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Arabidopsis Transcription Factors and the Regulation of Flowering Time: A Genomic Perspective

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Abstract

The availability of the Arabidopsis genome sequence allows for novel approaches in the analysis of many aspects of plant biology. Approximately 6% of Arabidopsis genes code for transcription factors, which can be grouped into different families according to similarities within the DNA binding domains. Transcription factors are critical regulatory components of the pathways that underpin many aspects of plant growth, development, and physiology. In particular, a substantial number of them are emerging as having crucial roles in controlling one of the most important, but complex, steps in the plant life cycle: the transition to flowering. Genome-wide studies offer the opportunity to gain a comprehensive understanding of this polygenic process, making it possible to appreciate both the large number of genes involved, as well as the complex regulatory networks into which those genes are integrated.

Introduction

The availability of the first plant genome sequence, that of *Arabidopsis thaliana*, (Lin *et al*., 1999; Mayer *et al*., 1999; Arabidopsis Genome Initiative, 2000; Salanoubat *et al*., 2000; Tabata *et al*., 2000; Theologis *et al*., 2000), allows for global, or genomic, analyses on many aspect of plant biology that, until recently, have been studied only through more traditional approaches. This shift from a 'gene-centric' to a 'genome-centric' perspective in eukaryotic biology is especially appropriate for the study of transcriptional regulation, and of transcription factors in particular (reviewed in: Riechmann and Ratcliffe, 2000; Riechmann, 2002). Transcription factors are the most numerous of the different types of proteins involved in transcription. They are the main (although not the only) protein components of the combinatorial logic of transcription, and the principal factors upon which mechanisms for selectivity of gene activation are built.

To gain a genomic appreciation of biological processes, it is necessary to compile complete lists of participating elements. A first step in this direction is the comprehensive analysis of the genome of interest through sequence comparisons. Transcription factor genes comprise a substantial fraction of any eukaryotic genome, and the majority can be grouped into a handful of different, often large, gene families according to the type of DNA-binding domain they encode. Within these families of related genes, functional redundancy or overlap is not unusual, and therefore the proper characterization of particular genes might require their study in the context of their closest relatives. The Arabidopsis complement of transcription factors has been the subject of an extensive genome-wide descriptive analysis, which also included a comparison with those of *Drosophila melanogaster*, *Caenorhabditis elegans*, and *Saccharomyces cerevisiae* (Riechmann *et al*., 2000). It was determined that the Arabidopsis genome codes for more than 1,500 transcription factors, or approximately 6% of its total number of genes. Less than 10% of these factors have been genetically and functionally characterized, usually through traditional genetic approaches whereby genes are first defined by a mutant phenotype and then isolated. For the majority of these transcriptional regulators, functional characterization is limited to the description of phenotypic differences between mutant and wild-type plants, and determination of their expression patterns. However, there is still very little knowledge of their modes of action; that is, of the genes that they regulate and of the mechanisms that they use to achieve that regulation. Thus, the function of the Arabidopsis complement of transcription factors, considered as a whole, and the dynamic relationship between the genome, the transcriptional regulators, and the transcriptome, remain largely unexplored (Riechmann, 2002).

Differential gene expression is a key element of developmental processes in multicellular eukaryotes, and thus transcription factors are often the master regulatory genes that direct the development of such organisms. In plants, the decision to flower is a critical developmental step in the life cycle, and a complex web of control pathways has evolved to ensure that this occurs at the most appropriate time. Studies in Arabidopsis have shown that more than 80 genetic loci are involved the regulation of the floral transition in response to a range of internal and external variables. Such variables or factors include day-length (photoperiod), prolonged cold periods (vernalization), the developmental state of the plant, and the action of hormones, such as gibberellins (Koornneef *et al*., 1991; Martínez-Zapater *et al*., 1994; Levy and Dean, 1998a, b; Simpson *et al*., 1999). Thus, the control of flowering time is under extreme polygenic control. Increasing numbers of genes that affect flowering time in Arabidopsis are being cloned, and many of them encode transcription factors (Table 1).

In this article, we first provide a succinct overview of the transcription factor gene complement of the Arabidopsis genome, and we particularly consider it in terms of biological complexity and developmental processes in

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Table 1. Flowering time genes cloned from Arabidopsis [1]

Gene	Symbol	Gene Product Functional Type	Pathway/Role	References
ANTHOCYANINLESS2	*ANL2*	Transcription factor (HB family)	Floral repressor	(Kubo *et al.*, 1999; Weigel *et al.*, 2000)
CIRCADIAN CLOCK ASSOCIATED 1	*CCA1*	Transcription factor (Myb-related group)	Circadian clock, floral repressor	(Wang *et al.*, 1997; Wang and Tobin, 1998)
CKB3	*CKB3*	Regulatory subunit of Ser/Thr protein kinase	Circadian clock	(Sugano *et al.*, 1998; Sugano *et al.*, 1999)
CONSTANS	*CO*	Transcription factor (Zinc coordinating type)	Floral promoter, photoperiod pathway	(Putterill *et al.*, 1995)
CRYPTOCHROME 1 / ELONGATED HYPOCOTYL 4	*CRY1 / HY4*	Photoreceptor	Light perception	(Ahmad and Cashmore, 1993)
CRYPTOCHROME 2 / FHA	*CRY2 / FHA*	Photoreceptor	Light perception, photoperiod pathway	(Guo *et al.*, 1998)
EARLY FLOWERING 3	*ELF3*	Novel nuclear protein	Circadian clock	(Covington *et al.*, 2001; Hicks *et al.*, 2001; Liu *et al.*, 2001b)
EMBRYONIC FLOWER 1	*EMF1*	Putative novel type of transcription factor	Floral repressor, multiple pathways	(Aubert *et al.*, 2001)
EMBRYONIC FLOWER 2	*EMF2*	Chromatin related protein	Floral repressor, multiple pathways	(Yoshida *et al.*, 2001)
FCA	*FCA*	RNA binding protein	Floral promoter, autonomous pathway	(Macknight *et al.*, 1997)
FERTILIZATION INDEPENDENT ENDOSPERM	*FIE*	Chromatin related protein	Floral repressor	(Kinoshita *et al.*, 2001)
FLAVIN BINDING, KELCH REPEAT, F BOX	*FKF1*	PAS protein	Circadian clock	(Nelson *et al.*, 2000)
FLORAL PROMOTING FACTOR 1	*FPF1*	Novel class of protein	Floral promoter	(Kania *et al.*, 1997)
FLOWERING LOCUS C	*FLC*	Transcription factor (MADS family)	Floral repressor, multiple pathways	(Michaels and Amasino, 1999a; Sheldon *et al.*, 1999)
FLOWERING LOCUS T	*FT*	Phosphatidylethanolamine binding protein	Floral promoter, multiple pathways	(Kardailsky *et al.*, 1999; Kobayashi *et al.*, 1999)
FPA	*FPA*	RNA binding protein	Floral promoter, autonomous pathway	(Schomburg *et al.*, 2001)
FRIGIDA	*FRI*	Novel class of protein	Floral repressor	(Johanson *et al.*, 2000)
FWA	*FWA*	Transcription factor (HB family)	Floral repressor	(Soppe *et al.*, 2000)
GA REQUIRING 1	*GA1*	Enzyme	GA regulation	(Sun and Kamiya, 1994)
GIBBERELLIC ACID INSENSITIVE	*GAI*	Transcription factor (GRAS family)	GA regulation	(Peng *et al.*, 1997)
GIGANTEA	*GI*	Novel nuclear localized protein	Floral promoter, photoperiod pathway	(Fowler *et al.*, 1999; Park *et al.*, 1999)
LATE ELONGATED HYPOCOTYL	*LHY*	Transcription factor (Myb-related group)	Circadian clock related, floral repressor	(Schaffer *et al.*, 1998)
LIKE HETEROCHROMATIN PROTEIN 1	*LHP1*	Chromatin related protein	Floral repressor	(Gaudin *et al.*, 2001)
LOV KELCH PROTEIN 2	*LKP2*	PAS protein	Circadian clock	(Schultz *et al.*, 2001)
LUMINIDEPENDENS	*LD*	Novel protein	Floral promoter, autonomous pathway	(Lee *et al.*, 1994)
MADS AFFECTING FLOWERING 1/ FLOWERING LOCUS M	*MAF1 / FLM*	Transcription factor (MADS family)	Floral repressor, multiple pathways	(Ratcliffe *et al.*, 2001; Scortecci *et al.*, 2001)
PHYTOCHROME A / ELONGATED HYPOCOTYL 8	*PHYA / HY8*	Photoreceptor	Light perception	(Sharrock and Quail, 1989)
PHYTOCHROME B / ELONGATED HYPOCOTYL 3	*PHYB / HY3*	Photoreceptor	Light perception	(Sharrock and Quail, 1989)
PHYTOCHROME INTERACTING FACTOR 3	*PIF3*	Transcription factor (bHLH family)	Photoreceptor signal transduction	(Ni *et al.*, 1998)
REPRESSOR OF GA1-3	*RGA*	Transcription factor (GRAS family)	GA regulation	(Silverstone *et al.*, 1998)
SHORT INTERNODES	*SHI*	Transcription factor (Zinc coordinating type)	GA regulation	(Fridborg *et al.*, 1999)
SHORT VEGETATIVE PHASE	*SVP*	Transcription factor (MADS family)	Floral repressor	(Hartmann *et al.*, 2000)
SQUAMOSA PROMOTER BINDING PROTEIN-LIKE 3	*SPL3*	Transcription factor (SBP family)	Floral promoter, multiple pathways	(Cardon *et al.*, 1997)
SUPPRESSOR OVEREXPRESSION CONSTANS 1/ AGAMOUS-LIKE 20	*SOC1 / AGL20*	Transcription factor (MADS family)	Floral promoter, multiple pathways	(Borner *et al.*, 2000; Lee *et al.*, 2000; Samach *et al.*, 2000)
TERMINAL FLOWER 1	*TFL1*	Phosphatidylethanolamine binding protein	Floral repressor, multiple pathways	(Bradley *et al.*, 1997)
TIMING OF CAB EXPRESSION 1	*TOC1*	Putative transcriptional regulator	Circadian clock	(Strayer *et al.*, 2000)
VERNALIZATION 2	*VRN2*	Chromatin related protein	Floral promoter, vernalization pathway	(Gendall *et al.*, 2001)
ZEITLUPE	*ZTL*	PAS protein	Circadian clock	(Somers *et al.*, 2000)

[1] Cloned Arabidopsis genes influencing the floral transition published prior to December 2001 are listed. A number of loci and genes that are primarily involved in light regulated development, general gibberellic acid metabolism, or starch metabolism, but that also influence flowering time, have been omitted (such genes are listed in Levy and Dean, 1998b).

plants. We then summarize the current understanding of flowering time in Arabidopsis, with an emphasis on transcriptional regulation (more comprehensive and general reviews on the control of the reproductive switch in plants have been published elsewhere: Koornneef *et al*., 1998; Levy and Dean, 1998b; Simpson *et al*., 1999; Reeves and Coupland, 2000). In the last section, we revisit and combine both topics in an attempt to provide a genomic view of the flowering time gene regulatory network, and of future research in the field.

The Arabidopsis Transcription Factor Gene Complement

The Arabidopsis genome (~125 Mbp of DNA) contains approximately 26,000 genes (Arabidopsis Genome Initiative, 2000). The corresponding complement of transcription factor coding genes has been described and reviewed in detail elsewhere (Riechmann *et al*., 2000; Riechmann, 2002), and only the most salient features are listed here.

- The Arabidopsis genome codes for at least 1,572 transcription factors (or ~6% of its total number of genes), which can be grouped into more than 45 different gene families. Such a content of transcriptional regulators is comparable to those of other eukaryotic organisms: transcriptional regulators represent approximately 3.5, 3.5, and 4.6% of the genes in yeast, *C. elegans*, and Drosophila, respectively, and 4.6-6.6% in humans.
- Many of the Arabidopsis families of transcription factors are large, with close to 100 members. The three largest families, AP2/ERF (APETALA2/ethylene response factor; this family was initially referred to as AP2/EREBP, for AP2/ethylene responsive element binding protein), bHLH (basic-region helix-loop-helix), and MYB-(R1)R2R3, each represent ~9% of the transcription factor gene complement.
- Approximately 45% of the Arabidopsis transcription factors belong to gene families that are specific to plants, and ~53% belong to families that are found in the three eukaryotic kingdoms of plants, animals, and fungi.
- Diversity in transcription factors among different organisms is large. In addition to differences in the composition of the transcription factor gene complement, the Arabidopsis factors that belong to families that are common to all eukaryotes do not share significant similarity with those from the other kingdoms, except in the conserved DNA binding domains that define the respective families. Furthermore, diversity in protein sequence and structure is increased by domain shuffling. Shuffling of some of the DNA-binding domains that are present in all eukaryotes has generated novel transcription factors with plant-specific combinations of modules.
- Arabidopsis transcription factor genes have followed duplication and rearrangement patterns that are similar to those of the genome as a whole. The genome contains many duplications, including small tandem duplications as well as large-scale duplications localized on different chromosomes (Arabidopsis Genome Initiative, 2000; Vision *et al*., 2000). Approximately 45% of the total number of transcription factors comprise pairs or groups of highly related sequences. These duplications are more frequently found in different chromosomes, than in tandem repeats.

In summary, analysis of the Arabidopsis genome revealed a substantial number of transcription factor genes, most of which have not been functionally characterized, and illustrated the large degree of diversity in transcriptional regulators that is present among the different eukaryotic kingdoms (Riechmann *et al*., 2000; Riechmann, 2002).

Transcription and Biological Complexity

Evolution of life on earth has progressed through a trend of increases in size, diversity, and complexity (Carroll, 2001). Biological complexity is a term for which the abstract or intuitive meaning is apparent, but which eludes precise definition. Despite this, however, there have been several proposed metrics and attempts to quantify biological complexity, by considering, for example, the number of different physical parts in an organism, such as cell types or genes (reviewed in Carroll, 2001). Determination of the genome sequence of different eukaryotes, however, has revealed that the association between gene number and complexity is not immediate: *Drosophila melanogaster* contains ~13,000 genes, whereas the arguably simpler nematode *Caenorhabditis elegans* has ~19,000, and 26,000 genes were identified in the genome of Arabidopsis (The *C. elegans* Sequencing Consortium, 1998; Adams *et al*., 2000; Arabidopsis Genome Initiative, 2000). More surprisingly, a mere ~30,000 genes were predicted from the human genome sequence (International Human Genome Sequencing Consortium, 2001; Venter *et al*., 2001), although there is uncertainty about this estimate (see, for example: Hogenesch *et al*., 2001; Wright *et al*., 2001). Alternative splicing, which is frequently observed for human genes, might be an important contributor to complexity, substantially increasing the number of different proteins that are derived from the genome. Nevertheless, since absolute numbers of genes or parts seem inadequate as a measure of biological complexity, other parameters have been used (reviewed in Carroll, 2001). Among such parameters is the number of interactions among parts. In particular, it has been proposed that biological complexity might be better explained by considering networks of transcription factors and the genes they regulate (connectivity of gene-regulation networks, Szathmáry *et al*., 2001), or the number of theoretical transcriptome states that a genome could achieve (Claverie, 2001). This reasoning was based in part on the observation that there is a trend to increase the number of transcription factors from yeast, to *C. elegans*, to Drosophila, and to humans (Szathmáry *et al*., 2001) (although the assertion that for all transcription factor families their members increase in

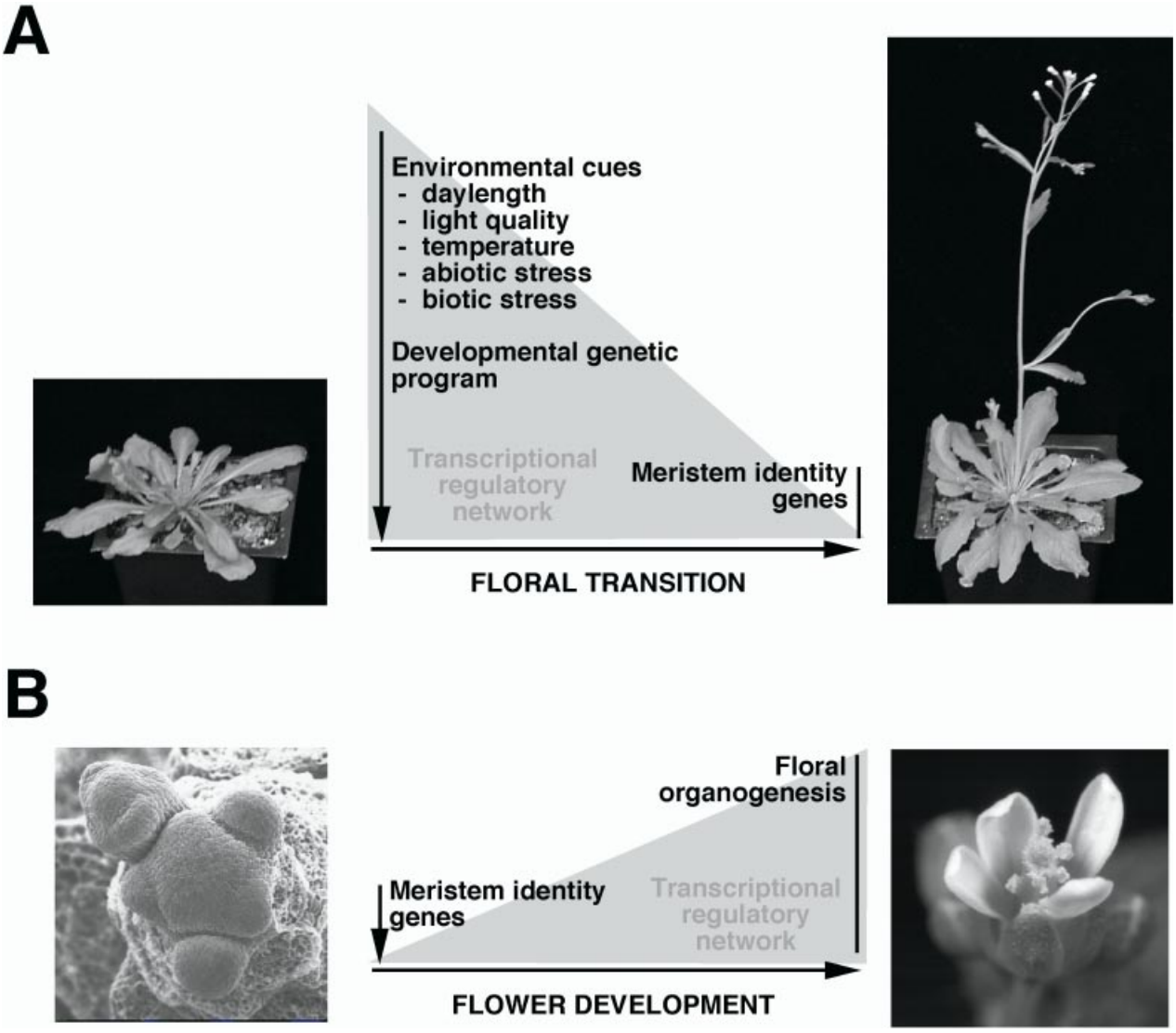


Figure 1. Transcription in plant developmental processes. (A) The floral transition, a plastic process. The reproductive switch is under the control of multiple different inputs, including the plant's intrinsic developmental program as well as many different environmental cues. A complex web of pathways responds to these inputs and controls the transition. Transcriptional regulation plays a prominent role in this network, and the inputs are eventually resolved into the upregulation of master meristem identity genes. (B) Flower development. This process is initiated by upregulation of master meristem identity genes, and is relatively inflexible, being achieved via the same sets of genes irrespective of the prevailing conditions.

number in such order, is not correct, since different gene families have been amplified to a different extent in each organism, see: Riechmann *et al*., 2000; Riechmann, 2002).

Following such reasoning, why do plants, as represented by Arabidopsis, have a complement of transcription factors that is more complex than that of Drosophila and *C. elegans*, and perhaps even similar in that respect to that of humans (Riechmann, 2002)? This 'peculiarity' has been interpreted in the context of the complexity of secondary metabolism in plants (Szathmáry *et al*., 2001). However, at least two other features might contribute to the effect. First, segmental duplications are frequent in the Arabidopsis genome (Arabidopsis Genome Initiative, 2000; Vision *et al*., 2000), somewhat more so than in the case of Drosophila or *C. elegans*, for instance. Second, plants, as sessile organisms, display a complex web of interactions with their environment (both biotic and abiotic), and many environmental variables evoke responses at the transcriptional level. In particular, and in contrast to animals, plant morphological development is, in many respects, a plastic process that is heavily influenced by the environment. A critical step in plant development is the floral transition, and the regulation of this switch is fundamentally different to the control of other developmental events that have well-defined end points, such as the patterning of a Drosophila embryo or a floral meristem. In these latter processes, which are very tractable to genetic studies, development is relatively

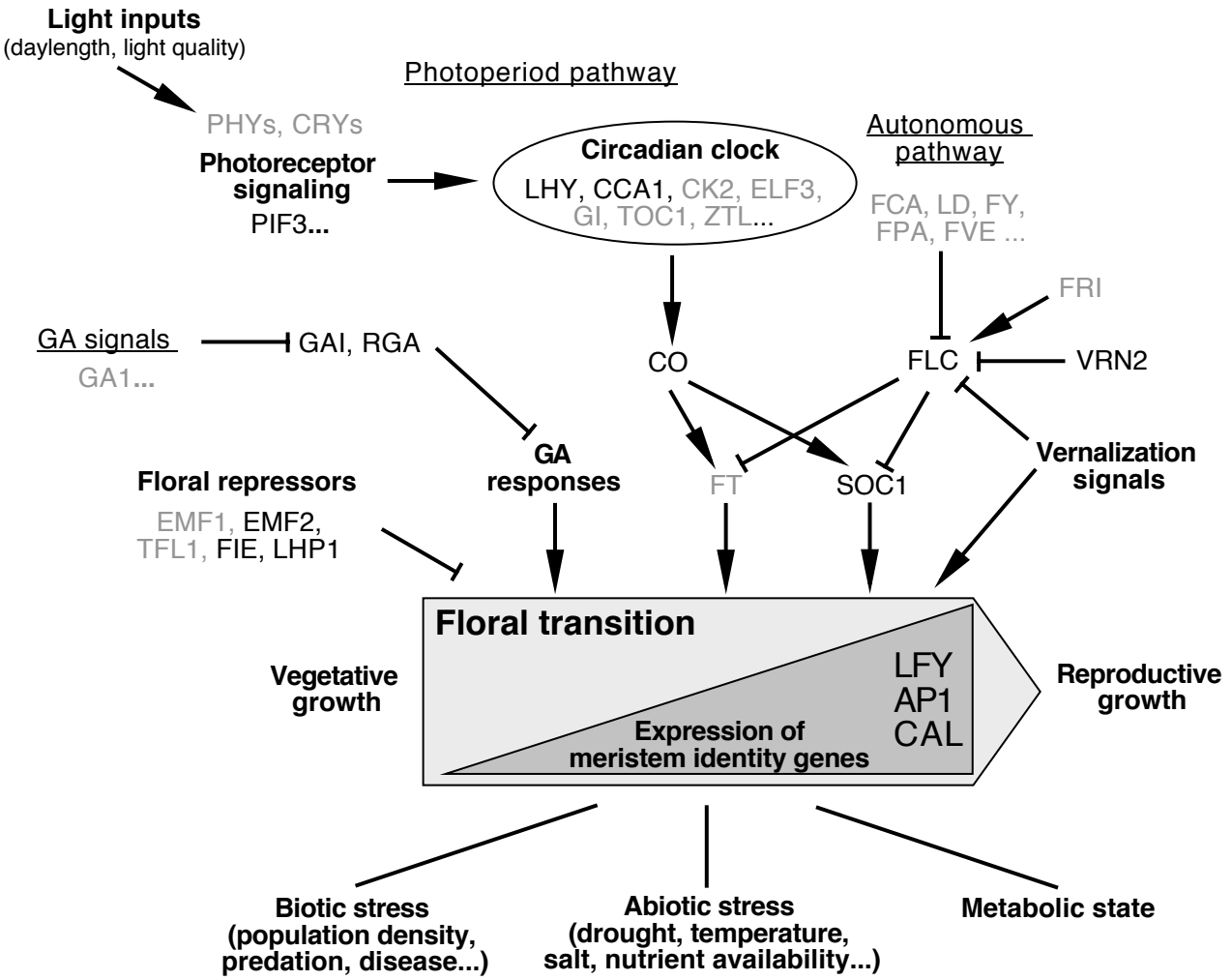


Figure 2. Control of the floral transition in Arabidopsis. The diagram represents a summary of the different pathways known to control the reproductive switch in Arabidopsis. The three major characterized pathways are the autonomous pathway (which monitors the developmental state of the plant), the photoperiod pathway (which mediates the response to light inputs, such as daylength), and the gibberellin pathway. Many variables that influence the floral transition (biotic and abiotic stress, metabolic state of the plant) remain to be studied, and the molecular mechanisms by which those inputs operate are not known. Some of the genes or loci that form the different pathways are listed; genes that code for transcription factors or chromatin related proteins are written in black, and those that code for other types of proteins are shown in gray. Some of these latter genes, however, might also be involved in transcriptional regulation, since they code for novel nuclear localized proteins (such as GI, and ELF3). The multiple positive and negative inputs of the regulatory network are eventually resolved into the upregulation of meristem identity genes, such as *LFY*, *AP1*, and *CAL*. Arrows represent positive inputs, either at the physiological level (promotion of the floral transition) or at the molecular level (induction of gene expression or activity). Blunt-ended arrows represent negative inputs: repressors of the reproductive switch (physiological level), or of gene expression or activity (molecular level).

inflexible, and is achieved using the same sets of genes irrespective of the prevailing conditions. In contrast, although the reproductive switch is in itself a well-defined end point, flowering time is a highly plastic trait, and multiple channels exist via which the decision can be influenced by any of a number of very diverse inputs (Figure 1).

Transcriptional Regulation and the Control of Flowering Time in Arabidopsis

Genetic analyses of Arabidopsis mutants and natural variants (accessions and ecotypes) have identified several major pathways that regulate flowering time (Figure 2), including the photoperiod pathway, the autonomous pathway, and the gibberellin pathway (Koornneef *et al.*, 1991; Martínez-Zapater *et al.*, 1994; Koornneef *et al.*, 1998; Reeves and Coupland, 2001). From our current knowledge, it appears that each one of these major pathways is founded upon key steps of transcriptional regulation. Ultimately, the flowering time regulatory pathways influence the expression of additional transcription factors that promote floral meristem development, such as LEAFY (LFY) and APETALA1 (AP1; a MADS domain protein) (Mandel *et al.*, 1992; Weigel *et al.*, 1992; Simon *et al.*, 1996; Ruiz-García *et al.*, 1997; Nilsson *et al.*, 1998; Parcy *et al.*, 1998). In fact, the promoter of the *LEAFY* gene serves as a convergence point for the different inductive pathways

(Blázquez and Weigel, 2000), in accordance with the concept of promoters acting as information processing systems (reviewed in Riechmann, 2002). CONSTANS (CO) appears to be the central transcriptional regulator within the photoperiod pathway, whereas FLOWERING LOCUS C (FLC) and GIBBERELLIN INSENSITIVE (GAI) are key transcription factors within the autonomous and gibberellin pathways, respectively (Putterill *et al*., 1995; Peng *et al*., 1997; Michaels and Amasino, 1999a; Sheldon *et al*., 1999).

Transcriptional Regulation Within the Photoperiod Pathway

Arabidopsis is a facultative long day (LD) plant in which flowering is accelerated by daylengths of 16 or more hours light. Mutants such as *co*, *gigantea* (*gi*), *fha, ft*, *fd*, *fe*, and *fwa* are defective in this response (Rédei, 1962; Koornneef *et al*., 1991): they flower later than wild-type plants under inductive LD conditions, but flower at the same time as wild type when grown in short day (SD) conditions of 8 or 10 hours light. Additionally, these mutants show little or no response to vernalization, further indicating that the corresponding genes are specifically involved in the response to daylength.

CO is a central component of the photoperiod floral promotion pathway (Figure 2), and a potent activator of flowering; 35S::*CO* Arabidopsis transgenic plants, in which the gene is constitutively expressed, flower extremely early under all photoperiodic conditions (Onouchi *et al*., 2000). *CO* encodes a putative transcriptional regulator with a C_2C_2 zinc finger motif (Putterill *et al*., 1995), and defines a subfamily of 33 genes in Arabidopsis which, together with the GATA, Dof, and YABBY transcription factors, comprise the C_2C_2 superfamily (Riechmann *et al*., 2000). The molecular mechanism of CO action still remains to be elucidated, and one of the hallmarks of typical transcription factors (sequence-specific binding to DNA) has not been demonstrated yet for the CO protein. However, several lines of evidence suggest a direct role for CO in transcriptional regulation.

A glucocorticoid inducible system has been used to trigger CO activity in plants, to follow its effects on the expression of specific genes over time or, in combination with differential display, to identify putative CO targets (Simon *et al*., 1996; Samach *et al*., 2000). These experiments showed that upregulation of first *LEAFY*, and then *AP1,* occurs relatively rapidly following induction of CO activity, and identified *SUPPRESSOR OF OVEREXPRESSION OF CONSTANS 1* (*SOC1*) and *FT* as early targets of CO. In an independent experiment, both *soc1* and *ft* alleles were identified in mutagenesis screens as suppressors that attenuated the early flowering phenotype of 35S::*CO* transgenic lines, corroborating the conclusion that they act downstream of *CO* in the regulatory network to promote flowering (Onouchi *et al*., 2000).

The molecular mode of action of *FT* remains unclear, since it encodes a putative phosphatidyl ethanolamine binding protein of uncharacterized cellular role (Kardailsky *et al*., 1999; Kobayashi *et al*., 1999). However, *SOC1* codes for a MADS domain transcription factor (SOC1 has also been described as AGAMOUS-LIKE 20, or AGL20, and was independently identified by two other groups as a positive regulator of flowering: Borner *et al*., 2000; Lee *et al*., 2000). *FT* and *SOC1* likely represent integration points at which the different flowering pathways converge prior to upregulation of floral meristem identity genes (Figure 2) (Lee *et al*., 2000; Onouchi *et al*., 2000; Samach *et al*., 2000).

The suppressor mutagenesis screens performed with the 35S::*CO* transgenic lines also identified novel alleles of another gene, *FWA*, that attenuated the early flowering phenotype of the plants. Unlike *FT*, *SOC1*, and *CO* itself, *FWA* appears to act as a floral repressor, with late flowering *fwa* mutants corresponding to dominant gain of function alleles (Onouchi *et al*., 2000; Soppe *et al*., 2000). Additionally, null mutants for *FWA* appear wild-type, suggesting that it might act redundantly with another gene, or function in wild-type plants under very specific conditions (Soppe *et al*., 2000). *FWA* encodes a homeodomain transcription factor of the GL2 class (Soppe *et al*., 2000), that bears considerable homology to another GL2-like transcription factor, ANTHOCYANINLESS2 (ANL2) (Kubo *et al*., 1999). The *anl2* loss-of-function mutant does not show alterations in flowering time, but displays a pleiotropic phenotype comprising defects in anthocyanin accumulation and in root development (Kubo *et al*., 1999). However, activation tagged Arabidopsis lines in which *ANL2* is upregulated are late flowering (Weigel *et al*., 2000). Nevertheless, regardless of whether *FWA* and *ANL2* correspond to bona fide flowering time loci or not, the fact that the upregulation or miss-expression of both genes alters flowering time, suggests that evolution could tinker with the trait by modifying the expression of genes that have other defined functions.

In summary, *CO* is a central component of the photoperiod floral promotion pathway, which appears to depend heavily on transcriptional regulatory switches. But how is the activity of *CO* regulated, and how are changes in light conditions detected and relayed into the pathway?

CO transcript levels show daily oscillations, falling following dawn and accumulating through the day, reaching high levels by the afternoon or evening (Suárez-López *et al*., 2001). Importantly, the ability of CO to activate target genes such as *FT* likely depends on whether *CO* levels become high while the plants are still in a light period. In SD conditions, under which CO does not induce flowering, *CO* levels do not become sufficiently high until the plants are once again in darkness. Studies of *FT* expression in LD grown 35S::*CO* lines show that *FT* mRNA abundance is much higher in the light than in the dark, indicating that light exposure might influence activity of the CO protein (Suárez-López *et al*., 2001). The rhythmic expression pattern of *CO* indicates a role for the circadian clock in its regulation and, in fact, *CO* transcript levels are altered, and expression becomes arrhythmic, in mutants for clock-associated genes, such as *LATE ELONGATED HYPOCOTYL* (*LHY*), *EARLY FLOWERING 3* (*ELF3*), and *GIGANTEA* (*GI*) (Suárez-López *et al*., 2001). Thus, CO is itself a link between the circadian clock, which is entrained by light signals and measures light/dark cycles, and downstream floral promoters in the photoperiod pathway. This is illustrated by the observation that *FT* transcript levels reflect those of *CO* (Suárez-López *et al*., 2001).

Circadian clocks are considered to have three basic conceptual components. The first is an input pathway(s) that transmits information from the environment and sets the phase of a second component, the central oscillator, which in Drosophila and *Neurospora crassa* consists of a feedback loop comprising positive and negative elements. The final component is an output pathway that relays information from the clock to the many pathways and processes that it regulates (reviewed in: Barak *et al*., 2000; Harmer *et al*., 2001; McClung, 2001).

In Arabidopsis, a pair of homologous MYB-related transcription factors, LHY and CIRCADIAN CLOCK ASSOCIATED 1 (CCA1), appear to be components of the oscillator (Wang *et al*., 1997; Schaffer *et al*., 1998; Wang and Tobin, 1998). *LHY* and *CCA1* show regular oscillations in transcript levels through the day/night cycle that persist if plants are moved into either continuous light or dark conditions, and both genes appear to display feedback inhibition of their own transcription. The constitutive expression of either *CCA1* or *LHY* in transgenic plants causes late flowering, repression of the expression of the endogenous *CCA1* and *LHY* genes, and many other alterations related to a disruption of clock function (Schaffer *et al*., 1998; Wang and Tobin, 1998). Another gene associated with the circadian clock in Arabidopsis is *TOC1,* which encodes a protein with a region that is also found in CO-like transcription factors, and another segment of similarity to the receiver domains of response regulators from two-component signal transduction systems (Makino *et al*., 2000; Strayer *et al*., 2000). The molecular mechanism of TOC1 action is somewhat unclear, but it has been shown that it forms a feedback loop with CCA1 and LHY that is critical for clock function. Both LHY and CCA1 can bind to a region within the *TOC1* promoter, and they negatively regulate *TOC1* expression; reciprocally, TOC1 appears to activate both its own transcription and that of *LHY* and *CCA1* (Alabadí *et al*., 2001). In addition to their regulation at the transcriptional level, CCA1 and LHY also appear to be regulated by phosphorylation, and have been shown to associate with protein kinase CK2 (Sugano *et al*., 1999). Transgenic plants in which CKB3, a regulatory subunit of CK2, is overexpressed show altered flowering time and shorter periods of rhythmic expression of *CCA1* and *LHY*, suggesting that CK2 can influence flowering via the circadian clock (Sugano *et al*., 1999).

The clock-associated genes *ELF3* and *GI* have long been implicated in the photoperiodic regulation of flowering (Rédei, 1962; Koornneef *et al*., 1991; Zagotta *et al*., 1996; Fowler *et al*., 1999; Park *et al*., 1999; Huq *et al*., 2000; Covington *et al*., 2001; Hicks *et al*., 2001; Liu *et al*., 2001b). These genes have opposing effects, with *ELF3* acting as a floral repressor and *GI* functioning to promote the floral transition. *GI* likely functions upstream of *CO* (because overexpression of *CO* corrects the *gi* late flowering phenotype), and it encodes a novel nuclear localized protein (Fowler *et al*., 1999; Park *et al*., 1999; Huq *et al*., 2000). *GI* is expressed in a circadian pattern, and influences both its own transcription and expression of *LHY* and *CCA1* (Fowler *et al*., 1999; Park *et al*., 1999). *ELF3* encodes a novel type of nuclear protein, is also under circadian control, and appears to inhibit both light signal inputs and clock outputs (Covington *et al*., 2001; Hicks *et al*., 2001; Liu *et al*., 2001b).

The main input, or entrainment stimulus, for the circadian clock in plants is light (reviewed in: Barak *et al*., 2000; Harmer *et al*., 2001; McClung, 2001), which is sensed by different classes of photoreceptors. Arabidopsis perceives light using different types of light-absorbing photoreceptors, such as phytochromes (phyA through phyE), which absorb red and far-red light, and cryptochromes (CRY1 and CRY2), which absorb blue and UV-A light (for review: Batschauer, 1998; Nagy and Schäfer, 2000). Because light conditions influence many different aspects of plant physiology and development, genes encoding photoreceptors and light-signaling components have frequently been characterized on the basis of mutants that show changes in seedling photomorphogenesis. However, many of these mutants (e.g. *cop1*, *det1*, *det2*, *hy1*, *hy2*, *phyA*, *phyB*, *pef1*, *pef2*, and *pef3*) also display alterations in flowering time (Levy and Dean, 1998b, and references therein). Conversely, a number of mutants (e.g. *elf3*, *elg*, *lhy*, and *fha*) identified via alterations in flowering time display abnormalities in photomorphogenesis (Levy and Dean, 1998b, and references therein).

The photoreceptors phyA and CRY2 appear to have a prominent role in photoperiod perception, whereas phyB plays a major role in determining flowering time in response to light quality (Koornneef and Peeters, 1997; Guo *et al*., 1998). CRY2 is now known to be the product of the *FHA* gene (Guo *et al*., 1998), which was one of the initial set of flowering time loci that were placed in the photoperiod pathway (Koornneef *et al*., 1991). Accordingly, CRY2 appears to markedly influence *CO* activity; *CO* transcript levels are elevated in transgenic lines that overexpress *CRY2*, and lowered in the *cry2* mutant (Guo *et al*., 1998). Levels of both phyA and CRY2 proteins fall rapidly in the light, further supporting the notion that they are involved in sensing light/dark transitions (Sharrock and Quail, 1989; Lin *et al*., 1998). CRY1 also has a role in the promotion of flowering, but its interaction with flowering time pathways is less clear (Bagnall *et al*., 1996; Koornneef and Peeters, 1997; Simpson *et al*., 1999). In addition, some photoreceptors likely influence flowering time independently of the circadian clock (Koornneef *et al*., 1995; Millar *et al*., 1995; Simpson *et al*., 1999).

Transcription factors are involved in photoreceptor signal transduction. PHYTOCHROME INTERACTING FACTOR3 (PIF3) is a transcription factor of the bHLH family that participates in signaling by phyB (Ni *et al*., 1998; Halliday *et al*., 1999). PIF3 binds to a cis-element present in several light-regulated promoters, and phyB (which is translocated to the nucleus in a light dependent manner: Kircher *et al*., 1999; Yamaguchi *et al*., 1999) reversibly binds to DNA-bound PIF3 upon the light-triggered conversion to its biologically active form (Ni *et al*., 1998; Martínez-García *et al*., 2000; Zhu *et al*., 2000). Thus, phytochromes might act as light-switchable components of transcription complexes, and their interaction with transcription factors might provide a short, direct pathway from light perception to photoresponsive nuclear gene expression (Martínez-García *et al*., 2000). Plants in which *PIF3* activity is reduced flower early, indicating that the gene is necessary for proper

regulation of flowering time (Ni *et al*., 1998).

In summary, genetic analysis and gene expression studies on mutant and transgenic gain-of-function lines have revealed that regulation within the photoperiod pathway is heavily dependent on cascades of transcriptional activity mediated via the action of transcription factors. Such transcriptional regulatory events are central to the perceptions of the inputs for the pathway and to its initial steps (photoreceptor signal transduction and the circadian clock), to its global regulation (built around CO), and to its downstream, effector steps. Pathway architecture that is based on transcriptional regulation also appears to be a recurring theme for the other known pathways that control the switch to flowering.

Transcriptional Regulation Within the Autonomous Pathway

The autonomous pathway monitors the developmental state of the plant and, in contrast to the photoperiod pathway, it does not respond to daylength (Koornneef *et al*., 1991; Martínez-Zapater *et al*., 1994). Loci that promote flowering within this pathway include *LUMINIDEPENDENS* (*LD*), *FCA*, *FY*, *FPA*, *FVE*, and *FLD*; mutants for these genes flower later than wild-type plants in either long day or short day conditions. Additionally, two dominant factors that repress flowering, *FLOWERING LOCUS C* (*FLC*) and *FRIGIDA* (*FRI*), were identified via genetic analysis of naturally occurring early and late flowering ecotypes (Burn *et al*., 1993; Lee *et al*., 1993; Clarke and Dean, 1994; Koornneef *et al*., 1994; Lee *et al*., 1994; Lee and Amasino, 1995; Sanda and Amasino, 1996; Johanson *et al*., 2000). *FRI* and *FLC* act synergistically, and ecotypes that contain active alleles of both of these genes are very late flowering. Importantly, such ecotypes and late flowering autonomous pathway mutants display a strong vernalization response, and exhibit much earlier flowering if given a prolonged cold treatment of 4-8 weeks at the germinating seedling stage.

Many of the loci within the autonomous pathway have now been cloned (Figure 2). In a comparable manner to CO occupying a central role in the photoperiod pathway, FLC is a novel MADS domain transcription factor that has a central function within the autonomous pathway, acting as a repressor of the floral transition (Michaels and Amasino, 1999b; Sheldon *et al*., 1999; Michaels and Amasino, 2001). In particular, *FLC* plays an important role in the maintenance of a vernalization response, with *FLC* transcript levels declining during cold treatments. In addition, it has been shown that overexpression of *FLC* is sufficient to severely delay or even prevent flowering in early flowering Arabidopsis accessions, such as Landsberg *erecta* (L*er*) and Columbia, in agreement with *FLC* acting as a repressor of the transition (Michaels and Amasino, 1999a; Sheldon *et al*., 1999; Ratcliffe *et al*., 2001). Plants carrying dominant *FRI* alleles and autonomous pathway mutants all contain high steady state levels of *FLC* transcript. Thus, *FRI* appears to support *FLC* levels, and genes such as *LD*, *FCA*, and *FVE* have inhibitory effects (Michaels and Amasino, 1999b; Sheldon *et al*., 1999; Michaels and Amasino, 2001). *FCA*, *FPA,* and possibly also *LD,* encode putative RNA binding proteins and could therefore potentially regulate *FLC* post-transcriptionally (Macknight *et al*., 1997; Aukerman *et al*., 1999; Schomburg *et al*., 2001). The cellular function of FRI is unknown, since it represents a novel type of protein (Johanson *et al*., 2000), and the molecular mechanisms by which *FLC* transcript levels are reduced following cold treatments remain elusive.

Intriguingly, it seems likely that other genes could also act alongside *FLC* in the maintenance of a vernalization response, since *flc* null mutants still respond to vernalization (Michaels and Amasino, 2001). It has recently been shown that the Arabidopsis genome encodes five other MADS domain transcription factors that are highly homologous to *FLC*, and it appears that these genes could perform similar functions (Ratcliffe *et al*., 2001; Scortecci *et al*., 2001). An additional MADS box gene, *SHORT VEGETATIVE PHASE* (*SVP*), also acts as a floral repressor, although its position within the regulatory network has not been established (Hartmann *et al*., 2000). A key question is to identify the downstream components of the pathway through which FLC exerts floral repression. As mentioned above, it has been shown that the photoperiod and autonomous pathways converge on at least two genes, *FT* and *SOC1*, prior to activation of floral meristem identity genes (Borner *et al*., 2000; Lee *et al*., 2000; Onouchi *et al*., 2000; Samach *et al*., 2000). However, it is likely that FLC acts through additional targets, in addition to influencing *SOC1* and *FT* (Michaels and Amasino, 2001).

Transcriptional Regulation Within the Gibberellin Pathway

The third major characterized pathway of floral promotion operates in response to gibberellic acid (GA) signals. Many of the mutants that are defective in GA metabolism show alterations in flowering time. In Arabidopsis, there appears to be a critical requirement for gibberellins in short days; mutants such as *ga-1*, which are unable to synthesize GA, do not flower under such conditions (Wilson *et al*., 1992; Blázquez *et al*., 1998; Nilsson *et al*., 1998; Reeves and Coupland, 2001). In addition, triply mutant plants that are defective in the GA, autonomous, and photoperiod pathways do not flower under either long or short days, indicating that gibberellins are required for flowering under all photoperiodic conditions (Reeves and Coupland, 2001). Finally, the floral meristem identity gene *LEAFY* is rapidly upregulated in response to GA applications (Blázquez *et al*., 1998).

As in the case of the autonomous and photoperiod pathways, the GA pathway appears to be organized around key transcription factors. In particular, the *GIBBERELLIN INSENSITIVE* (*GAI*) and *REPRESSOR OF GA1-3* (*RGA*) loci encode highly related transcription factors of the GRAS family that act as negative regulators of GA responses (Peng and Harberd, 1997; Harberd *et al*., 1998; Silverstone *et al*., 1998; Dill and Sun, 2001; King *et al*., 2001). GAI and RGA are themselves repressed by GA signals, thereby permitting responses to occur, a mode of action that resembles the manner by which *FLC* acts within the autonomous pathway. Unlike *FLC*, however, which is down-regulated at the transcriptional level in response to vernalization, GAI and RGA appear to be modulated

posttranslationally on receipt of GA signals (Peng *et al.*, 1997; Peng *et al.*, 1999). The GAI and RGA proteins also provide an example of the recurring theme of functional redundancy (Dill and Sun, 2001; King *et al.*, 2001); in numerous instances, spanning different biological pathways, key Arabidopsis transcription factors have highly related paralogs that serve partially overlapping functions (reviewed in Riechmann, 2002).

A Genomic View of Flowering Time Regulation

The picture that emerges from the current understanding of flowering time control in Arabidopsis is thus one of three major pathways that operate in response to different environmental or internal variables. In these three pathways, transcriptional regulation plays a prominent role, and evidence of interconnectivity (or 'cross-talk') between them is starting to accumulate (Figure 2). However, such an understanding has been derived from classical genetic and molecular studies that have focused on the effects of, and interactions between, a relatively small number of genes. Hence, our current models are likely to be incomplete. In particular, screens for loci affecting flowering have been performed in only a limited number of conditions. Many different biotic and abiotic variables that influence the reproductive switch remain to be examined, such as growth temperature, water availability, light intensity, and various other abiotic and biotic factors. If the photoperiod, autonomous, and gibberellin pathways are an example for what remains to be discovered, responses to these unexplored variables will also likely be controlled by specific genes, and transcriptional regulation will be found to play a prominent role in each process. Thus, it is very probable that a substantial number of novel regulators of flowering time remain to be identified, and that a large proportion of them will be transcription factors. Importantly, the control of the transcriptional regulation events that control the floral transition has not been delegated to a single, or a few, transcription factor families. Rather, regulators that belong to many different gene families are involved in the process (Table 1). In addition, functional overlap or redundancy appears to be relatively common in Arabidopsis, and it has already been demonstrated, in several instances, for transcription factor genes (reviewed in Riechmann, 2002). This peculiarity, derived from the abundance of segmental duplications in the Arabidopsis genome (Vision *et al.*, 2000), suggests that many important loci might have been missed in forward genetic screens. A potential example is provided by the transcription factor SPL3, a member of the SBP family (for SQUAMOSA promoter binding protein). *SPL3* triggers early flowering when overexpressed, but plants in which its activity is reduced through antisense RNA display a wild-type phenotype (Cardon *et al.*, 1997).

In summary, the list of regulatory components that control the reproductive switch in Arabidopsis is incomplete. In addition, little progress has been made in understanding the genome-wide changes that occur at the transition. Despite such limited knowledge, evidence has begun to accumulate indicating that the reproductive switch indeed involves broad ranging effects in the genome. Large-scale alterations in gene expression in response to light signals, and the involvement of chromatin associated proteins and of other epigenetic changes, such as DNA methylation, in flowering time regulation, appear to point in that direction.

Genome-Wide Alterations in Gene Expression in Response to Light Signals

DNA microarrays that monitor up to ~8,500 different Arabidopsis genes, or approximately one third of the genome, have been used in experiments designed to catalogue genes that are expressed in response to particular stresses or stimuli, or in certain tissues or developmental processes. These early studies have included the response to different nutrient concentrations, to drought and cold stresses, to wounding and insect feeding, the disease response, and light-related processes, such as the circadian clock, the light/dark transition, and phytochrome A signaling (reviewed in Riechmann, 2002). The most extensive dynamic reprogramming of the expression of the genome has been observed upon light stimulus or in light-related processes (Harmer *et al.*, 2000; Ma *et al.*, 2001; Schaffer *et al.*, 2001; Tepperman *et al.*, 2001). For example, one of these studies showed that up to 6% of the genes represented in the microarray exhibited circadian regulation (Harmer *et al.*, 2000), and other experiments revealed that up to one third of genes were regulated by light (Ma *et al.*, 2001). Furthermore, transcription factors appear to play a very significant role in phytochrome signaling: more than 40% of the genes that were immediately activated by the phyA pathway in response to a far-red light treatment were transcription factors (Tepperman *et al.*, 2001). This result illustrates how a change in light conditions could be rapidly converted into differential regulation of expression of batteries of genes further down the response pathways.

Chromatin Associated Proteins in Flowering Time Control

The involvement of genome-wide transcriptional regulation in the control of flowering time is further suggested by the identification of a variety of chromatin associated proteins as important components of the machinery that controls the reproductive switch. Two well-established flowering time loci, *EMBRYONIC FLOWER 2* (*EMF2*) and *VERNALIZATION 2* (*VRN2*), encode zinc finger proteins similar to the *Drosophila* Polycomb Group (PcG) protein Suppressor of zeste 12 (Su(z)12), and likely act to maintain repressed states of gene expression (Birve *et al.*, 2001; Gendall *et al.*, 2001; Yoshida *et al.*, 2001). *VRN2* is required to maintain the stable reduction in *FLC* transcript levels that occurs following vernalization treatments, and this appears to involve a change in chromatin accessibility at the *FLC* locus (Gendall *et al.*, 2001). However, it is not known whether VRN2 acts specifically on *FLC*, or on a broader range of targets within the genome. *EMF2* is critical for the general repression of flowering that occurs during seedling development, as mutants for this gene lack a rosette phase and flower very early, immediately following

germination (Sung *et al*., 1992; Yang *et al*., 1995; Yoshida *et al*., 2001). Another Arabidopsis protein that, like EMF2, is involved in floral repression in early development is FERTILIZATION INDEPENDENT ENDOSPERM (FIE) (Kinoshita *et al*., 2001). FIE shows homology to PcG proteins with WD repeats, such as Drosophila extra sex combs (esc) (Ohad *et al*., 1999). Both EMF2 and FIE repress floral meristem and organ identity genes at early seedling stages, but whether this occurs directly or indirectly is not yet clear (Chen *et al*., 1997; Kinoshita *et al*., 2001; Yoshida *et al*., 2001).

Mutations in *LIKE HETEROCHROMATIN PROTEIN 1* (*LHP1*), which codes for a homolog of Drosophila heterochromatin protein 1 (HP1), affect flowering time and plant architecture (Gaudin *et al*., 2001). Drosophila HP1 is involved in silencing gene expression through the generation and maintenance of inactive heterochromatin states (reviewed in Eissenberg and Elgin, 2000). The structural hallmark of HP1 proteins is the presence of two conserved domains, the chromo domain and the related chromo-shadow domain, both of which are critical for protein function. Arabidopsis LHP1 contains both domains and is a typical member of the HP1 family, and thus likely operates in a similar manner to HP1 (Gaudin *et al*., 2001). Arabidopsis *lhp1* mutants flower much earlier than wild-type plants, both in SD and in LD conditions, and show a reduced response to the influence of photoperiod. This result could be explained, at least in part, because *CO* is upregulated in the *lhp1* mutant at the early stages of seedling development (two cotyledon stage), at which point *CO* expression levels are very low in wild-type plants (Gaudin *et al*., 2001). However, LHP1 shows subnuclear localization in distinct foci, suggesting the existence of multiple targets within the genome (Gaudin *et al*., 2001).

In summary, and as exemplified by EMF2, FIE, and LHP1, it appears that chromatin related proteins play critical roles in maintaining the vegetative phase of plant development through repression of gene expression, and thus the pathways that promote the floral transition must ultimately overcome this repression. Where transcription factors act as repressors of the reproductive switch, as in the case of FLC, chromatin related proteins might operate to decrease their expression, and thus to promote flowering by repressing a repressor, as exemplified by VRN2. In addition, some genes coding for other types of chromatin associated proteins might be involved in the control of the reproductive switch, since alteration in their activity results in flowering time defects. For instance, Arabidopsis plants in which transcript levels of *AtHD1* (a histone deacetylase-coding gene, also referred to as *AtRPD3A*) were reduced, by using antisense RNA, were late flowering (Wu *et al*., 2000). Similarly, Arabidopsis lines in which DNA methylation (another epigenetic change that influences transcription levels) is reduced also display an abnormal flowering time (Ronemus *et al*., 1996). In both cases, it is not clear whether such phenotypes arise from broad-spectrum alterations in transcriptional activity across the entire genome, or from changes in the activity of a few key regulatory loci.

Genetics, Genomics, and Regulatory Networks

The view of flowering time regulation that is unfolding, then, mostly from studies in Arabidopsis, is one in which a large number of diverse stimuli are integrated via genetic networks that are centered upon, or based on, regulation at the transcriptional level. Given that only a limited set of conditions or variables has been analyzed, a large number of loci that impact the decision to flower likely remain to be discovered. A complex gene regulatory network probably exists underlying the control of flowering time, and such a network might be only partially captured in the current regulatory models, which are mostly based on linear genetic pathways. The flowering time regulatory network might turn out to be one of the most complex regulatory systems in a plant, perhaps together with that of the disease responses. The shape of the network itself is an open question, but it appears that information is eventually resolved into the upregulation of a small number of transcription factor genes, such as *LFY*, *AP1*, and *CAULIFLOWER* (*CAL*) (Mandel *et al*., 1992; Weigel *et al*., 1992; Kempin *et al*., 1995; Parcy *et al*., 1998), that control the development of floral meristems. In turn, these factors trigger the activity of larger numbers of downstream genes that pattern the meristem into whorls of floral organs (Figure 1).

The extent to which the regulation of flowering time in Arabidopsis also represents that of diverse plant species is still an open question. It is possible that some areas of the regulatory network (i.e., pathways) play more prominent roles in some plant species than in others, and that the mode by which the pathways or their components operate has been altered through evolution. For instance, *CO* is the central component of the photoperiod pathway in Arabidopsis, which is a facultative long day plant (flowering is promoted by long days). Similarly, *CO* homologs also appear to regulate the photoperiod flowering response in rice and in *Pharbitis nil*, which are short day plants (flowering is induced by long nights) (Yano *et al*., 2000; Liu *et al*., 2001a). How *CO* and orthologous genes regulate the photoperiod pathway in response to either long days or short days in different plant species is not clear, although it appears likely that changes at the level of transcriptional regulation, and not of protein sequence, are involved (reviewed in Samach and Gover, 2001). Interestingly, the expression of Pharbitis *CO* correlates with the SD requirement for flowering, since it is increased by long nights; conversely, Arabidopsis *CO* expression is promoted by long days. Thus, *CO*, and its role in the floral transition in diverse species, could provide another example of the importance of alterations in gene expression as a major source of the diversity and change that underlie the adaptation and evolution of eukaryotic organisms (Doebley and Lukens, 1998; Cubas *et al*., 1999; Carroll, 2000; Tautz, 2000).

In contrast to the case of the photoperiod pathway and of its components, whether regulation of the vernalization response is conserved between Arabidopsis and other plant species is still unclear. Furthermore, Arabidopsis is an annual plant whereas many other species exhibit a perennial growth habit. In Arabidopsis, floral meristem initiation is rapidly followed by flower emergence, whereas

in numerous woody perennials, floral meristems arrest development for long periods following their initiation (Sedgley and Griffin, 1989). In many cases, it is not the actual initiation of floral meristems, but rather the time at which the dormancy of those meristems is broken, that is heavily dependent on the environmental conditions (Battey, 2000; Battey and Tooke, 2002). It has been suggested that the annual habit evolved from that of the perennial plants (Battey, 2000; Battey and Tooke, 2002). It is thus possible that regulatory genes exist within the Arabidopsis genome that are specific to annuals and that and are not represented in perennial plants. Alternatively, numerous genes involved in modulating perennialism might still be present in the Arabidopsis genome, but having a much less prominent regulatory role than in the ancestral species. If such loci exist, it is unlikely that they would be revealed in mutant screens performed under standard growth conditions.

To conclude, genome-wide approaches, made feasible by the availability of the Arabidopsis genome sequence (and of those of other plants in the future), and by the novel genomic techniques, offer the opportunity of a broader understanding of the control of the floral transition. Given the importance of transcriptional regulation in the pathways that are being elucidated, it appears that the network that regulates this developmental switch will eventually be interpreted and explained in terms of changes in transcriptional activity at a genome-wide level.

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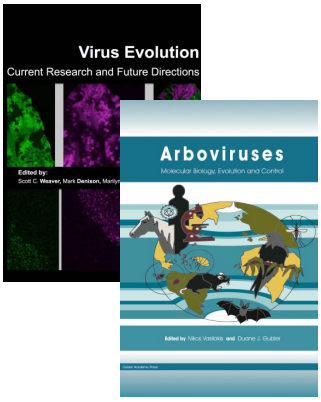
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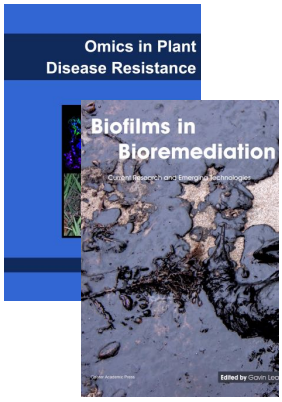
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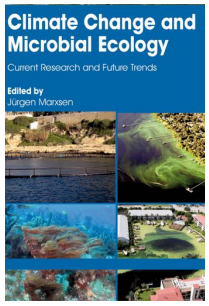
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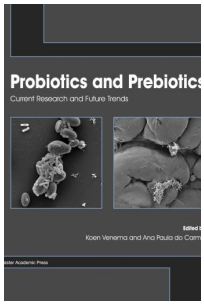
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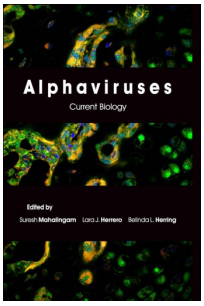
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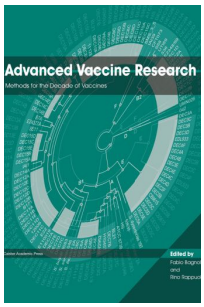


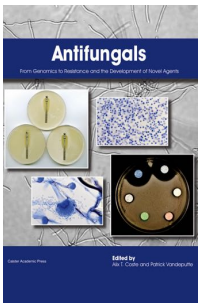












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