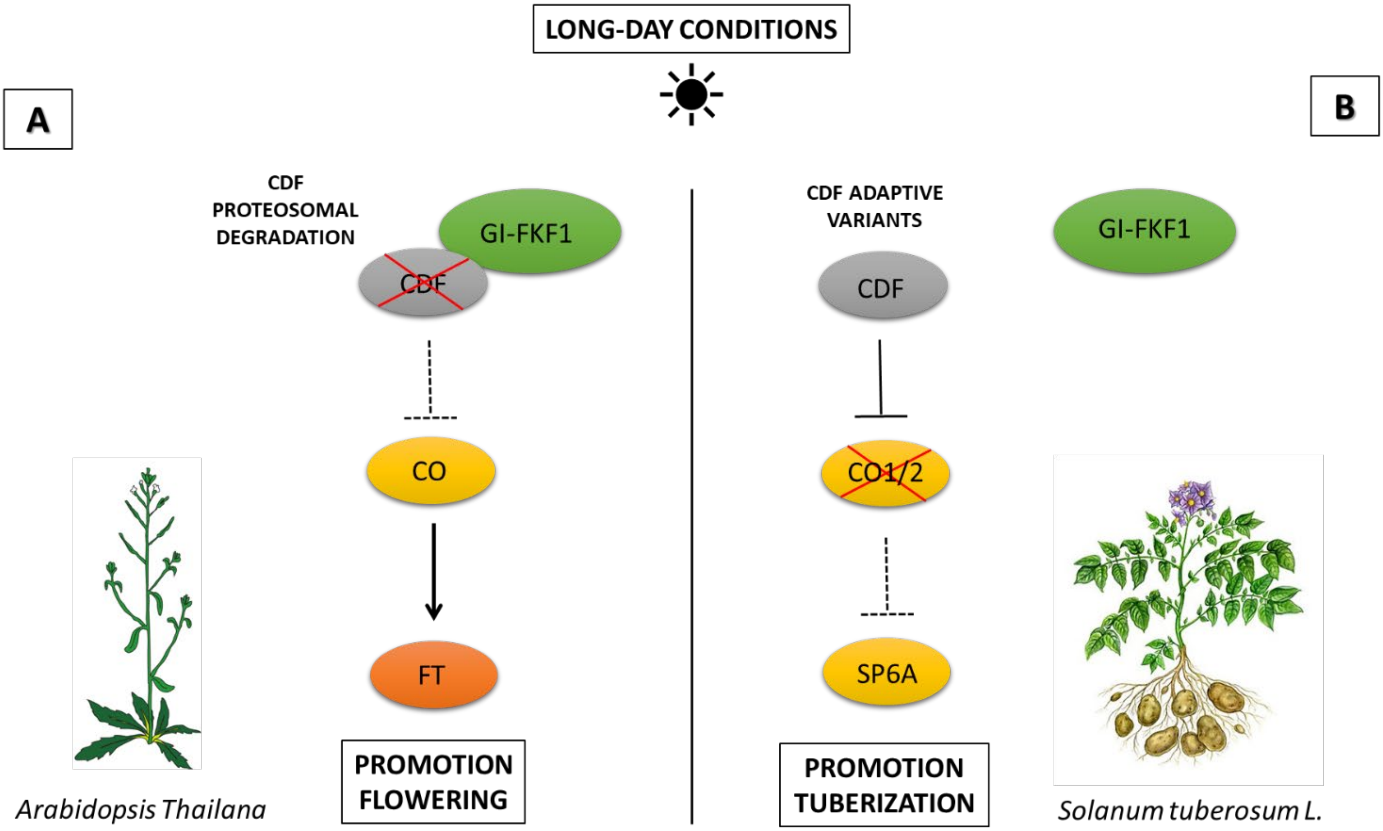
LONG-DAY CONDITIONS
A
B
CDF
PROTEOSOMAL
DEGRADATION
GI-FKF1
CDF
CO
FT
PROMOTION
FLOWERING
CDF ADAPTIVE
VARIANTS
GI-FKF1
CDF
CO1/2
SP6A
PROMOTION
TUBERIZATION
Arabidopsis Thailana
Solanum tuberosum L.

Figure 3

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