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REVIEW ARTICLE

The Transition to Flowering

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INTRODUCTION

The general body plan of plants is established during embryogenesis, when the undifferentiated meristematic regions of root and shoot are set aside. However, much of plant development occurs postembryonically, through the reiterative production of organ primordia at the shoot apical meristem (SAM). In most species, the SAM initially gives rise to vegetative organs such as leaves, but at some point the SAM makes the transition to reproductive development and the production of flowers.

This change in the developmental fate of primordia initiated at the SAM is controlled by environmental and endogenous signals (Bernier, 1988; McDaniel et al., 1992). However, unlike many developmental transitions in animals, the SAM of plants is not irreversibly "committed" to reproductive development once flowering commences. In some species and genotypes under certain environmental conditions, leafy shoots are formed after flowers in a phenomenon known as inflorescence reversion (see, e.g., Battey and Lyndon, 1990; Pouteau et al., 1997). This observation implies that the genes and processes involved in the transition to flowering are required to both initiate and maintain reproductive development.

Because many species must reach a certain age or size before they can flower, the vegetative meristem is thought to first pass through a "juvenile" phase in which it is incompetent to respond to internal or external signals that would trigger flowering in an "adult" meristem. The acquisition of reproductive competence is often marked by changes in the morphology or physiology of vegetative structures—leaf shape offers one example—in a process known as vegetative phase change (Poethig, 1990; Lawson and Poethig, 1995). It is likely that some of the genes identified as important in controlling the transition from vegetative to reproductive development are also involved in vegetative phase change.

In some species, the timing of flowering is primarily influenced by environmental factors, which serve to communicate the time of year and/or growth conditions favorable for sexual reproduction and seed maturation. These factors include photoperiod (i.e., day length), light quality (spectral composition), light quantity (photon flux density), vernalization (exposure to a long period of cold), and nutrient and water availability. Other species are less sensitive to environmental variables and appear to flower in response to internal cues such as plant size or number of vegetative nodes. Flowering can also be induced by stresses such as nutrient deficiency, drought, and overcrowding. This response enables the plant to produce seeds, which are much more likely to survive the stress than is the plant itself.

Over the years, physiological studies have led to three models for the control of flowering time (reviewed in Bernier, 1988; Thomas and Vince-Prue, 1997). The florigen concept (reviewed in Lang, 1952; Evans, 1971) was based on the transmissibility of substances or signals across grafts between reproductive "donor" shoots and vegetative "recipients." It was proposed that florigen, a flower-promoting hormone, was produced in leaves under favorable photoperiods and transported to the shoot apex in the phloem. The identification of a graft-transmissible floral inhibitor also led to the concept of a competing "antiflorigen." Many research years were consumed hunting for florigen in the phloem sap, but its chemical nature has remained elusive.

The inability to separate the hypothetical flowering hormones from assimilates led to a second model, the nutrient diversion hypothesis. This model proposed that inductive treatments result in an increase in the amount of assimilates moving to the apical meristem, which in turn induces flowering (reviewed in Sachs and Hackett, 1983; Bernier, 1988).

The view that assimilates are the only important component in directing the transition to flowering was superseded by the multifactorial control model, which proposed that a number of promoters and inhibitors, including phytohormones and assimilates, are involved in controlling the developmental transition (Bernier, 1988). According to this model, flowering can only occur when the limiting factors are present at the apex in the appropriate concentrations and at the right times. This model attempted to account for the diversity of flowering responses by proposing that different factors could be limiting for flowering in different genetic backgrounds and/or under particular environmental conditions.

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Genetic analysis of flowering time in pea, cereals, and Arabidopsis supports the hypothesis that the transition to flowering is under multifactorial control (reviewed in Snape et al., 1996; Weller et al., 1997; Koornneef et al., 1998b). Indeed, multiple genes that control flowering time have been identified in all three of these species. Moreover, some of these genes act to promote flowering and others to repress it; some interact with environmental variables and others appear to act autonomously.

The most striking recent advances in our understanding of the genetic control of the timing of flowering have come from work on Arabidopsis. This area of research has been extensively reviewed (see Martínez-Zapater et al., 1994; Haughn et al., 1995; Weigel, 1995; Amasino, 1996; Aukerman and Amasino, 1996; Dennis et al., 1996; Hicks et al., 1996; Madueño et al., 1996; Peeters and Koornneef, 1996; Wilson and Dean, 1996; Coupland, 1997; Koornneef et al., 1998b; Levy and Dean, 1998; Piñeiro and Coupland, 1998), and a number of key findings have emerged. Flowering involves the sequential action of two groups of genes: those that switch the fate of the meristem from vegetative to floral (floral meristem identity genes), and those that direct the formation of the various flower parts (organ identity genes). Therefore, genes that control flowering time can be expected to interact with floral meristem identity genes, which in Arabidopsis include *LEAFY* (*LFY*), *APETALA1* (*AP1*), *CAULIFLOWER* (*CAL*), *AP2*, and *UNUSUAL FLORAL ORGANS* (*UFO*). The floral meristem identity genes are themselves capable of influencing flowering time. For example, overexpression of *LFY* and *AP1* causes early formation of determinate floral meristems (Mandel and Yanofsky, 1995; Weigel and Nilsson, 1995), whereas mutations in *TFL1* affect both flowering time and meristem identity (Shannon and Meeks-Wagner, 1991). The regulation of floral meristem identity genes is under intense investigation. However, because of space constraints, this topic is covered here only briefly (for recent reviews, see Ma, 1997; Piñeiro and Coupland, 1998).

To complement earlier reviews, we describe here the current view of the control of flowering time and discuss the classic physiological studies in the context of recent molecular genetic advances. We begin by introducing the genes and mutations identified in Arabidopsis that are known to influence the timing of flowering. On the bases of their phenotypes under different growth conditions and genetic epistasis experiments, these mutants and genes are grouped into separate pathways that either promote or repress flowering. The role of DNA methylation in flowering is covered in two places to discuss separately its possible role in repression of flowering and its hypothesized role in vernalization.

In the second section, we examine the role of substances such as phytohormones that classically have been implicated in the control of flowering time and attempt to place these substances in the promotive and repressive genetic pathways. In the final section, we discuss recent data on genetic interactions that control the floral transition, and we present an updated model that attempts to summarize some of the known interactions.

GENETIC CONTROL OF FLOWERING

Arabidopsis is a facultative long-day plant; thus, long-day photoperiods are inductive, and short-day photoperiods are noninductive. The majority of Arabidopsis ecotypes are winter annuals, that is, they flower late unless they have experienced a vernalization period. This feature allows them to overwinter vegetatively and to delay flowering until favorable conditions arrive in the spring. Genes that affect flowering time in Arabidopsis have been identified through analyses of natural variation in different ecotypes and through characterization of induced mutations. The currently identified genes that are considered to play a role in flowering-time control are summarized in Figure 1 and Table 1.

Most of the genes identified by mutagenesis are derived from three rapid-cycling progenitor ecotypes: Landsberg *erecta* (L*er*), Wassilewskija (WS), and Columbia (Col). The analysis of flowering-time variation in the naturally late-flowering ecotypes therefore complements the mutagenic approach, particularly regarding repressors of the floral transition. A number of genes—*FRI*, *FLC*, *FKR*, *JUV*, and *KRY*—and quantitative trait loci (QTLs) that are not represented in the mutant collections have been identified by this approach (Figure 1 and Table 1; reviewed in Koornneef et al., 1998b). Taken together, there are currently ~80 loci in Arabidopsis that are known to affect flowering time.

The response of flowering-time mutants to environmental treatments, such as vernalization and photoperiod (Table 1), combined with genetic analyses of epistasis, have established the existence of at least four pathways that control flowering time in Arabidopsis (Figure 2). Two of these pathways appear to monitor the endogenous developmental state of the plant. The floral repression pathway(s) may be a built-in mechanism that prevents flowering until the plant has reached a certain age or size, whereas the autonomous promotion pathway is believed to increasingly antagonize this repression as the plant develops. The other two pathways mediate signals from the environment: the photoperiodic promotion pathway is responsible for floral induction in response to inductive photoperiods, and the vernalization promotion pathway allows flowering to occur after experiencing an extended period of cold temperature (Figure 2).

Floral Repression Pathways

The identification of loss-of-function mutations that accelerate flowering in rapid-cycling ecotypes such as L*er* reveals that even in early-flowering ecotypes, some genes act to repress flowering. Most early-flowering mutants have been categorized by their response to photoperiod (Table 1); some (e.g.,

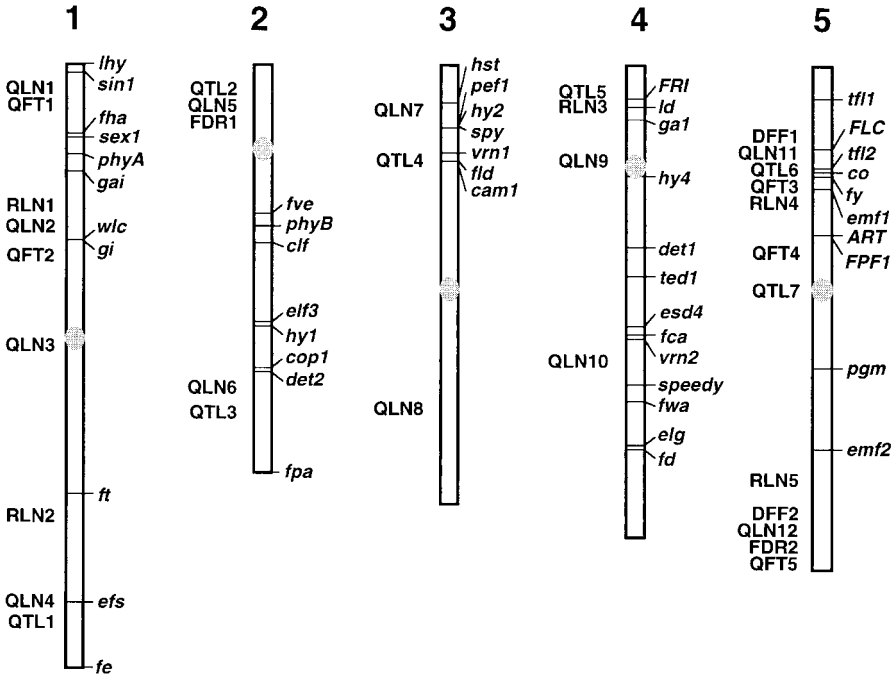

Figure 1. Genetic Map Showing the Approximate Positions of the Genes and Quantitative Trait Loci That Affect Flowering Time in Arabidopsis.

This map, which has been updated from that shown in Koornneef et al. (1998b), shows the five chromosomes as vertical bars, with the centromeres indicated by gray ellipses. Mutant loci are given in lowercase, whereas loci identified in natural populations are given in uppercase. The QTLs were initially described in the following publications: QLN1-12, Jansen et al. (1995); QFT1-5 and QTL1-7, Koornneef et al. (1998b); FDR1-2, Mitchell-Olds (1996); RLN1-5, Clarke et al. (1995); and DFF1-2, Kowalski et al. (1994).

clf, *elf1*, *elf2*, *elg*, *esd4*, *pef1*, *pef2*, *pef3*, *phyB*, *speedy*, *tfl1*, *tfl2*, and *wlc*) retain a response to photoperiod, whereas others (*elf3*, *emf1*, *emf2*, and *pif*) do not. Because this division is not absolute, the early-flowering mutants are considered here collectively, and the products of the corresponding wild-type genes are thought to act in repression of flowering.

The *EMF* genes have been considered to play a major role in repression of flowering because *emf1* and *emf2* mutants flower with essentially no preceding vegetative phase (Sung et al., 1992; Yang et al., 1995). The *EMF* genes may mediate the repression of flowering via their interactions with certain floral meristem identity genes (Figure 2). For example, *AP1* and *AG* are expressed very early in germinating *emf* seedlings, and constitutive expression of *LFY* enhances the phenotype of weak *emf1* alleles, These observations suggest that the *EMF* genes and *AP1* and *AG1* reciprocally regulate each other in a negative fashion (Figure 2; Chen et al., 1997).

Some gene products that promote flowering may act, in part, by directly or indirectly repressing *EMF* function. For example, *emf1* and *emf2* are, respectively, epistatic to *gi* and *co* (two late-flowering mutants in the photoperiodic promotion pathway; Figure 2) (Yang et al., 1995). However, when the *emf* mutations are combined with *fca* and other mutations that result in late flowering, the double-mutant plants flower after they have produced an intermediate number of leaves (Haung and Yang, 1998), which suggests that the corresponding wild-type products of these genes do not act by repressing *EMF* function.

TFL1, another floral repressor (Table 2), was cloned recently on the basis of its similarity to its Antirrhinum ortholog *CENTRORADIALIS* (*CEN*) (Bradley et al., 1997) and by T-DNA tagging (Ohshima et al., 1997). The *tfl1* mutant flowers early, and the normally indeterminate shoot apex terminates with a flower. Ordinarily, therefore, *TFL1* must function to suppress flower formation at the apex and to delay the transition from vegetative to reproductive development. Consistent with this role, overexpression of *TFL1* greatly extends the vegetative and inflorescence growth phases (Ratcliffe et al., 1998). It is likely that *TFL1* exerts this delay in flowering by repressing the function of genes such as *FCA*, *FVE*, and *FPA*, which operate in the autonomous promotion pathway (Figure 2). This is because the late-flowering phenotype conferred by mutations in these genes is epistatic to *tfl1* (Ruiz-García et al., 1997; T. Page and C. Dean, unpublished results).

CLF and *WLC* (Table 2) act to delay flowering by repressing certain floral meristem identity genes. The *clf* mutant expresses *AG* ectopically in leaves, inflorescence stems, and flowers (Goodrich et al., 1997), and *wlc* expresses *AG* and

Table 1. Genes and Mutations That Affect Flowering Time in Arabidopsis[a]

Locus		Description[b]	Environ. Response[c] Ppd.	Vern.	References
ADG1	*ADP GLUCOSE PYROPHOSPHORYLASE1*	Mutants lack leaf starch and flower late, primarily in SDs	+	ND	Lin et al. (1998)
ART	*AERIAL ROSETTE*	In combination with another locus, probably *FRI*, delays flowering of the axillary meristems, giving rise to aerial rosettes in LDs	+	+	Grbic and Bleecker (1996)
CAM1	*CARBOHYDRATE ACCUMULATION MUTANT1*	Mutants flower late and have increased starch in leaves	−	−	Eimert et al. (1995)
CCA1	*CIRCADIAN CLOCK ASSOCIATED1*	Overexpression results in long hypocotyls, abolished circadian rhythms, and late flowering	−	ND	Wang and Tobin (1998)
CLF	*CURLY LEAF*	Mutants flower early, have upwardly curled leaves, and express *AGAMOUS* ectopically	+	ND	Goodrich et al. (1997)
CO (=*FG*)	*CONSTANS*	Mutants flower late	−	−	Rédei (1962)
COP1 (=*FUS1*)	*CONSTITUTIVE PHOTOMORPHOGENIC1*	Mutants flower early in SDs and are constitutively photomorphogenic when germinated in the dark	−	ND	Deng et al. (1991)
DET1 (=*FUS2*)	*DEETIOLATED1*	Mutants have a phenotype similar to *cop1*	−	ND	Chory et al. (1989b)
DET2	*DEETIOLATED2*	Mutants flower late and exhibit pleiotropic defects in dark- and light-grown development	ND	ND	Chory et al. (1991)
ELF1, 2	*EARLY FLOWERING1* and *2*	Mutants flower early	+	ND	Zagotta et al. (1992)
ELF3	*EARLY FLOWERING3*	Mutants flower early in SDs, and have a long hypocotyl primarily in B and no circadian rhythm in cL	−	ND	Zagotta et al. (1992)
ELG	*ELONGATED*	Mutants flower early and have long hypocotyls	+	ND	Halliday et al. (1996)
EMF1,2	*EMBRYONIC FLOWER1* and *2*	Mutants flower extremely early and have severe pleiotropic effects on leaf and flower morphology	−	ND	Sung et al. (1992)
ESD4	*EARLY IN SHORT DAYS4*	Mutants flower early, have club-shaped siliques, and form a terminal flower	±	ND	Coupland (1995)
FCA		Mutants flower late and are strongly responsive to vernalization	+	+	Koornneef et al. (1991)
FD		Mutants flower late	±	−	Koornneef et al. (1991)
FE		Mutants flower late	±	±	Koornneef et al. (1991)
FHA (=*CRY2*)	(=*CRYPTOCHROME2*)	Mutants flower mildly late and have a long hypocotyl in low intensity B	−	±	Koornneef et al. (1991)
FKR	*FLOWERING KIRUNA*	Recessive alleles cause late flowering			J.E. Burn et al. (1993)
FLC	*FLOWERING LOCUS C*	Dominant alleles such as *FLC*-Col enhance the effect of late alleles at *FRI* and *LD* and of mutations at *fca*, *fpa*, and *fve*, in the L*er* background	+	+	Koornneef et al. (1994); Lee et al. (1994b)
FLD	*FLOWERING LOCUS D*	Dominant alleles cause late flowering, which requires a late allele of *FLC* for full effect	+	+	Sanda and Amasino (1996)
FPF1	*FLOWERING PROMOTING FACTOR1*	Overexpression causes early flowering in LDs and SDs	+	ND	Kania et al. (1997)
FPA		Mutants flower late	+	+	Koornneef et al. (1991)
FRI (=*FLA*)	*FRIGIDA*	Dominant alleles cause late flowering, which is suppressed by vernalization	+	+	Napp-Zinn (1957)
FT		Mutants flower late	±	±	Koornneef et al. (1991)
FVE		Mutants flower late	+	+	Koornneef et al. (1991)
FWA (=*FTS*)		Mutants flower late	−	±	Koornneef et al. (1991)
FY		Mutants flower late	+	+	Koornneef et al. (1991)
GA1		Mutants flower late in LDs and do not flower in SDs	+	±	Koornneef and van der Veen (1980)
GAI	*GIBBERELLIN INSENSITIVE*	Mutants flower late in SDs	+	−	Koornneef et al. (1985)
GI (=*FB*)	*GIGANTEA*	Mutants flower late and have increased starch in leaves	−	−	Rédei (1962)

(continued)

Table 1. Continued

Locus		Description[b]	Environ. Response[c] Ppd.	Vern.	References
HST	*HASTY*	Mutants have a shortened juvenile vegetative phase and flower early	+	ND	Telfer and Poethig (1998)
HY1,*2*	*LONG HYPOCOYTL1* and *2*	Mutants flower early and have pale-green young rosettes and long hypocotyls	+	ND	Koornneef et al. (1980); Chory et al. (1989a)
HY4 (=*CRY1*)	*LONG HYPOCOTYL4* (=*CRYPTOCHROME1*)	Mutants have long hypocotyls in B and flower late in certain ecotypic backgrounds	+	ND	Koornneef et al. (1980)
JUV	*JUVENALIS*	Recessive alleles cause late flowering, which is suppressed by vernalization	+	+	Napp-Zinn (1957)
KRY	*KRYOPHILA*	Recessive alleles cause late flowering, which is suppressed by vernalization	+	+	Napp-Zinn (1957)
LD	*LUMINIDEPENDENS*	Mutants flower late in combination with a late allele of *FLC*	+	+	Rédei (1962)
LHY	*LATE ELONGATED HYPOCOTYL*	Overexpression results in long hypocotyls, abolished circadian rhythms, and late flowering	−	−	Schaffer et al. (1998)
PEF1	*PHYTOCHROME-SIGNALING EARLY-FLOWERING*	Mutants flower early and are similar to *hy1* and *hy2*	+	ND	Ahmad and Cashmore (1996)
PEF2, *3*	*PHYTOCHROME-SIGNALING EARLY-FLOWERING2* and *3*	Mutants flower early and are similar to *phyB*	+	ND	Ahmad and Cashmore (1996)
PGM	*PHOSPHOGLUCOMUTASE*	Mutants lack starch and flower late, primarily in SDs	+	+	Caspar et al. (1985)
PHYA (=*HY8, FHY2*)	*PHYTOCHROME A* (=*LONG HYPOCOTYL8*)	Mutants have long hypocotyls in far-red light and are impaired in day-length perception	−	ND	Whitelam et al. (1993)
PHYB (=*HY3*)	*PHYTOCHROME B* (=*LONG HYPOCOTYL3*)	Mutants flower early, are pale green, and have long hypocotyls and petioles	+	ND	Koornneef et al. (1980)
PIF	*PHOTOPERIOD INSENSITIVE*	Mutants flower early, have small curled leaves, and are dwarfed	−	ND	Hicks et al. (1996)
SEX1	*STARCH EXCESS1*	Mutants have increased starch in leaves and flower late (except in cL)	+	+	Caspar et al. (1991)
SIN1	*SHORT INTEGUMENT1*	Mutants flower late and are female sterile	+	−	Ray et al. (1996)
SPEEDY (=*EBS*)	(=*EARLY BOLTING IN SHORT DAYS*)	Mutants flower early	±	ND	Koornneef et al. (1998b)
SPY	*SPINDLY*	Mutants flower early and resemble plants treated with gibberellins	ND	ND	Jacobsen and Olszewski (1993)
TED1		Mutants suppress *det1* and flower late	+	ND	Pepper and Chory (1997)
TFL1	*TERMINAL FLOWER1*	Mutants flower early and have determinate shoot growth and replacement of coflorescences with flowers	+	ND	Shannon and Meeks-Wagner (1991)
TFL2	*TERMINAL FLOWER2*	Mutants are similar to *tfl1* but flower even earlier and are markedly reduced in size	±	ND	Hicks et al. (1996)
VRN1	*VERNALIZATION1*	Mutants flower late only after vernalization	+	−	Chandler et al. (1996)
VRN2	*VERNALIZATION2*	Mutants flower moderately late in combination with *fca* and have a reduced vernalization response	+	−	Chandler et al. (1996)
WLC	*WAVY LEAVES AND COTYLEDONS*	Mutants flower early, have reduced size, and display a characteristic waving and rolling of the leaves	±	ND	Bancroft et al. (1993)

[a] For up-to-date information on the cloning of genes involved in flowering time, refer to "The Flowering Web" (http://www.salk.edu/LABS/pbio-w/flower_web.html).

[b] B, blue light; cL, continuous light; LD, long day; SD, short day.

[c] Environmental response of the mutant or otherwise indicated allele to flower earlier under inductive photoperiods (Ppd.) and after vernalization (Vern.). (+), strongly sensitive; (±), weakly sensitive; (−), insensitive; ND, not determined.

AP3 ectopically in leaves. Thus, the wild-type function of *CLF* and *WLC* is to prevent the expression of the floral meristem identity genes in vegetative tissue. The *CLF* gene shares sequence homology with the Drosophila polycomb group of genes, which are involved in maintaining the repression of homeotic genes (Goodrich et al., 1997). The *wlc* mutant displays hypomethylation of repetitive sequences associated with the centromeres (C. Hutchison and C. Dean, unpublished results); thus, reduced methylation may directly alleviate the repression of *AG* and *AP3* expression in leaves. Similarly, induced hypomethylation resulting from constitutive expression of an antisense methyltransferase gene resulted in ectopic expression of *AG* and *AP3* and early flowering (Finnegan, 1996). Thus, methylation may play an important role in the repression of the floral transition.

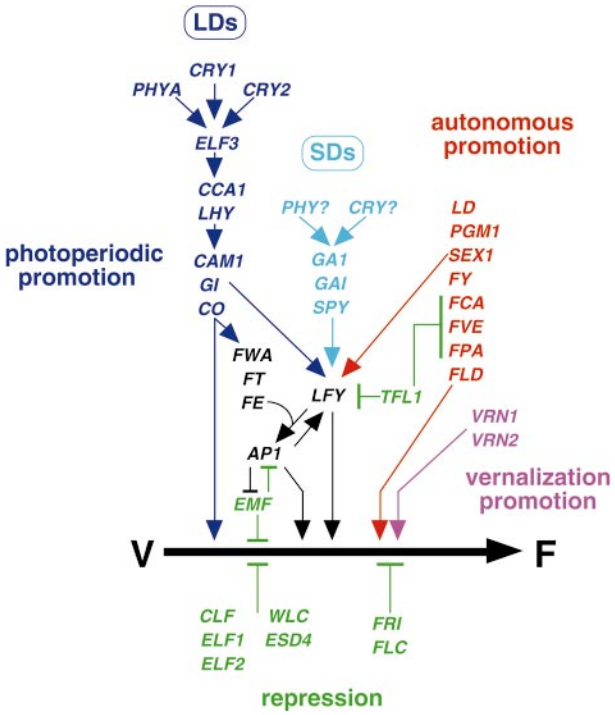

Figure 2. Genetic Pathways That Control Flowering Time in Arabidopsis and Proposed Interactions among Some of the Genes Involved.

The horizontal line symbolizes the vegetative (V) to floral (F) transition, with the promotive and repressive pathways exerting their influence on this switch. Four pathways are shown: repression (green), autonomous promotion (red), photoperiodic promotion under long days (LDs; dark blue) and short days (SDs; light blue), and vernalization promotion (pink). Genes that influence both floral meristem identity and flowering time are shown in black. Promotive (arrows) and repressive (T-bars) interactions are based on genetic epistasis experiments and analysis of gene expression in mutant and overexpressing lines. Not all interactions have been tested directly, and little is known about how the floral repressors interact with the various promotive pathways; thus, most of the repressors have simply been represented below the horizontal line. Therefore, this model, which is an updated combination of those published by Koornneef et al. (1998b) and Nilsson et al. (1998), does not fully represent the complexity of the interactions between genes and pathways that control flowering time in Arabidopsis.

Methylation appears to play a role in the regulation of flowering time by the *FWA* gene. Working with the *ddm1* mutant, which has decreased DNA methylation but unaltered methyltransferase activity (Richards, 1997), Kakutani et al. (1996) noted late flowering as a frequently appearing phenotype in repeatedly self-pollinated *ddm1* lines. *FTS*, the dominant locus conferring this late-flowering phenotype, was mapped genetically (Kakutani, 1997) and localized close to *FWA*, which was previously characterized by Koornneef et al. (1991) as a dominant mutation conferring late flowering. Subsequent analysis of the methylation status of the genomic region surrounding the *FWA* locus in *ddm1* and in EMS-induced *fwa* alleles showed the region to be hypomethylated (Koornneef et al., 1998b). Therefore, the wild-type product of the *FWA* gene may encode a repressor of flowering that normally is downregulated by methylation. However, because there is precedence for local hypermethylated sites within a hypomethylated region of a gene (see, e.g., Jacobsen and Meyerowitz, 1997), it is difficult to predict whether or not *FWA* expression will be up- or downregulated in the *fwa* mutant. Ronemus et al. (1996) speculated that a general and gradual increase in methylation during development could serve to change meristem competency and determinacy as a plant ages. It will interesting to test whether such a gradient of methylation exists in Arabidopsis and whether alleviation of the autonomous repression of flowering depends, at least in part, on changes in methylation at specific loci such as *FWA.*

Analysis of the natural variation in flowering time has revealed that the early-flowering ecotypes such as L*er* and Col can themselves be considered as mutants in genes conferring strong repression of the floral transition. Crosses between a number of winter and spring Arabidopsis ecotypes revealed that late flowering and a requirement for vernalization segregated as a dominant monogenic trait (Sanda et al., 1997) that mapped to the *FRI* locus (J.E. Burn et al., 1993; Lee et al., 1993; Clarke and Dean, 1994). The recent map-based cloning of *FRI* has revealed that L*er* and Col are likely to carry loss-of-function *FRI* alleles (U. Johanson and C. Dean, unpublished data).

Dominant alleles at a second locus, *FLC*, are required for the full repression of flowering by *FRI* (Lee et al., 1994b; Aukerman and Amasino, 1996). Most ecotypes carry dominant alleles at *FLC*, but L*er* and the C24 ecotype carry recessive alleles (Michaels and Amasino, 1995). Map-based cloning of *FLC* is nearing completion (S.D. Michaels and R.M. Amasino, personal communication), and therefore, the basis of this variation can soon be analyzed at the molecular level. Future studies will also be able to address how the

Table 2. Cloned Arabidopsis Genes That Affect Flowering Time[a]

Gene	Sequence Similarity and Probable Function
Promoters of flowering	
ADG-1	ADP glucose pyrophosphorylase, involved in starch metabolism
CO	Putative transcription factor with two zinc fingers
DET2	Steroid 5α-reductase, an enzyme involved in brassinolide biosynthesis
FCA	RNA binding protein with a protein–protein interaction domain
FHA	Cryptochrome 2, a flavin-containing blue light photoreceptor
FPF-1	Novel protein that may be involved in signaling or response to GAs
FT	*TFL1* homolog[b]
GA1	*ent*-kaurene synthetase A, an enzyme involved in GA biosynthesis
GAI	Member of a novel family of putative transcription factors
GI	Novel protein with putative membrane-spanning regions[c]
LD	Glutamine-rich homeobox transcription factor
PGM	Phosphoglucomutase, involved in starch metabolism
PHYA	Light-labile R-FR light photoreceptor
Repressors of flowering	
CCA1	MYB-related transcription factor; *LHY* homolog
CLF	Homology to *Enhancer of Zeste*, a Drosophila polycomb-group gene
ELF3	Novel protein[d]
ESD4	Novel protein
LHY	MYB-related transcription factor; *CCA1* homolog
PHYB	Light-stable R-FR light photoreceptor
SPY	*O*-linked *N*-acetylglucosamine transferase, involved in modification of proteins
TFL1	Similarity with phosphatidylethanolamine binding proteins
WLC	Novel protein[e]

[a] For up-to-date information on the cloning of genes involved in flowering time, refer to "The Flowering Web" (http://www.salk.edu/LABS/pbio-w/flower_web.html).
[b] T. Araki and D. Weigel, personal communication.
[c] K. Lee, G. Coupland, S. Fowler, and J. Putterill, personal communication.
[d] D.R. Meeks-Wagner, personal communication.
[e] C. Hutchison and C. Dean, unpublished data.

vernalization promotion pathway (see below) is able to bypass the repression of flowering mediated by *FRI* and *FLC* (Figure 2).

Given that so many genes are involved in the regulation of flowering time in Arabidopsis, it is interesting that a major determinant of both the natural variation in flowering time and the requirement for vernalization is allelic variation at *FRI. FRI* maps close to one of the two major QTLs that confer a vernalization requirement in *Brassica* spp (Osborn et al., 1997). Thus, an important question to address in the future is whether *FRI* orthologs correspond to flowering-time loci in a number of plant species.

Autonomous Promotion Pathway

The identification of loss-of-function mutations that delay flowering of rapid-cycling ecotypes reveals genes that act to promote flowering. Many of these late-flowering mutants have been categorized by their response to vernalization and photoperiod and in epistasis experiments (Table 1; Koornneef et al., 1991, 1998a). One group of mutants (*co*, *fd*, *fe*, *fha*, *ft*, *fwa*, and *gi*) show little response to photoperiod or vernalization, and the corresponding genes are thought to act in the photoperiodic promotion pathway (Figure 2). A second group of mutants (*fca*, *fpa*, *ld*, *fve*, and *fy*) respond strongly to vernalization but flower even later under noninductive photoperiods. Because the products of the corresponding wild-type genes appear to promote flowering independently of photoperiod, these genes are considered to act in the autonomous promotion pathway (Figure 2). Moreover, the fact that these mutants respond to vernalization suggests that the vernalization promotive pathway acts redundantly with the autonomous promotion pathway in these early-flowering ecotypes.

Two genes of the autonomous promotion pathway encode proteins whose function may be to regulate the expression of other genes (Table 2). *LD* encodes a putative homeodomain protein, and although the *LD* transcript is expressed throughout the plant, it is most abundant in the shoot and root apices (Lee et al., 1994a; Aukerman and Amasino, 1996). *FCA* encodes a protein with RNA binding and protein–protein interaction domains (Macknight et al., 1997). The RNA binding domains of FCA are similar to those

of the Drosophila proteins SX-1 and ELAV, which regulate alternative splicing of pre-mRNA transcripts important for sex determination and neuronal differentiation (Macknight et al., 1997). The *FCA* transcript is itself alternatively spliced, and increasing the levels of specific *FCA* transcripts results in earlier flowering (R. Macknight and C. Dean, unpublished results).

Analysis of the interaction of *FCA* with meristem identity genes indicates that *FCA* function is required for both activation and competence to respond to *LFY* and *AP1* (T. Page and C. Dean, unpublished results). FCA, or downstream gene products, appear to act in a cell non-autonomous manner, because even in plants in which a large proportion of the two inner layers of the SAM (i.e., L2 and L3) are genotypically *fca*, bolting and flowering are normal (Furner et al., 1996).

Transmissible signals that promote flowering are also the focus of recent work by Colasanti et al. (1998). The maize *id1* mutation confers late flowering and altered floral development. *ID1* encodes a protein with zinc finger motifs, suggesting that it acts as a transcriptional regulator. Several observations led Colasanti et al. (1998) to propose that *ID1* may be involved in the production or transport of a transmissible signal. For example, *id1* plants do not flower under field conditions, and plants containing an increasing proportion of transposon-induced wild-type *ID1* sectors in a mutant *id1* background flower progressively earlier (Colasanti et al., 1998). Taken together, these experiments suggest that ID1 is required to produce and/or modulate the activity of a signal that originates in immature leaves and influences reproductive development in the SAM.

That leaves are required to determine the developmental potential of the apex has also been established using cultured maize apices. Excised apices revert to producing a full set of leaves before they produce flowers, irrespective of how many leaves had been produced before they were placed in culture (Irish and Jegla, 1997). However, leaving the four to six youngest leaf primordia on the excised apices prevents the resetting of the developmental program, indicating that some signal from the leaves influences development of the apex.

Photoperiodic Promotion Pathway

Plants detect light in at least five regions of the visible spectrum by using at least three classes of photoreceptors. Blue light and ultraviolet-A are detected by the cryptochromes, red (R) and far-red (FR) light are detected by the phytochromes, and ultraviolet-B is detected by an as-yet-unidentified photoreceptor (Thomas and Vince-Prue, 1997). In Arabidopsis, there are at least five phytochromes (PHYA to PHYE) and two cryptochromes (CRY1 and CRY2) (Thomas and Vince-Prue, 1997). These photoreceptors typically have been characterized by the effect they have on seedling morphogenesis under different light conditions. Several Arabidopsis mutants that were originally isolated based on abnormal seedling photomorphogenesis are also affected in flowering time. These include *cop1*, *det1*, *det2*, *hy1*, *hy2*, *hy4*, *phyA*, *phyB*, *pef1*, *pef2*, and *pef3* (Table 1). Conversely, several mutants isolated based on their flowering-time phenotypes were subsequently found to exhibit abnormal seedling photomorphogenesis. These include *elf3*, *elg*, *fha*, and *lhy* (Table 1).

The role of photoperiod in flowering was conclusively demonstrated by Garner and Allard in the 1920s in their classic experiments with the Maryland Mammoth mutant of tobacco and the Biloxi variety of soybean (reviewed in Thomas and Vince-Prue, 1997). Recent genetic studies have begun to identify molecular components of the photoperiodic promotion pathway (Figure 2), and an overall picture of how Arabidopsis perceives and responds to inductive photoperiods is beginning to emerge.

The pathway begins with photoreceptors (such as PHYA and CRY2), which initiate signals that interact with a circadian clock and entrain the circadian rhythm. Somehow, day length is measured, and when the length of the dark period decreases below a critical length, genes that promote flowering (such as *CO*) are activated. This activation leads, in turn, to the upregulation of floral meristem identity genes and, thereafter, flowering.

In Arabidopsis, light quality affects flowering time, with R light inhibiting and FR light promoting flowering (Martínez-Zapater et al., 1994). The phenotype of *phyB* mutants (Table 1) suggests that PHYB normally plays a role in inhibiting flowering under high R to FR conditions but is not involved in day-length perception (Koornneef and Peeters, 1997). Physiological studies on multiple mutant combinations suggest that in addition to PHYB, other light-stable phytochromes also regulate flowering in response to light quality (Koornneef and Peeters, 1997). In contrast, mutations in *PHYA*, which encodes a light-labile photoreceptor, prevent perception of low-fluence-rate, FR-enriched day-length extensions that promote flowering. These observations suggest that PHYA is involved in both day-length perception and promotion of flowering by inductive photoperiods (Figure 2; Koornneef and Peeters, 1997).

Blue light alone promotes flowering in Arabidopsis, and the product of the *FHA* gene has recently been shown to encode CRY2, one of the two cryptochromes thus far identified in Arabidopsis (Guo et al., 1998). Transgenic plants overexpressing *CRY2* flowered earlier than did the wild type and had increased levels of *CO* mRNA (Guo et al., 1998), suggesting that blue light promotes flowering via CRY2 and CO (see below). Furthermore, the level of *CO* mRNA was found to be reduced in *cry2* mutants grown under long days but not under short days (Guo et al., 1998), thereby providing a possible explanation for the basis of the original *fha* late-flowering phenotype. Because the levels of both PHYA and CRY2 proteins drop rapidly and dramatically in the light (Thomas and Vince-Prue, 1997), they could fulfill the role of providing information about light/dark transitions to the circadian clock.

CRY1, the other cryptochrome in Arabidopsis, was originally identified as the *hy4* mutant, which has a long hypocotyl under blue light (Table 1). *hy4* is sensitive to photoperiod and is not delayed in flowering in a L*er* background under white light and inductive photoperiods. However, in the presence of non-L*er* alleles of *FLC* and in blue-enriched light, *hy4* is late flowering and exhibits photoperiodic sensitivity (Bagnall et al., 1996; Koornneef and Peeters, 1997). Therefore, CRY1 is involved in the promotion of flowering, but its interaction with floral promotion pathways is unclear.

Several genes that affect photoperiodic sensitivity and that may encode components of the circadian clock itself have been identified. *CCA1* and *LHY* RNA levels oscillate in a rhythmic fashion, and overexpression of either gene results in long hypocotyls and late flowering (Schaffer et al., 1998; Wang and Tobin, 1998). Constitutive expression of either *CCA1* or *LHY* also abolishes or alters the circadian expression of their own transcripts as well as several other genes, which suggests that CCA1 and LHY negatively regulate their own expression (Wang and Tobin, 1998).

Another likely component of the circadian clock is *TOC1*, which was identified as a semi-dominant mutation that shortened the period length of the circadian clock by 2 to 3 hr (Somers et al., 1998). The *toc1* mutation reduces the sensitivity of plants to photoperiod and causes early flowering under short days, indicating that quantitative changes in the pace of the circadian clock, not rhythmicity/arhythmicity alone, can alter flowering time.

ELF3 may mediate the interaction of light signals generated by the photoreceptors with the circadian clock (Figure 2). The phenotype of the *elf3* mutant (Table 1) suggests that the wild-type product of this gene is involved in repressing flowering under noninductive photoperiods. However, the conditional arhythmicity of the *elf3* mutant suggests that *ELF3*, which has recently been cloned (Table 2), does not function in the circadian clock itself (Hicks et al., 1996; Koornneef and Peeters, 1997).

The circadian clock is believed to affect the expression of downstream genes that operate in the photoperiodic promotion pathway, including *CO* (Table 2) (Putterill et al., 1995). *CO* mRNA is expressed throughout the plant and is more abundant in plants grown under long days compared with short days (Piñeiro and Coupland, 1998). *GI*, which has recently been cloned (Table 2), probably acts upstream of *CO* (Figure 2), because the phenotype of plants that overexpress *CO* is epistatic to the *gi* mutation (Piñeiro and Coupland, 1998).

Several lines of evidence suggest that the level of CO activity in L*er* plants is directly correlated with flowering time (reviewed in Piñeiro and Coupland, 1998). Using a glucocorticoid-inducible system, Simon et al. (1996) demonstrated that induction of CO activity is sufficient to rapidly cause flowering under short days and to initiate transcription of *LFY* and *TFL1* as rapidly as when these genes are induced by transfer to inductive photoperiods. However, levels of *AP1* mRNA increase more slowly after CO activation than they do in response to inductive photoperiods (Simon et al., 1996). These data suggest that CO acts in a pathway that is sufficient to activate *LFY* and *TFL1* transcription but that rapid activation of *AP1* requires an additional pathway (Figure 2). Interestingly, genetic analyses by Ruiz-García et al. (1997) have placed *CO* and *TFL1* in different genetic pathways, so the rapid activation of *TFL1* transcription remains to be explained.

Vernalization Promotion Pathway

Another seasonal cue in temperate zones is a winter period, and many species require exposure of imbibed seeds or vegetative plants to a period of cold temperature (typically 2 to 8 weeks at ~4°C) in order to flower. This process, known as vernalization, is slow and quantitative but requires active metabolism (reviewed in Chouard, 1960; Vince-Prue, 1975). The site of perception of vernalization is the shoot apex (e.g., Curtis and Chang, 1930; Metzger, 1988), but all actively dividing cells, not only those at the shoot apex, may be capable of responding to vernalization (Wellensiek, 1964). Unlike photoperiodic induction, vernalization prepares the plant to flower but does not itself evoke flowering. That is, there is a clear temporal separation between cold treatment and flowering, which commonly occurs after a period of growth at warmer temperatures. Vernalization is required in each generation for winter annuals and biennials and each growth year for perennials, which suggests that meiosis or some other aspect of reproductive growth resets the requirement for vernalization.

The features of vernalization suggest that an epigenetic mechanism may be responsible for the establishment, persistence, and resetting of whatever self-perpetuating changes occur during or subsequent to exposure to cold. The observations that the flowering of late-flowering, vernalization-sensitive Arabidopsis mutants is accelerated by azacytidine treatment (J.B. Burn et al., 1993) and that cold treatment leads to specific changes in gibberellin (GA) metabolism (Hazebroek and Metzger, 1990; Hazebroek et al., 1993) led J.B. Burn et al. (1993) to propose that vernalization causes a specific reduction in cytosine methylation. This reduction, J.B. Burn et al. (1993) hypothesized, results in the activation of the gene encoding kaurenoic acid hydroxylase, an enzyme that catalyzes an early step in GA biosynthesis. Indeed, when general levels of methylation were reduced in wild-type plants by introducing a transgene expressing an antisense version of a methyltransferase gene (antisense-*MET1*), developmental abnormalities and early flowering were observed (Finnegan, 1996; Finnegan et al., 1998). However, the role of methylation in vernalization is still unclear, because substantial demethylation did not prevent vernalization from fully accelerating flowering in these lines, nor did it prevent resetting of the vernalization requirement in the progeny of antisense-*MET1* plants (Finnegan et al., 1998).

One approach to understanding the molecular basis of vernalization has been to isolate mutants of Arabidopsis that

are specifically impaired in their response to cold treatment (Chandler et al., 1996). The starting point for this genetic screen was *fca*, a late-flowering mutant whose phenotype can be completely corrected by a period of vernalization. *fca* plants were mutagenized, and a population of progeny plants were vernalized and screened for individual plants that flowered late, that is, which no longer exhibited a strong response to vernalization. Of these candidate double mutants, those that flowered no later than *fca* itself without cold treatment were selected for further characterization (Chandler et al., 1996). Such *vrn* mutants may be defective either in the perception of cold temperature or in the transduction of the cold signal by the vernalization promotion pathway (Figure 2). An initial screen identified five independent recessive *vrn* mutations in at least three complementation groups (Chandler et al., 1996), and a second screen identified five additional mutants, which have not yet been assigned to complementation groups (Y.Y. Levy and C. Dean, unpublished results). Two mutants, *vrn1* and *vrn2* (Table 1), have been characterized in some detail and are being cloned by chromosome walking. Both *vrn1* and *vrn2* have a normal acclimation response, indicating either that they are downstream of a cold-perception pathway common to acclimation and vernalization or that cold perception occurs via independent pathways in these two responses (Chandler et al., 1996). Analysis of the *VRN* genes should reveal some of the molecular components involved in promotion of flowering by vernalization.

INTEGRATING PHYSIOLOGY AND GENETICS: FLORAL SIGNALS AND GENETIC PATHWAYS

Considerable physiological analysis has led to certain compounds and processes being implicated in controlling the floral transition. These include the role of sugars, cytokinins, and GAs. In this section, we discuss the role of these substances in flowering and try to place them within the promotive and repressive pathways.

The Role of Carbohydrates in Flowering

Compelling evidence that sucrose may function in long-distance signaling during floral induction comes from studies of *Sinapis alba*, a long-day plant in the mustard family. After induction of flowering in *S. alba* by either a single long day or a displaced short day, the concentration of sucrose in the phloem reaching the apex increases rapidly and transiently (Bernier et al., 1993). Furthermore, this pulse of sucrose precedes the increase in cell division that is normally observed in the SAM upon floral induction. The sucrose reaching the apex appears to be derived from the mobilization of stored carbohydrates, most likely starch in the leaves and stems, because plants induced by a displaced short day receive the same photosynthetic input as plants maintained under noninductive photoperiods (Bernier et al., 1993).

In Arabidopsis, L*er* plants grown in darkness with their apices in contact with sucrose-containing medium flower with the same number of leaves as do plants grown under long days (Roldán et al., 1997). In contrast, sucrose has a significant effect on the flowering of vernalization-requiring ecotypes Leiden and Stockholm, which flower early when grown under these conditions and with approximately the same number of leaves as L*er* (Roldán et al., 1997). Furthermore, sucrose alone, whether supplied in the dark or in the light, is responsible for most of this acceleration. Therefore, supplying sucrose to these late-flowering ecotypes bypasses the inhibition of flowering normally conferred by the existence of dominant alleles at *FRI* and *FLC* (Table 1). Sucrose also accelerates the flowering of *fve*, *fpa*, *fca*, *co*, and *gi* but not of *ft* and *fwa* (Roldán et al., 1997). This result implies that *FVE*, *FPA*, *FCA*, *CO*, and *GI* function in processes that are either upstream of or separate from control of sucrose availability to the vegetative apex, whereas *FT* and *FWA* function in processes downstream of this control point.

Further genetic evidence connecting carbohydrate metabolism with control of flowering is available, but the nature of this connection is unclear. For example, there are at least five Arabidopsis mutants, *adg1*, *cam1*, *gi*, *pgm*, and *sex1*, which are altered in starch synthesis, accumulation, or mobilization and which flower late under some conditions (Table 1). The flowering time of *cam1* and *gi* is not influenced by photoperiod, and therefore, both are likely to act in the photoperiodic promotion pathway (Eimert et al., 1995). *pgm* and *sex1* mutants flower later in short days than they do in long days and so fall into the autonomous promotion pathway. Flowering of these mutants is accelerated by cold treatment, suggesting that vernalization does not depend on normal starch metabolism (Bernier et al., 1993).

Phytohormones

The role of GAs in the transition to flowering has been difficult to establish. On the one hand, there are many examples in which the abundance or composition of endogenous GAs changes under conditions that induce flowering (Pharis and King, 1985). Furthermore, because applying certain GAs can induce flowering in some species, there has been an emphasis on the study of GAs in floral initiation and in the search for florigen (reviewed in Chouard, 1960; Evans, 1971; Zeevaart, 1983; Thomas and Vince-Prue, 1997). On the other hand, applied GAs are rarely effective at inducing flowering in short-day plants. Moreover, they generally inhibit flowering of woody angiosperms, although they do promote flowering of conifers (Pharis and King, 1985). Even within long-day plants, the same GA can have a different effect in different species. For example, 2,2-dimethyl GA_4 has potent florigenic activity when applied to *Lolium temulentum* but has no effect on flowering in *S. alba* (Bernier et al., 1993).

In Arabidopsis, signaling mediated by GAs appears to play a promotive role in flowering, particularly under noninductive photoperiods (Figure 2). Application of GAs accelerates flowering of wild-type plants under short days (Langridge, 1957) and of the late-flowering mutants *fb*, *fca*, *fd*, *fe*, *co*, *fpa*, *ft*, *fve*, and *fwa* (Table 1) under long days (Chandler and Dean, 1994). Under noninductive photoperiods, the *ga1* mutant (Table 1) does not flower unless provided with GAs (Wilson et al., 1992), and the *gai* mutant (Table 1) flowers very late. Furthermore, *spy* (Table 1), a mutant considered to exhibit constitutive GA-mediated signal transduction, flowers early (Jacobsen and Olszewski, 1993), as do plants constitutively expressing *FPF1*, a gene that appears to be involved in GA-mediated signal transduction or responsiveness to GAs (Table 1; Kania et al., 1997).

The role of GAs in activation of the *LFY* promoter has recently been analyzed (Blázquez et al., 1998). The basal level of *LFY* promoter activity is lower in *ga1* mutants, and the upregulation by long days is delayed. In contrast, *LFY* activity is slightly higher in a *spy* mutant grown in short days, correlating with an acceleration of flowering. A cauliflower mosaic virus 35S–*LFY* transgene was also found to rescue flowering in *ga1* mutant plants in short days. Thus, GAs promote flowering in Arabidopsis at least in part by activating *LFY* expression. Blázquez et al. (1998) also analyzed the direct effect of GA_3 with and without sucrose on *LFY* promoter activity. GA_3 alone had no effect, sucrose produced a small increase, and both together had a synergistic effect. This requirement for two activation signals for maximal effect may account for observations with excised *Lolium* apices (McDaniel and Hartnett, 1996). In this study, photoperiodic induction was found to result from two signals acting at the apex. One of these signals has not been identified (but from this analysis, it is possibly sucrose), and the other is GA (McDaniel and Hartnett, 1996).

The role of GAs in vernalization has received particular attention because in some species, application of GAs to vegetatively growing plants can substitute for cold treatment (see Chouard, 1960; Lang, 1965; Evans, 1971; Zeevaart, 1983; Martínez-Zapater et al., 1994). However, in the majority of species examined, including most cereals and nonrosette plants, application of GAs is not sufficient to overcome a requirement for vernalization (Chouard, 1960; Lang, 1965; Evans, 1971; Zeevaart, 1983). Because GAs are involved in flowering processes such as floral evocation (McDaniel and Hartnett, 1996) and bolting (Metzger, 1990), which occur well after the cold treatment, it is possible that application of GAs can simply bypass vernalization completely. Consistent with this possibility is the notion that vernalization may increase the sensitivity of plants to GAs but that GAs have no direct role in the process of vernalization itself (Chouard, 1960).

Further indication that GAs may not play a role in vernalization in Arabidopsis comes from experiments with *ga1-3* (Table 1), a mutant severely impaired in GA biosynthesis (Sun and Kamiya, 1994). When combined with *fca*, which responds strongly to vernalization, the *ga1-3 fca* double mutants still exhibit a robust vernalization response (J. Chandler and C. Dean, unpublished data). However, because *ga1-3* plants still contain residual GAs (T.-p. Sun, personal communication; Zeevaart and Talón, 1992), this result must be interpreted with caution. In summary, the precise role of GAs in the transition to flowering is unclear. Potential tissue-specific changes in GA biosynthesis and sensitivity need to be addressed, as does the potential existence of as-yet-undiscovered florigenic GAs (for a discussion of this possibility, see Evans, 1971; Zeevaart, 1983).

GAs are not the only class of phytohormones that has been implicated in affecting the floral transition. For example, there is evidence from studies on *S. alba* that long-distance signaling by cytokinins might play a role in the transition to flowering in response to inductive photoperiods (reviewed in Bernier et al., 1993). As discussed above, inductive photoperiods cause the rapid and transient export of sucrose from the leaves to both the shoot and root meristems. In the root, this sucrose leads to the export of cytokinin, primarily zeatin riboside, to the shoot and leaves, presumably via the xylem. Subsequently, another cytokinin, isopentenyladenine riboside, moves out of the leaves, and some makes its way to the shoot apex, where its levels increase within 16 hr of induction (Bernier et al., 1993).

The relative importance of the cytokinin and sucrose fluxes to the floral transition in Arabidopsis remains to be established. Application of cytokinins provokes a phenotype similar to that of *deetiolated 1* mutants—early flowering and severe pleiotropic effects on growth (Chory et al., 1994). *emf2* has been shown to be allelic (Z.R. Sung, personal communication) to the cytokinin resistance mutant *cyr1* (Deikman and Ulrich, 1995), but the apparent lack of mutations that implicate cytokinins in flowering may be due to a high degree of redundancy in the genes involved. Alternatively, the mutant phenotypes may be so pleiotropic that such mutants have not been classified as cytokinin mutants.

In addition to GAs and cytokinins, other phytohormones, such as abscisic acid (ABA), ethylene, and polyamines, may be involved in flowering under certain circumstances and in some species (Martínez-Zapater et al., 1994). The ethylene-insensitive mutant *ein2* is slightly delayed in flowering, and ABA-deficient mutants flower somewhat early under noninductive photoperiods (Martínez-Zapater et al., 1994), suggesting a role for ethylene and ABA in floral promotion and repression, respectively.

GENETIC INTERACTIONS THAT CONTROL THE FLORAL TRANSITION

The genetic interactions that control the floral transition in Arabidopsis have been described in a model that is constantly updated and revised as new data become available (Figure 2; see, e.g., Schultz and Haughn, 1993; Martínez-Zapater et al., 1994; Coupland, 1995; Yang et al., 1995; Koornneef et al., 1998a). This model fits well with the multifactorial control

model, which was developed on the basis of physiological analyses of flowering time (Bernier, 1988). Its essential feature is that the time at which flowering occurs is determined by antagonism between the promotive action of parallel pathways that monitor developmental age and environment and the repressive action of floral inhibitors. The promotive pathways are functionally redundant, explaining why no single mutation that prevents flowering has yet been found.

How the long-day, autonomous promotion, and GA pathways integrate to activate the meristem identity genes is one of the most active areas of research in this field. Quantitative increases in *LFY* expression are clearly required, with flowering occurring only after a threshold concentration of LFY has been reached (Blázquez et al., 1998). Expression of *AP1* is more qualitatively linked to floral determination (Hempel et al., 1997). Unlike *LFY* and *AGL-8*, expression of *AP1* is upregulated after the point of floral determination. The connection between the flowering-time genes and *LFY* has been directly addressed (Blázquez et al., 1998; Nilsson et al., 1998). Indeed, *CO*, *GI*, *FCA*, *FVE*, *GA1*, and *GAI* all play a role in activation of *LFY* (Figure 2) and are required to some extent for full expression of *LFY* function. In contrast, *FWA*, *FE*, and *FT* appear to be necessary for plants to respond to *LFY* expression (Nilsson et al., 1998). *FT* has recently been cloned independently by T-DNA tagging (Araki et al., 1998) and activation tagging (D. Weigel, personal communication); it encodes a protein with pronounced similarity to another meristem identity gene, *TFL1* (Bradley et al., 1997). Despite their similarity, *TFL1* and *FT* have opposing functions, with one repressing and the other promoting flowering.

Genetic analyses by Ruiz-García et al. (1997) have distinguished *FWA* and *FT* from the other flowering-time genes, and it has been proposed that these two genes function to activate *AP1* in a pathway that runs parallel to the pathway leading to *LFY* activation (Figure 2). This separation of *FT* and *FWA* was also observed by Roldán et al. (1997) in their study of the sucrose-dependent acceleration of flowering in Arabidopsis flowering-time mutants (see The Role of Carbohydrates in Flowering, above). Thus, *FWA* and *FT* appear to act as intermediaries between some of the other floral promoters and floral meristem gene activation (Figure 2). How the many known floral meristem genes fit into this picture remains to be seen, but it is clear that different promotive pathways converge to redundantly activate a large set of floral meristem identity genes, which are themselves at least partially redundant in function. As stated previously, this area has been extensively reviewed recently and so is not covered in great detail here (see Figure 2; Koornneef et al., 1998b; Piñeiro and Coupland, 1998).

PERSPECTIVES

In summary, very rapid progress is being made in elucidating the molecular control of the floral transition. The next phase of the work will require the use of genetic screens designed, for example, to identify suppressors and enhancers of existing mutations. Creative genetic strategies that take advantage of the ability to constitutively express individual flowering-time genes or that use specific mutant backgrounds will help to identify both genes that operate downstream in the same pathway and genes with redundant functions. As more flowering-time genes are cloned, biochemical and cellular characterization of their products will become increasingly important. Several flowering-time genes that have already been cloned appear to encode regulators of gene expression (Table 2); identification of the upstream and downstream targets of these gene products will help to establish their regulatory role and, perhaps, to confirm genetically defined steps in the various signaling pathways.

As the genes controlling flowering time in Arabidopsis become better defined, an important question will be to address how they correspond to genes that regulate flowering time in other species. A focused effort on comparative mapping will be required to establish the potential correspondence of different genes in different species. With this goal in mind, we have assembled a list of possible orthologs from Arabidopsis, pea, sugar beet, barley, and wheat (all vernalization-responsive, quantitative, long-day plants), based on the physiological characteristics of the mutants or allelic variants and genetic dominance for late- or early-flowering phenotypes (Table 3).

Establishing correspondence among these different genes would clearly accelerate their cloning, and it would also provide useful information on gene function in Arabidopsis. The ability to combine grafting with genetic analysis in peas has provided important information on the role of the flowering-time genes. For example, the *Gigas* gene product is involved in the production of a graft-transmissible floral promoter, whereas the products of *Late flowering* and *Vegetative 2* are not graft transmissible and are thought instead to alter the threshold sensitivity of the meristem to the transmissible signals. Determining whether *Gigas*, *Late flowering*, and/or *Vegetative 2* correspond to *FCA* and/or *FRI* would significantly add to our understanding of the function of these Arabidopsis genes. Although gene function may have diverged during evolution, the identification of orthologs in different species would inform a working model, which could then be tested.

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Table 3. Possible Orthologs of Arabidopsis Flowering-Time Genes[a]

	Species					
Class of Gene Product	Arabidopsis	Brassica[b]	Pea	Sugar Beet	Barley	Wheat
Promotes flowering independent of photoperiod	*FCA* *FVE* *LD*	–[c]	*Gigas*	*B*	*Spring habit 2*	*Vernalization 1*
Promotes flowering in response to inductive photoperiods	*CO* *GI*	Bn *LG2*, *8*	–	–	*Photoperiod HI* (Igri)	*Photoperiod 1* and *2*[d]
Inhibits flowering in response to non-inductive photoperiods	*ELF3*	–	*Sterile node* *Day neutral* *Photoperiod response*	–	–	–
Inhibits flowering and confers vernalization requirement	*FRI* *FLC*	Bn *VFN1* Br *VFR1* Bn *VFN2* Br *VFR2*	*Late flowering* *Vegetative 2*	–	*Spring habit 1*	*Group 6* gene(s)

[a] Restricted to vernalization-responsive, quantitative, long-day plant species. See Bezant et al. (1996); Snape et al. (1996); Laurie (1997); Law and Worland (1997); and Osborn et al. (1997).
[b] QTLs. Bn, *Brassica napus*; Br, *Brassica rapa*.
[c] None detected.
[d] In contrast to *CO*, *Photoperiod 1* and *Photoperiod 2* confer early flowering in both long days and short days. They may represent dominant gain-of-function alleles (Laurie, 1997).

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