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How to be early flowering: an evolutionary perspective

Fabrice Roux[1,3], Pascal Touzet[1], Joël Cuguen[1] and Valerie Le Corre[2]

[1] Laboratoire de Génétique et Evolution des Populations Végétales, UMR-CNRS 8016, FR CNRS 1818, Université de Lille I, F-59655 Villeneuve d'Ascq Cedex, France
[2] UMR 1210 Biologie et Gestion des Adventices, Institut National de la Recherche Agronomique, 17 rue Sully, F-21065 Dijon Cedex, France
[3] Present address: Department of Ecology and Evolution, University of Chicago, 1101 East 57th Street, Chicago, IL 60637, USA

In wild and cultivated annual plant species, flowering time is an important life-history trait that coordinates the life cycle with local environmental conditions. Extensive studies on the genetic basis of flowering time in the model species *Arabidopsis thaliana* have revealed a complex genetic network that can detect environmental and internal signals. Based on this knowledge and on known pleiotropic effects associated with flowering time genes, we suggest that a natural shift towards an early-flowering life cycle might involve only particular functional regions in a limited number of genes. Our predictions are supported by genetic theories of adaptation and by recent data about genes associated with natural variation. We analyse the extent to which these predictions can also apply to crop species.

Flowering time: a keystone in plant adaptation

Flowering time is a major life-history trait that contributes to fitness (see Glossary) in annual plants. Depending on abiotic (photoperiod, temperature, nutrients) and biotic (competition, pollinators, herbivores) conditions, different flowering time strategies can be adopted by different wild plant species and also different strategies can be adopted within a wild plant species. In optimal growing conditions, late flowering leads to a longer vegetative growth period that promotes the accumulation and allocation of more resources to seed production, whereas early flowering is selected in environments with a short or unpredictable growing season [1–3]. The trade-off between resource accumulation and stress avoidance is also of primary importance for crop yield and quality, and the identification of molecular variation associated with flowering time is a key step when selecting varieties adapted to different latitudes and cropping seasons. Our knowledge of the genetic regulation of flowering time in the model plant *Arabidopsis thaliana* has rapidly increased recently. Current data show that floral development is a repressible process when flowering time genes are naturally expressed, which suggests that late flowering is the ancestral character (Box 1) [2,4]. Genes that regulate flowering time have been identified mainly by analysing *Arabidopsis* laboratory mutants with an altered flowering phenotype, many of which are early flowering. However, unlike laboratory-generated variation, adaptive natural variation results from the long process of natural selection, screening mutations according to their global phenotypic effect. We propose to elucidate the genetic determinism of naturally occurring early flowering in *Arabidopsis* using the following approach: (i) examination of the genetic network controlling flowering time, which should enable likely targets of selection for early flowering to be identified; (ii) the study of their associated negative pleiotropic effects should reduce the number of these potential targets; (iii) the number and distribution of the genetic effects that are eventually fixed under selection can be predicted using recent genetic theories of adaptation. Deciphering the genetic determinism of quantitative variation is of interest not only to evolutionary biologists studying the genetics of adaptation in wild species, but also to crop breeders because it could provide useful guidelines for quantitative trait loci (QTL) studies and identification of target genes for selection as well as Marker Assisted Selection [5]. In the last part of this article we extend our approach to the study of evolution towards early flowering in crop species.

Flowering time: a complex trait well described in *Arabidopsis*

The genetic network of flowering time has been reviewed in detail elsewhere [6–9]. In summary, environmental and internal cues are mainly detected by four genetic pathways (Figure 1). The light-dependent pathway involves the perception and integration of changes in photoperiod, light quality and intensity [10]. The light-dependent pathway has also been associated with the response to ambient temperature [6]. Long periods of cold accelerate flowering time via the vernalization pathway [11]. The promotive autonomous pathway is thought to respond to internal developmental signals because mutants associated with this pathway are still able to respond to light and vernalization [8]. Signals from the light-dependent pathway are synthesized by the activity of the floral activator *CONSTANS* (*CO*), whereas signals from the vernalization and autonomous pathways are synthesized at the level of the floral repressor *FLOWERING LOCUS C* (*FLC*). The fourth pathway, the gibberellin (GA) pathway, promotes flowering via the action of hormonal inputs. A prominent

Corresponding author: Le Corre, V. (lecorre@dijon.inra.fr)
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Glossary

Adaptive walk: number, phenotypic size and temporal sequence of genetic changes during the entire approach of a population to a new phenotypic optimum.
CArG box: MADS-domain protein binding element.
Circadian clock: components that synchronize an organism to daily rhythms with a ~24 hour periodicity.
Fisher's infinitesimal model: hypothesis that mutations underlying quantitative variation and adaptation are of extremely small phenotypic sizes, with effects approaching zero. A population therefore approaches a new phenotypic optimum by accumulating slight successive variations.
Fitness: the average number of viable, fertile offspring produced by individuals with a certain genotype relative to the number produced by individuals with other genotypes.
Pleiotropic effect: the phenotypic effect of a gene on more than one trait.
Selective sweep: elimination of much of the neutral variation linked to an advantageous mutation driven by directional selection to fixation in a population.
Vernalization: acceleration of flowering by a long period of cold temperature.

feature of the flowering regulatory network is that all pathways ultimately regulate a common set of key integrator genes, *SUPPRESSOR OF OVEREXPRESSION OF CONSTANS1* (*SOC1*), *FLOWERING TIME* (*FT*) and *LEAFY* (*LFY*), which act on the floral meristem identity genes to initiate flowering [6–9]. It has also been shown that each of the upstream regulators *CO*, *FLC* and the GA pathway act on separate regulatory elements within the *cis*-regulatory regions of the integrator genes *SOC1*, *FT* and *LFY* [12]. Thus, natural selection for early flowering can modify the response to a given environmental cue while maintaining responses to other cues unchanged.

Box 1. Ecological and evolutionary significance of flowering time variation in *Arabidopsis thaliana*

Two distinct life cycles have been described among natural populations of *Arabidopsis thaliana*: winter annuals that germinate in the fall (autumn), overwinter as rosettes and flower in the spring; and single season annuals that germinate and flower in a short period, either in spring or fall. Because of the difference in the length of their vegetative phases these two phenotypes are referred to as 'late' and 'early' flowering. Several data suggest that flowering time is under selection in *Arabidopsis*, with early flowering being the derived state, although these issues are still debated.

Because the environmental cues used by plants to adjust their life cycle vary systematically with latitude, a latitudinal cline in flowering time would suggest local adaptation. However, in *Arabidopsis*, no clear and consistent patterns have been found across studies [16,18]. A systematic geographical trend might well be masked by the influence of other selective agents that vary locally. Although a correlation between flowering time and January precipitation has been found [16], the role of other factors has not been properly analysed yet because a precise local description of abiotic and biotic factors is lacking for most natural accessions.

Direct phenotypic analyses seeking correlations between fitness and variation in a trait have been rarely conducted. However, strong directional selection favouring early flowering was detected in a field study of two North American populations [45]. The among-population differentiation for flowering time has been either compared with neutral genetic differentiation [46,47] or examined using transplantation experiments [48]. Some evidence for local selection has been found in Western Europe, but not in the more peripheral regions of the range of the species (Scandinavia). Local adaptation might be hindered by demographic instability (extinction–recolonizations), so some populations might be transient and not locally adapted.

Finally, reverse genetic approaches have identified the *FRIGIDA* (*FRI*) gene as the main contributor to species-wide flowering time variation [18]. Most early-flowering accessions carry a *FRI* allele with a loss-of-function mutation. Numerous such alleles have been described, suggesting that early-flowering types have evolved independently from late-flowering ancestral types several times [14,18]. Furthermore, the selective sweep signature and extensive linkage disequilibrium associated with those alleles found in worldwide accessions [31,49] suggest that they have been driven by strong recent directional selection favouring earlier flowering at the species level.

Target elements of selection for early flowering

By integrating the known functions of the different proteins and their interaction with promoter regions in the flowering time pathways in *Arabidopsis*, we identified the target genes where molecular variation would be likely to result in a phenotypic change toward greater precocity. Although floral repressive genes are generally thought to be the main target of selection for early flowering, selection on floral promotive genes could also lead to adaptive early flowering (Tables 1 and 2).

Floral repressive genes

Floral repressive genes are: *FLC* and its activators, other repressor genes including some homologues of *FLC*, and the genes involved in gibberellin signalling, which are negative regulators of flowering in the absence of gibberellins. Disruption of any functional domain in these genes can result in early flowering. The loss of sensitivity of *FLC* to its upstream positive regulators is expected to have a similar effect. These points are supported by recent studies on natural variation in *Arabidopsis*. Indeed, several loss-of-function mutations in *FRIGIDA* confer early flowering [13–19]. Loss-of-function mutations were also found in *FLC* [20]. Moreover, the first intron of *FLC*, an important *cis*-regulatory region for the gene, has independent transposon insertions that reduce the *FLC* expression level [17,20,21]. A more peculiar case is the complete deletion of the *FLOWERING LOCUS M* (*FLM*), which is responsible for early flowering of the single accession Niederzenz [22].

Floral promotive genes

Floral promotive genes can be sorted according to the region affected by selection for early flowering. (i) The *cis*-regulatory regions of integrative and meristematic genes are likely targets. They consist of separate motifs, each regulated by a single pathway. In *Arabidopsis*, *FLC* specifically recognizes a CArG box within the *SOC1* promoter [23]. Altering this motif leads to an early-flowering phenotype in laboratory mutants. (ii) Early flowering can arise from mutations in specific domains of *CRYPTOCHROME 1 and CRYPTOCHROME 2* (*CRY1* and *CRY2*) and *PHYTOCHROME A* (*PHYA*) that enhance their own protein stability and, therefore, *CO* activation. A point mutation in *CRY2* confers early flowering under short-day conditions in one tropical accession of *Arabidopsis* [24].

Negative pleiotropic effects can limit the number of target genes

The almost complete dissection of the flowering time genetic network in Arabidopsis gives us functional

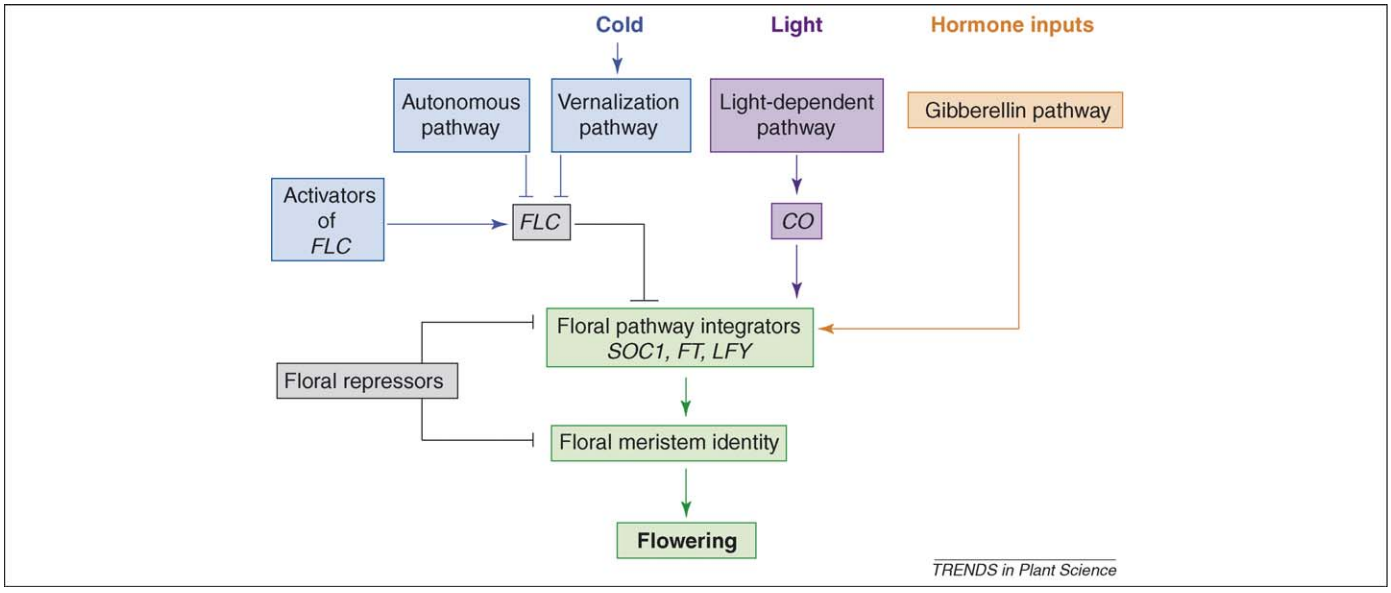

Figure 1. Interacting flowering time genetic pathways. Although complex interactions occur among the different flowering-time genetic pathways (See Ref. [9] for example), we have intentionally simplified the overall network of flowering-time regulation for a better understanding. Abbreviations: *CO, CONSTANS*; *FLC, FLOWERING LOCUS C*; *FT, FLOWERING TIME*; *LFY, LEAFY*; *SOC1, SUPPRESSOR OF OVEREXPRESSION OF CONSTANS*.

arguments to discriminate the potential genes selected for early flowering. However, this knowledge of the molecular genetic pathways does not necessarily indicate which genes are variable and likely to contribute to the evolutionary response to selection. In addition, because natural selection acts on phenotypes, the number of target elements selected for early flowering can be limited by negative pleiotropic effects. For example, mutations in the *EMBRYONIC FLOWER 1* (*EMF1*) and *EMBRYONIC FLOWER 2* (*EMF2*) floral repressors confer an extremely early-flowering phenotype but are also associated with a drastic reduction in seed production [6]. In the light-dependent pathway, mutations in *PHYTOCHROME B* (*PHYB*) and *EARLY-FLOWERING 3* (*ELF3*) alter seed germination and the circadian clock, respectively [25]. Under natural conditions, such mutations would be disadvantageous and, therefore, would be selected against. To take this into account, we classified the genes according to their negative pleiotropic effects in laboratory mutants of *Arabidopsis*: group A, no pleiotropic effects observed; group B, pleiotropic effects observed for life-history traits; and group C, pleiotropic effects observed for seed production, a major component of fitness in *Arabidopsis* (Tables 1 and 2). Groups A, B and C indicate a high, medium and low probability of selection for early flowering, respectively. However, this classification suffers from three limitations. First, Tables 1 and 2 are incomplete. The negative pleiotropic effects of many *Arabidopsis* flowering-time mutants have not yet been described. We therefore encourage physiologists to describe the phenotypes thoroughly during the characterization of their mutant lines. Second, its predictive value depends on the conservation of the negative pleiotropic effects between *Arabidopsis* and other species. Research characterizing pleiotropy of gene function in a comparative manner and its conservation across species would be useful. Third, the pleiotropic effects noted in Tables 1 and 2 are preliminary, and would need confirmation based on investigations of pleiotropic effects under natural conditions [26].

Selection for early flowering: an adaptive walk?

Flowering time is a quantitative trait controlled by multiple genes. For decades, predicting the evolution of adaptive quantitative traits has mainly relied on Fisher's infinitesimal model, but recent genetic theories of adaptation have shed new light on the matter (Box 2) [27–29]. During adaptive evolution, the response to selection is mostly achieved via the fixation of a few mutations having large fitness effects and several additional mutations that have much smaller effects. Mutations that have large fitness effects are those that confer the largest progress towards the optimal phenotype (flowering time in this case) while having the lowest negative pleiotropic effects.

Although the relative importance of standing genetic variation as opposed to new mutations as a source of beneficial alleles is still a matter of debate among evolutionists, some predictions could be tested in a model species such as *Arabidopsis* by measuring the fitness effects of alleles that show evidence of selective sweep [29]. To our knowledge, this approach has never been undertaken. Future research in this area should test whether loci with small effects on phenotypes show less evidence of selection at the molecular level. However, the theoretical expectations agree with the results of genetic mapping studies of QTL for flowering time variation in *Arabidopsis*. Among the 14 different QTLs identified [30], the major effect loci *FRI* and *FLC* were repeatedly identified in crosses involving one late-flowering accession and one early-flowering accession. Loss-of-function mutations at *FRI* account for as much as 70% of the flowering time variation [18]. The adaptive nature of the variation at *FRI* was also suggested by molecular signatures [31] (Box 1). Loss-of-function can appear in multiple ways, and thus at a high rate, whereas adjusting the function of a protein requires specific amino-acid changes.

Table 1. Potential floral repressive genes under selection for early flowering

Gene name[a]	Abbreviation	Target of selection for early flowering	Negative pleiotropic effects based on studies in *Arabidopsis thaliana*[b,c]	Class[b,d]
Activators of *FLC*				
FRIGIDA	*FRI*	Coding regions	Modified water-use efficiency (a character genetically correlated with flowering time)	A
FRIGIDA-LIKE1 and *2*	*FRL1, FRL2*	Coding regions	No pleiotropic effects observed	A
FRIGIDA-ESSENTIAL1	*FES1*	Coding regions	No pleiotropic effects observed	A
PAF1 complex				
EARLY-FLOWERING7 and *8*	*ELF7, ELF8*	Coding regions	Smaller rosette leaves, altered petal number (pleiotropic effects are background dependent)	B
EARLY FLOWERING IN SHORT DAYS	*EFS*	Coding regions	Reduction in fertility, plant size and apical dominance	C
EARLY IN SHORT DAYS4	*ESD4*	Coding regions	Premature termination of the shoot, no rosette leaves under long days, smaller cauline leaves	B
PHOTOPERIOD INSENSITIVE1	*PIE1*	Coding regions	Narrow serrated leaves in a Ws background, reduced fertility in a Col background	C
VERNALIZATION INDEPENDENCE 3	*VIP3*	Coding regions	Overall reduced plant size, predominately male sterile	C
VERNALIZATION INDEPENDENCE 4	*VIP4*	Coding regions	Smaller rosette leaves, altered petal number, predominately male sterile	C
Floral repressors				
EARLY BOLTING IN SHORT DAYS	*EBS*	Coding regions	Reduction in seed dormancy, plant size and fertility	C
EMBRYONIC FLOWER1 and *2*	*EMF1, EMF2*	Coding regions	Abnormal vegetative phase (no rosette development), abnormal and incomplete flowers	C
FLOWERING LOCUS C	*FLC*	Coding regions (+ first intron)	Modified water-use efficiency (a character genetically correlated with flowering time)	A
	HUA2	Coding regions	No pleiotropic effects observed	A
MADS AFFECTING FLOWERING 1	*MAF1/FLM*	Coding regions	No pleiotropic effects observed	A
MADS AFFECTING FLOWERING 2, 3 and *4*	*MAF2, MAF3, MAF4*	Coding regions	?	?
SCHLAFMUTZE	*SMZ*	Coding regions	?	?
SCHNARCHZAPFEN	*SNZ*	Coding regions	?	?
SHORT VEGETATIVE PHASE	*SVP*	Coding regions	No pleiotropic effects observed	A
TARGET OF EAT1 and *2*	*TOE1, TOE2*	Coding regions	?	?
TERMINAL FLOWERING LOCUS1	*TFL1*	Coding regions	Determinate inflorescence, reduced seed production	C
TERMINAL FLOWERING LOCUS2	*TFL2*	Coding regions	Formation of a terminal flower and dwarfism, reduced photoperiod sensitivity	B
Light-dependent pathway				
CIRCADIAN CLOCK ASSOCIATED1	*CCA1*	Coding regions	Incorrect matching of circadian rhythms to environmental rhythms (photoperiod) results in: reduced leaf chlorophyll content, reduced assimilation, reduced growth and increased mortality	B
EARLY-FLOWERING3	*ELF3*	Coding regions		B
LATE ELONGATED HYPOCOTYL	*LHY*	Coding regions		B
PHYTOCHROMEB	*PHYB*	Coding regions		B
TIMING OF CAB1	*TOC1*	Coding regions		B
Gibberellin pathway				
GIBBERELLIC ACID INSENSITIVE	*GAI*	Coding regions except DELLA domains	Shorter siliques and reduction in fertility	C
REPRESSOR OF GA1-3	*RGA*	Coding regions except DELLA domains	Shorter siliques and reduction in fertility	C
RGA-LIKE 1	*RGL1*	Coding regions except DELLA domains	Shorter siliques and reduction in fertility	C
SPINDLY	*SPY*	Coding regions except DELLA domains	Pale-green foliage, partial male sterility, parthenocarpic fruit development	C
Vernalization pathway				
HIGH EXPRESSION OF OSMOTICALLY RESPONSIVE GENES 1	*HOS1*	Coding regions	Deficiency in cold tolerance	B

[a]The molecular identification of the genes is described in recent reviews [6–9].
[b]'?' indicates no available data to predict potential negative pleiotropic effects (because of recent molecular identification of corresponding genes).
[c]See Table S1 in the Online Supplementary Material for references describing the negative pleiotropic effects associated with flowering time genes.
[d]Probability of selection for early flowering: A, high probability; B, medium probability; C, low probability.

Table 2. Potential floral promotive genes under selection for early flowering

Gene name[a]	Abbreviation	Target of selection for early flowering	Negative pleiotropic effects based on studies in *Arabidopsis thaliana*[b,c]	Class[b,d]
Floral pathways integrators				
FLOWERING TIME	*FT*	Promoters	Unexpected pleiotropic effects for mutations localized in the promoter regions	A
LEAFY	*LFY*	Promoters	Unexpected pleiotropic effects for mutations localized in the promoter regions	A
SUPPRESSOR OF OVEREXPRESSION OF CONSTANS	*SOC1*	Promoters	Unexpected pleiotropic effects for mutations localized in the promoter regions	A
Floral meristem identity genes				
APETALA1	*AP1*	Promoters	Unexpected pleiotropic effects for mutations localized in the promoter regions	A
Light-dependent pathway				
CRYPTOCHROME1 and *2*	*CRY1, CRY2*	Coding regions	Shorter fruit length, reduction in ovule number and fertility	C
PHYTOCHROMEA	*PHYA*	Coding regions	Deficiency in germination	B

[a]The molecular identification of the genes is described in recent reviews [6–9].
[b]'?' indicates no available data to predict potential negative pleiotropic effects (because of recent molecular identification of corresponding genes).
[c]See Table S1 in the Online Supplementary Material for references describing the negative pleiotropic effects associated with flowering time genes.
[d]Probability of selection for early flowering: A, high probability; B, medium probability; C, low probability.

Loss-of-function is also expected to result in greater phenotypic effects. Therefore, the first and largest mutations selected during a bout of adaptation towards early flowering are likely to be loss-of-function mutations [32].

Box 2. Genetic theories of adaptation

Most of the recent genetic theories of adaptation stem from Fisher's geometric model [27–29]. This model pictures an organism as a point in an n-dimensional space, with each dimension representing a phenotypic trait value. A given point in this phenotypic space represents a fitness optimum. A recent environmental change can move a population away from the optimum. The Fisher–Orr model [28] describes the entire adaptive walk taken by a population to move towards the new optimum. The optimum is assumed to be fixed during adaptation and fitness is a continuous function of the phenotype. Although standing genetic variation can be a source of beneficial alleles, the model considers evolution from new mutations. Each of the successive steps during the walk similarly results in the fixing of a new mutation. The main predictions of the model are:

- The distribution of factors fixed during adaptation is nearly exponential.
- Fixed effects approximate a geometric sequence over time, with mutations with a larger phenotypic effect generally substituted first, and mutations with a smaller phenotypic effect substituted later.
- The size of the largest factor fixed is fairly large (large adaptive jumps are thus expected at the beginning of the walk).

This model was further modified to account for the molecular basis of phenotypic variation [29]. The theory of adaptation of DNA sequences or the 'mutational landscape model' makes the same assumptions as the Fisher–Orr model and assumes in addition strong selection and weak mutation, so that a population is essentially fixed for a single sequence at any time. The chance that a particular beneficial mutant sequence is the next substituted sequence is proportional to the fitness effect of that sequence. The predictions of this model are similar to those of the phenotypic model. The main prediction is that the distribution of the fitness effects of the mutations fixed during adaptation is a decreasing exponential.

When adaptation originates from standing genetic variation, the fixation probability of an allele depends on its deleterious and beneficial effects before and after the environmental change, respectively [50]. If a beneficial allele is originally neutral or weakly deleterious, its fixation probability is weakly dependent on its selection coefficient after the environmental change. The reason is the high initial frequency of the fixed allele. Therefore, adaptation from standing variation might result in the selection of alleles with smaller effects than adaptation from new mutations.

Several QTLs with smaller effects have been identified in crosses involving early-flowering accessions. These QTLs differ among different crosses and are strongly environment-dependent [33]. A high level of diversity in flowering time responses to various environmental cues was also detected among non-functional *FRI Arabidopsis* accessions [17]. Several different small-effect alleles belonging to all regulatory pathways also seem to have been selected during the evolution towards early flowering, depending on local key environmental factors (Box 1). Further characterization of the natural variation underlying QTLs with smaller effects are needed to validate our list of potential target genes under selection for early flowering (Tables 1 and 2).

Future prospects for the genetic dissection of flowering time variation in crop species

Our predictions are largely based on our present knowledge of the model plant *Arabidopsis* and on genetic theories of adaptation developed for natural populations. The relevance of these predictions must be adjusted to the specificities of crop species.

Flowering time evolves under different ecological constraints in different crop species

Under temperate climates, the main constraint on flowering time is set by cold temperatures during winter: vernalization is the major stimulus used by plants to adjust their flowering date, whereas photoperiod is less decisive. This is the case for *Arabidopsis* (Box 1). In temperate crop species, such as wheat, barley, pea or oilseed rape, both winter and spring varieties exist, indicating a strong potential for evolution of the response to vernalization. By contrast, most tropical species such as rice and maize are short-day plants that are highly responsive to photoperiod, an indicator that acts as a cue to the alternation of dry and humid seasons. Other plants can respond preferentially to ambient temperatures or to internal hormonal signals (e.g. tomato) [9]. The regulatory pathway within which selection for early flowering is more likely to occur

would thus depend on the principal features of the biology and environment of each plant species.

Conservation among species of the genetic pathways controlling flowering time

For the light-dependent, autonomous, GA, integration and meristematic pathways, comparative genetic approaches show that flowering time genes are conserved between *Arabidopsis* and a large range of crop species, including legumes [34] and cereals [35–38]. The light-dependent pathway is particularly well conserved. The light receptors (phytochromes and cryptochromes) are found across all plant taxa [39], and a single base substitution in *PHYA* was associated with early flowering in a laboratory mutant of *Pisum sativum* [40]. Other genes are conserved but have developed distinct functions among species with different photoperiod requirements: *CO* only has a promoting action under long days in *Arabidopsis*, but has both a repressing action under long days and a promoting action under short days in rice [37]. By contrast, the vernalization pathway is only partially conserved. In *Arabidopsis*, the two major genes *FRI* and *FLC* do not seem to exist in dicots other than *Brassicaceae* [34], and the response to vernalization involves another set of genes in the monocots [4,38]. However, the two recently identified vernalization genes *VRN1* and *VRN2* in cereals are not new genes but are homologues of the *Arabidopsis* meristematic gene *APETALA1* (*AP1*) and the widely conserved *CONSTANS*-like gene family, respectively [4,41]. Therefore, in other species, potential genes under selection for early flowering described in Tables 1 and 2 must be reconsidered according to the consistency of genetic architecture among plant families, particularly for the vernalization-dependent pathway.

Adaptive evolution under human selection

The notion of a few QTLs with a large effect playing a major role in adaptation has not only been verified in *Arabidopsis* but is also supported by results from divergent crop species. For example, in rice, allelic variation of the *CONSTANS*-like gene *Hd1* explains more than 60% of the variation in flowering time [5]. In wheat, *VRN* genes completely explain the differentiation into winter and spring varieties [4,41]. However, selection pressures acting on wild and domesticated species are qualitatively and quantitatively different so theoretical predictions from models of adaptation might differ.

(i) In crop species, some negative pleiotropic effects found in *Arabidopsis* can be considered harmless by the plant breeder under agronomic conditions. For example, in maize, polymorphisms at the *Dwarf8* gene (a homologue of the *GAI* gene in *Arabidopsis*) that are associated with early flowering also confer dwarfism [42], a character that should be considered as neutral under agronomic conditions with weed control but should be counter-selected under natural conditions.

(ii) Natural selection is thought to operate generally via a smooth increase of fitness to an optimum, whereas artificial selection often operates via strong truncation selection. Under artificial selection, any factor capable of crossing the selection threshold will be fixed. Adaptation in domesticated species might therefore more frequently involve a single factor with a large effect rather than multiple factors with exponentially distributed effects [28]. Even though this view is extreme (because domestication and subsequent plant breeding involve several rounds of selection), it is likely that fewer small-effect loci have been fixed in domesticated species than in wild species.

(iii) Because human selection operates over short time scales and rare beneficial variants are likely to be missed by breeders [43], adaptation in crops probably involves the occurrence of a high level of variation, such as loss-of-function mutations with a large phenotypic effect. Indeed, many of the natural mutations associated with early flowering in crops cause loss-of-function of repressive genes: complete deletion of *LATE FLOWERING*, a homologue of the *TFL1* gene, in *P. sativum* [44]; deletion of *VRN2* (a functional homologue of *FLC*) in diploid wheat (*Triticum monococcum*) and barley [41]; alteration of a key domain in the coding region of *Dwarf8* in maize [42]. Loss-of-function in the regulatory part of a promotive gene is also known: for example, the independent natural deletions of the CArG box in *VRN1* in *T. monococcum* and in bread wheat [4].

Conclusion

Using a functional approach, we have identified flowering time genes that are likely to be targets of selection for early flowering. We have proposed that their number might be reduced because of negative pleiotropic effects. The number and distribution of the genetic effects fixed under selection for early flowering in *Arabidopsis* seems consistent with general expectations of genetic theories of adaptation, suggesting that many QTLs remain to be identified. To achieve this, a better comprehension of the ecological determinants of flowering time evolution in this species is needed as well as an assessment of the allelic phenotypic size of candidate genes.

In addition to *Arabidopsis*, the genetic architecture of flowering time is mainly being deciphered in rice. Even though these two species are different, they do not span the range of phylogenetic and ecological diversification of crops. Comparative studies of additional model species are needed to uncover the diversity of evolutionary trajectories leading to early flowering. However, one of our main predictions is that a few genes with large effects are probably involved in early flowering in domesticated species, making the analysis of this trait easier in crops than in wild species such as *Arabidopsis*.

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Supplementary data

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