Check for updates

RNA Splicing of *FLC* Modulates the Transition to Flowering

Hao-Dong Qi[1], Yi Lin[1], Qiu-Ping Ren[2], Yu-Yi Wang[1], Feng Xiong[1], and Xiu-Ling Wang[1]*†

[1] National Key Laboratory of Crop Biology, College of Life Sciences, Shandong Agricultural University, Taian, China, [2] College of Agronomy, Liaocheng University, Liaocheng, China

Flowering is a critical stage of plant development and is closely correlated with seed production and crop yield. Flowering transition is regulated by complex genetic networks in response to endogenous and environmental signals. FLOWERING LOCUS C (FLC) is a central repressor in the flowering transition of *Arabidopsis thaliana*. The regulation of *FLC* expression is well studied at transcriptional and post-transcriptional levels. A subset of antisense transcripts from *FLC* locus, collectively termed cold-induced long antisense intragenic RNAs (*COOLAIR*), repress *FLC* expression under cold exposure. Recent studies have provided important insights into the alternative splicing of *COOLAIR* and *FLC* sense transcripts in response to developmental and environmental cues. Herein, at the 20th anniversary of *FLC* functional identification, we summarise new research advances in the alternative splicing of *FLC* sense and antisense transcripts that regulates flowering.

Keywords: alternative splicing, *FLOWERING LOCUS C*, *COOLAIR*, flowering transition, splicing factor, vernalization

HIGHLIGHTS

FLOWERING LOCUS C (FLC) is a key repressor in flowering transition. The alternative splicing of *FLC* sense and antisense transcripts regulated by external and internal cues modulates flowering transition.

INTRODUCTION

RNA splicing is a critical step in the post-transcriptional regulation of gene expression. This process occurs by removing intronic sequences and joining exons by spliceosome and numerous splicing factors (Jurica and Moore, 2003; Wahl et al., 2009; Matera and Wang, 2014; Vosseberg and Snel, 2017). Spliceosome is a highly dynamic ribonucleoprotein complex that catalyses RNA splicing and is composed of five small nuclear ribonucleoprotein (snRNP) particles (U1, U2, U4/U6 and U5) (Will and Lührmann, 2011; Fica et al., 2019). Splicing factors are one of the key determinants as accessory non-snRNP proteins regulating RNA splicing (Cho et al., 2011; Liu et al., 2016; Long et al., 2019; Wang et al., 2019; Xiong et al., 2019a; Xiong et al., 2019b). A pre-mRNA may undergo different splicing patterns, creating various mature transcripts that encode distinct functional proteins (Samach et al., 2011; Wang et al., 2015; Zhu et al., 2017; Lockhart, 2018; Okumoto et al., 2018). This phenomenon is called alternative splicing (AS).

AS fulfils important biological functions in plants, such as flowering transition and flower development (Wang et al., 2014; Melzer, 2017; Rodríguez-Cazorla et al., 2018; Park et al., 2019a; Park et al., 2019b; Wang et al., 2019). AS is also implicated in plant response to circadian rhythm regulation (Filichkin and Mockler, 2012), phytohormone (Hrtyan et al., 2015; Wang et al., 2015; Zhu

et al., 2017; Xiong et al., 2019a), ambient temperature (Verhage et al., 2017) and abiotic and biotic stresses (Lyons and Kazan, 2016; Huang et al., 2017; Mei et al., 2017; Shang et al., 2017; Laloum et al., 2018). These cues are all important for flowering transition; therefore, AS plays multiple roles in flowering by integrating endogenous developmental and exogenous environmental signals. The flowering inhibitor gene flowering locus c *(FLC)* encodes a MADS-box transcription factor and is a key regulator of vernalisation and autonomous pathways in *Arabidopsis* and related species (Michaels and Amasino, 1999; Sheldon et al., 1999; Sheldon et al., 2000; Chen et al., 2019; Coupland, 2019). FLC inhibits flowering by repressing the expression of a subset of key genes in promoting flowering, such as flowering locus t *(FT)*, suppressor of overexpression of constans 1 *(SOC1)* and target of flc and svp1 *(TFS1)* (Helliwell et al., 2006; Searle et al., 2006; Luo et al., 2019; Richter et al., 2019). Thus, *FLC* regulation is central for flowering at the transcriptional, post-transcriptional and post-translational levels (Michaels et al., 2003; Lempe et al., 2005; Li et al., 2016; Kwak et al., 2017; Whittaker and Dean, 2017; Xiong et al., 2019a). The AS of *FLC* sense and antisense transcripts is required for flowering transition in *Arabidopsis* and other dicots (Michaels and Amasino, 1999; Sheldon et al., 1999; Helliwell et al., 2006; Yuan et al., 2009; Wu et al., 2012).

Twenty years ago, the works of Michaels and Amasino (1999), and Sheldon et al. (1999) provided a first glimpse of the central functions of *FLC* in flowering and the molecular basis of *FLC* in vernalisation (Coupland, 2019). Subsequent research works have demonstrated the regulation of *FLC* at the transcriptional and post-transcriptional levels, especially the epigenetic silencing of *FLC* by histone methylation in vernalisation, and the splicing regulation of *FLC* sense and antisense transcripts by splice factors (Bastow et al., 2004; Liu et al., 2007; Liu et al., 2010; Marquardt et al., 2014). In this review, we describe the current understanding of the AS of *FLC* sense and antisense transcripts in modulating flowering time and the splice factors involved in these processes.

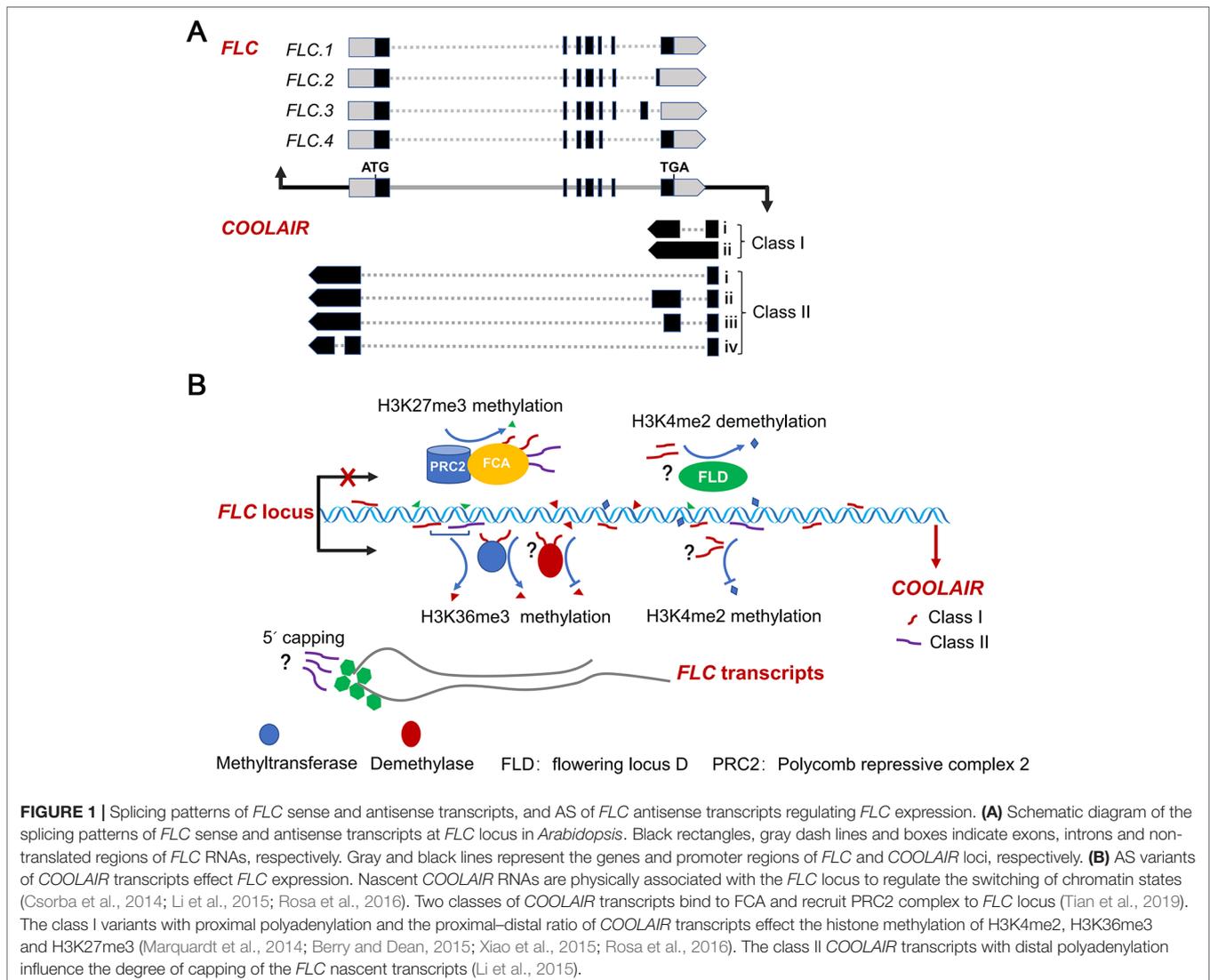## AS OF *FLC* SENSE TRANSCRIPTS MEDIATES FLOWERING TIME

Arabidopsis accessions exhibit markedly different flowering behaviour from different environments. The AS of *FLC* sense transcripts in these accessions generate multiple splice isoforms (**Figure 1A**). The naturally occurring splice variants of *FLC* are related to different vernalisation responses of various *Arabidopsis* accessions (Bloomer and Dean, 2017). *Arabidopsis* ecotype Bur-0 is late flowering and vernalisation insensitive. *FLC* cDNA from Bur-0 contains 64 bp of intron sequence immediately upstream of exon 7, causing a mutation at the final position of intron 6. The 64 bp intron retention causes a frame shift and a premature stop codon in *FLC* cDNA. Thus, the encoded FLC lacking the C-terminal 33 amino acid residues is a null function protein in Bur-0 (Werner et al., 2005). Similarly, in variations of Cen-0 and Cal-0, alternative splice acceptor sites in the last exon and last intron are used, respectively. These aberrant splicing forms all lead to a frame shift of cDNA sequences and severely compromise protein function (Lempe et al., 2005). In Col-0 *Arabidopsis*,

there are several additional splicing variants from *FLC* locus besides the canonical transcript (Severing et al., 2012; Park et al., 2019a); however, their roles in flowering transition remains to be investigated. An additional shorter transcript from *FLC* locus is induced after vernalisation treatment for 15 days in Est-0 and Le-0 ecotypes, which is not observed at normal temperature (Caicedo et al., 2004). Whether this short transcript is involved in vernalisation-induced flowering in *Arabidopsis* is unknown.

In other plant species, the naturally occurring splice variants of the *FLC* locus also reveal that *FLC* AS is important for the control of flowering time. For example, four different transcripts of the *FLC* homologs in *Brassica rapa BrFLC1* and *BrFLC2* have been identified from naturally occurring splicing mutations (Yuan et al., 2009; Zhao et al., 2010; Wu et al., 2012). These different splice types of *BrFLCs* are significantly associated with a natural variation of flowering time in different germplasms of *B. rapa*. Additionally, differential splicing variants of *BnFLC.A3b*, a *FLC* homolog in *B. napus*, have been observed in leaves at the seedling stage between winter cultivar Tapidor and semi-winter cultivar Ningyou7. The transcripts from Tapidor are usually spliced canonically, but numerous incompletely spliced transcripts have been identified in Ningyou7, causing decreased functional transcripts (Zou et al., 2012). In tetraploid *Capsella bursa-pastoris*, splice site polymorphisms in the *FLC* loci create different transcripts which are nonfunctional (Slotte et al., 2009). These findings partially explain the differential flowering times of *C. bursa-pastoris* from different districts. A natural splicing site mutation in the *BrpFLC1* gene causes early flowering in the cultivated variety of purple flowering stalk (*Bras. campestris L. ssp. chinensis* var. *purpurea*) compared with that of pakchoi (*Bras. campestris ssp. chinensis* var. *communis*) (Hu et al., 2011). Additionally, in an early flowering trifoliate orange (*Poncirus trifoliata*) mutant, five alternatively spliced transcripts of *PtFLC* have been identified; furthermore, their abundances are variable at the juvenile and adult stages, suggesting that the AS of *PtFLC* is related to flowering time (Zhang et al., 2009). Therefore, the AS of *FLC* is a target of natural selection for flowering regulation under natural conditions.

AS OF *FLC* ANTISENSE TRANSCRIPTS REGULATES *FLC* EXPRESSION

COOLAIR is a set of long noncoding RNAs expressed at the *FLC* locus in the antisense direction that was first identified in *Arabidopsis* (Liu et al., 2007; Swiezewski et al., 2007; Swiezewski et al., 2009; Ietswaart et al., 2012). *COOLAIR* RNAs functionally repress *FLC* sense expression at an early stage of cold exposure (vernalisation) *via* different ways, such as by directly associating with *FLC* chromatin or affecting H3K36me3 and H3K27me3 levels (Csorba et al., 2014; Berry and Dean, 2015; Rosa et al., 2016; Pajoro et al., 2017; Whittaker and Dean, 2017; Tian et al., 2019) (**Figure 1B**). The AS of antisense transcripts generated from the *FLC* locus produces two main classes of *COOLAIR* isoforms, terminating at proximal (sense intron 6, class I) and distal (sense promoter, class II) sites of *FLC* locus (Liu et al., 2007; Swiezewski et al., 2009; Marquardt et al., 2014). Each class contains several

FIGURE 1 | Splicing patterns of *FLC* sense and antisense transcripts, and AS of *FLC* antisense transcripts regulating *FLC* expression. **(A)** Schematic diagram of the splicing patterns of *FLC* sense and antisense transcripts at *FLC* locus in *Arabidopsis*. Black rectangles, gray dash lines and boxes indicate exons, introns and non-translated regions of *FLC* RNAs, respectively. Gray and black lines represent the genes and promoter regions of *FLC* and *COOLAIR* loci, respectively. **(B)** AS variants of *COOLAIR* transcripts effect *FLC* expression. Nascent *COOLAIR* RNAs are physically associated with the *FLC* locus to regulate the switching of chromatin states (Csorba et al., 2014; Li et al., 2015; Rosa et al., 2016). Two classes of *COOLAIR* transcripts bind to FCA and recruit PRC2 complex to *FLC* locus (Tian et al., 2019). The class I variants with proximal polyadenylation and the proximal–distal ratio of *COOLAIR* transcripts effect the histone methylation of H3K4me2, H3K36me3 and H3K27me3 (Marquardt et al., 2014; Berry and Dean, 2015; Xiao et al., 2015; Rosa et al., 2016). The class II *COOLAIR* transcripts with distal polyadenylation influence the degree of capping of the *FLC* nascent transcripts (Li et al., 2015).

subclasses produced by AS *associated with the usage of alternative 3′ polyadenylation* in spliced variants (**Figure 1A**). These multiple spliced variants with alternative polyadenylation are linked to different *FLC* expression states. Class I *COOLAIR* RNAs with proximal polyadenylation are associated with *FLC* repression (Liu et al., 2007; Swiezewski et al., 2009; Liu et al., 2010; Hornyik et al., 2010; Csorba et al., 2014). By contrast, class II *COOLAIR* transcripts are associated with high *FLC* expression levels. These *COOLAIR* RNAs with distal polyadenylation affect the capping of *FLC* nascent transcripts (Li et al., 2015).

The efficient splicing of class I intron promotes proximal polyadenylation in the antisense transcripts of *FLC*. As a result, this proximal polyadenylation inhibits the transcription of *FLC* through triggering H3K4me2 demethylation in the *FLC* locus (Marquardt et al., 2014). A few 3′-end processing factors containing RNA-recognition motifs, such as flowering control locus a (FCA) and FPA, glycine-rich rna-binding protein7 (GRP7), cleavage stimulation factor 64 (CstF64), CstF77, and nuclear speckle RNA binding protein a (NSRa), affect the splice

site selection and polyadenylation site usage of *COOLAIR* transcripts, leading to an altered ratio of proximal–distal spliced variants (Liu et al., 2007; Streitner et al., 2008; Liu et al., 2010; Hornyik et al., 2010; Streitner et al., 2012; Xiao et al., 2015; Bazin et al., 2018). Loss-of-function mutations in these factors decrease or increase the usage of *COOLAIR* proximal polyadenylation site, leading to upregulated or downregulated *FLC* transcription.

The AS of *COOLAIR* is altered by environmental conditions and natural intronic polymorphisms. Cold exposure influences *COOLAIR* splicing (Swiezewski et al., 2009). For example, class I *COOLAIR* RNAs increase more rapidly than do class II ones during vernalisation (Csorba et al., 2014; Eom et al., 2018). *Arabidopsis* accessions show variable *COOLAIR* splicing patterns that affect FLC expression and flowering time. A single nucleotide polymorphism (SNP) specifically regulates *COOLAIR* AS (Li et al., 2015). This SNP is located next to the acceptor splice site of the intron of class IIi *COOLAIR*. In later flowering accessions, such as Var2-6 and Eden-1, this SNP reduces use of the splice acceptor site of the class IIi *COOLAIR* intron, leading to a shift to

a downstream distal splice acceptor site and the inclusion of an internal exon. This change of splicing site produces isoforms with altered secondary structure and upregulates *FLC* expression (Li et al., 2015; Hawkes et al., 2016).

SPLICING FACTORS REGULATE THE PROCESSING OF *FLC* TRANSCRIPT

Splice sites, including 5′ donor splice site, branch point site, polypyrimidine tract and 3′ acceptor splice site, in pre-mRNA introns are precisely recognized by some splicing factors. Numerous splicing factors, such as BRR2, SC35 and SC35-like (SCL), RZ-1B and RZ-1C, are involved in the splicing of *FLC* in *Arabidopsis* flowering transition (**Table 1**). BRR2, an ATP-dependent RNA helicase, is an integral component of the U5 snRNP that is required for the activation of the spliceosome complex (Raghunathan and Guthrie, 1998). A missense mutation in *Arabidopsis BRR2a* results in defective *FLC* splicing and reduced *FLC* transcript levels (Mahrez et al., 2016). SC35 is a serine/arginine-rich (SR) protein that functions in the selection of splice sites (Valcárcel and Green, 1996). SC35 and SC35-like (SCL) proteins in *Arabidopsis* simultaneously modulate the splicing and transcription of *FLC* (Yan et al., 2017). *Arabidopsis* RZ-1B and RZ-1C, two heterogeneous nuclear ribonucleoproteins (hnRNPs), regulate *FLC* splicing and transcription by directly interacting with the SR protein (Wu et al., 2016). Interestingly, the retention of *FLC* introns 1, 5 and 6 in the *brr2a* mutant increases and the splicing efficiency of *FLC* intron 1 decreases in *rz-1b rz-1c* double mutants. These findings suggest that BRR2a, RZ-1B and RZ-1C promote the splicing of *FLC* introns. By contrast, the splicing efficiency of intron 1 in *FLC* increases compared with that in wild-type seedlings in quintuple mutants of *SC35* and *SCL* genes, indicating that SC35 and SCL proteins inhibit the splicing of the first intron of *FLC*. The splicing efficiency of *FLC* introns is also inhibited by KHZ1 and KHZ2, two RNA-binding proteins containing CCCH zinc-finger and K homology (KH) domain (Yan et al., 2019).

U2 auxiliary factor (U2AF) regulates flowering *via* modulating *FLC* splicing. U2AF65, a large subunit of *U2AF* in mammalians, recognises and binds to the 3′ polypyrimidine tract of introns (Wang et al., 2008; Shao et al., 2014). The binding site of U2AF65 with RNA is regulated and shifted in noncanonical introns (Shao et al., 2014; Howardet al., 2018). The genes *AtU2AF65a* and

AtU2AF65b encode the *U2AF* large subunit in *Arabidopsis* (Jang et al., 2014). AtU2AF65b plays roles in regulating flowering transition by splicing the introns 1 and 6 of *FLC* (Xiong et al., 2019a) (**Table 1**). *AtU2AF65b* expression is responsive to ABA, by which *AtU2AF65b* is involved in ABA-regulated flowering. *AtU2AF65a is* also *implicated in FLC splicing (*Park et al., 2019a*). Strikingly, the* loss-of-function mutants of *AtU2AF65a* and *AtU2AF65b* display opposite flowering phenotypes. Mutations in *atu2af65a* cause late flowering, whereas *AtU2AF65b* mutants exhibit early flowering (Park et al., 2019a; Xiong et al., 2019a). The differences in the noncanonical splicing variants between *atu2af65a* and *atu2af65b* null mutants (Park et al., 2019a) indicate that AtU2AF65a and AtU2AF65b might recognise different *FLC* introns.

In addition, some proteins play roles in RNA splicing by interaction with splicing factors. For example, the mRNA cap-binding complex (CBC) is involved in modulating pre-mRNA splicing activities *via* interaction with the splicing factors that recognise the 5′ splice site of the cap proximal intron (Izaurralde et al., 1994; Lewis et al., 1996). The CBP80/ABA Hypersensitive 1 (ABH1) and CBP20 are the large and small subunits of CBC protein complex in *Arabidopsis*, respectively (Hugouvieux et al., 2001). Knockout mutants of *ABH1/CBP80* and *CBP20* showing early-flowering phenotypes result from the defective splicing of *FLC* introns, especially the large first intron (Kuhn et al., 2007) (**Table 1**). In the *abh1* knockout mutant, the most prominent products are the splice intermediates containing the first intron, causing the downregulation of *FLC* transcript and the early-flowering phenotypes (Kuhn et al., 2007). Similarly, *CBP20* null mutation also results in increased unspliced–spliced ratio of *FLC* introns and low *FLC* mRNA levels (Geraldo et al., 2009).

To date, little is known about the splicing regulation of *COOLAIR* transcripts mediated by splicing factors. Only one splice factor, PRP8, a core spliceosome component, is found to function in modulating *COOLAIR* RNAs splicing (Marquardt et al., 2014) (**Table 1**). PRP8 is specifically required for the splicing of antisense transcripts *COOLAIR* but not for that of *FLC* sense transcripts. Single-base mutations of *PRP8* reduce the splicing efficiency of *COOLAIR* introns, especially class Ii introns. The decreased splicing efficiency of *COOLAIR* class Ii reduces proximal poly(A) site usage, leading to increased H3K4me2 and the transcriptional upregulation of *FLC* expression (Liu et al., 2010; Marquardt et al., 2014). NSRa, as a nuclear speckle RNA binding protein, modules flowering time through regulation of

TABLE 1 | Proteins involved in pre-mRNA splicing of *FLC* and *COOLAIR*.

Proteins	Type of Proteins	Splicing	References
U2AF65a, U2AF65b	Subunits of U2 auxiliary factors	*FLC* introns	Park et al., 2019a; Xiong et al., 2019a
SC35, SCL28,30,30A,33	SR proteins	*FLC* intron 1	Yan et al., 2017
BRR2a	U5 snRNP	*FLC* introns 1, 5 and 6	Mahrez et al., 2016
RZ-1B, RZ-1C	hnRNP proteins	*FLC* intron 1	Wu et al., 2016
ABH1/CBP80, CBP20	CAP-binding complex subunits; Interaction proteins of splicing factor	*FLC* introns	Geraldo et al., 2009; Kuhn et al., 2017
KHZ1, KHZ2	RNA-binding proteins	*FLC* introns	Yan et al., 2019
PRP8	Core spliceosome component	*COOLAIR* introns	Marquardt et al., 2014
NSRa	Nuclear speckle RNA binding protein	*COOLAIR* introns	Bazin et al., 2018

the *COOLAIR* AS (**Table 1**). Only distal variants are decrease in the *nsra* mutant. This change in relative variant usage of proximal-distal RNAs leads to a down-regulation of *FLC* mRNA and an early flowering phenotype of *nsra* mutant (Bazin et al., 2018).

CONCLUSION AND PERSPECTIVE

FLC is a key inhibitor in flowering transition in *Arabidopsis* and other dicots (Michaels and Amasino, 1999; Sheldon et al., 1999; Helliwell et al., 2006; Yuan et al., 2009; Wu et al., 2012). Therefore, the regulation of FLC is central to the transition to flowering in these plants. The AS of *FLC* sense and antisense transcripts is a critical step for *FLC* expression regulation. In *Arabidopsis*, multiple spliced variants of *FLC* sense and antisense transcripts have been determined (Kuhn et al., 2007; Severing et al., 2012; Li et al., 2015; Hawkes et al., 2016; Park et al., 2019a); however, we know little about functions *in vivo* of these spliced isoforms, especially, the *COOLAIR*-mediated regulation of switching of chromatin states at *FLC* and processing of *FLC* sense transcripts (**Figure 1B**). The further investigation will focus on how regulation of *COOLAIR* AS is linked to *FLC* chromatin modifications in response to external and internal influences.

Alternative splicing is regulated by splicing factors; however, only few splicing factors have been identified to be involved in the AS of *FLC*, especially those in the AS of *COOLAIR* transcripts. The identification of splicing factors and their functions is important for understanding the AS regulation of *FLC* sense and antisense transcripts in flowering transition. Additionally, the patterns of *FLC* AS is altered in response to environmental and signal stimuli (Swiezewski et al., 2009; Hornyik et al., 2010; Liu et al., 2010; Xiong et al., 2019a). Thus, the mechanisms by which the activities of splicing factors are regulated in response to external and internal cues must be investigated to study the AS of *FLC* sense and antisense transcripts in flowering regulation.

In agriculture, flowering is a prerequisite for crop production. Changes in the splicing patterns of *FLC* sense and antisense transcripts have enabled adaptation in response to changing environment for *Arabidopsis* accessions. Moreover, cold-induced sense and antisense RNAs of *FLC* are evolutionarily conserved in *Arabidopsis* perennial relatives and sugar beet (Reeves et al., 2007; Castaings et al., 2014; Li et al., 2015; Hawkes et al., 2016). Therefore, the molecular dissection of the diversity in splicing patterns of *FLC* across natural populations of *Arabidopsis* provides an important insight into how splicing regulation influences the switch from vegetative to reproductive growth. These findings propose a possible application for cultivating new varieties and augmenting the control of flowering time to adapt the environmental changes *via* modulating *FLC* expression in some crops, such as *Brassicaceae*.

AUTHOR CONTRIBUTIONS

X-LW designed the concept, organized and drafted the text. H-DQ performed the meta-analysis, drafted text, and prepared figures. H-DQ and YL edited the manuscript with help of Q-PR, Y-YW and FX.

FUNDING

REFERENCES

Bastow, R., Mylne, J. S., Lister, C., Lippman, Z., Martienssen, R. A., and Dean, C. (2004). Vernalization requires epigenetic silencing of *FLC* by histone methylation. *Nature* 427 (6970), 164–167. doi: 10.1038/nature02269

Bazin, J., Romero, N., Rigo, R., Charon, C., Blein, T., Ariel, F., et al. (2018). Nuclear speckle RNA binding proteins remodel alternative splicing and the non-coding *Arabidopsis* transcriptome to regulate a cross-talk between auxin and immune responses. *Front. Plant Sci.* 9 (1209). doi: 10.3389/fpls.2018.01209

Berry, S., and Dean, C. (2015). Environmental perception and epigenetic memory: mechanistic insight through *FLC*. *Plant J.* 83 (1), 133–148. doi: 10.1111/tpj.12869

Bloomer, R., and Dean, C. (2017). Fine-tuning timing: natural variation informs the mechanistic basis of the switch to flowering in *Arabidopsis thaliana*. *J. Exp. Bot.* 68 (20), 5439–5452. doi: 10.1093/jxb/erx270

Caicedo, A. L., Stinchcombe, J. R., Olsen, K. M., Schmitt, J., and Purugganan, M. D. (2004). Epistatic interaction between *Arabidopsis FRI* and *FLC* flowering time genes generates a latitudinal cline in a life history trait. *Proc. Natl. Acad. Sci. U.S.A.* 101 (44), 15670–15675. doi: 10.1073/pnas.0406232101

Castaings, L., Bergonzi, S., Albani, M. C., Kemi, U., Savolainen, O., and Coupland, G. (2014). Evolutionary conservation of cold-induced antisense RNAs of *FLOWERING LOCUS C* in *Arabidopsis thaliana* perennial relatives. *Nat. Commun.* 5, 4457. doi: 10.1038/ncomms5457

Chen, Y., Shen, Q., Lyu, P., Lin, R., and Sun, C. (2019). Identification and expression profiling of selected MADS-box family genes in *Dendrobium officinale*. *Genetica* 147 (3-4), 303–313. doi: 10.1007/s10709-019-00071-5

Cho, S., Hoang, A., Sinha, R., Zhong, X. Y., Fu, X. D., Krainer, A. R., et al. (2011). Interaction between the RNA binding domains of Ser-Arg splicing factor 1 and U1-70K snRNP protein determines early spliceosome assembly. *Proc. Natl. Acad. Sci. U.S.A.* 108 (20), 8233–8238. doi: 10.1073/pnas.1017700108

Coupland, G. (2019). *FLOWERING LOCUS C* isolation and characterization: two articles that opened many doors. *Plant Cell* 31 (6), 1190–1191. doi: 10.1105/tpc.19.00325

Csorba, T., Questa, J. I., Sun, Q., and Dean, C. (2014). Antisense *COOLAIR* mediates the coordinated switching of chromatin states at *FLC* during vernalization. *Proc. Natl. Acad. Sci. U.S.A.* 11; 111 (45), 16160–16165. doi: 10.1073/pnas.1419030111

Eom, H., Park, S. J., Kim, M. K., Kim, H., Kang, H., and Lee, I. (2018). TAF15b, involved in the autonomous pathway for flowering, represses transcription of FLOWERING LOCUS C. *Plant J.* 93 (1), 79–91. doi: 10.1111/tpj.13758

Fica, S. M., Oubridge, C., Wilkinson, M. E., Newman, A. J., and Nagai, K. (2019). A human postcatalytic spliceosome structure reveals essential roles of metazoan factors for exon ligation. *Science* 363 (6428), 710–714. doi: 10.1126/science.aaw5569

Filichkin, S. A., and Mockler, T. C. (2012). Unproductive alternative splicing and nonsense mRNAs: A widespread phenomenon among plant circadian clock genes. *Bio. Direct.* 7, 20. doi: 10.1186/1745-6150-7-20

Geraldo, N., Bäurle, I., Kidou, S., Hu, X., and Dean, C. (2009). FRIGIDA delays flowering in *Arabidopsis via a* cotranscriptional mechanism involving direct interaction with the nuclear cap-binding complex. *Plant Physiol.* 150 (3), 1611–1618. doi: 10.1104/pp.109.137448

Hawkes, E. J., Hennelly, S. P., Novikova, I. V., Irwin, J. A., Dean, C., and Sanbonmatsu, K. Y. (2016). *COOLAIR* antisense RNAs form evolutionarily conserved elaborate secondary structures. *Cell Rep.* 16 (12), 3087–3096. doi: 10.1016/j.celrep.2016.08.045

Helliwell, C. A., Wood, C. C., Robertson, M., James Peacock, W., and Dennis, E. S. (2006). The *Arabidopsis* FLC protein interacts directly *in vivo* with SOC1 and FT chromatin and is part of a high-molecular-weight protein complex. *Plant J.* 46 (2), 183–192. doi: 10.1111/j.1365-313X.2006.02686.x

Hornyik, C., Terzi, L. C., and Simpson, G. G. (2010). The spen family protein FPA controls alternative cleavage and polyadenylation of RNA. *Dev. Cell* 18 (2), 203–213. doi: 10.1016/j.devcel.2009.12.009

Howard, J. M., Lin, H., Wallace, A. J., Kim, G., Draper, J. M., Haeussler, M., et al. (2018). HNRNPA1 promotes recognition of splice site decoys by U2AF2 *in vivo*. *Genome Res.* 28 (5), 689–698. doi: 10.1101/gr.229062.117

Hrtyan, M., Slikova, E., Hejatko, J., and Ruzicka, K. (2015). RNA processing in auxin and cytokinin pathways. *J. Exp. Bot.* 66 (16), 4897–4912. doi: 10.1093/jxb/erv189

Hu, G., Hu, Z., Li, Y., Gu, F., Zhao, Z., and Chen, G. (2011). A splicing site mutation in *BrpFLC1* and repressed expression of *BrpFLC* genes are associated with the early flowering of purple flowering stalk. *Russ. J. Plant Physiol.* 58 (3), 431–438.

Huang, J., Gu, L., Zhang, Y., Yan, T., Kong, G., Kong, L., et al. (2017). An oomycete plant pathogen reprograms host pre-mRNA splicing to subvert immunity. *Nat. Commun.* 8 (1), 2051. doi: 10.1038/s41467-017-02233-5

Hugouvieux, V., Kwak, J. M., and Schroeder, J. I. (2001). An mRNA cap binding protein, ABH1, modulates early abscisic acid signal transduction in *Arabidopsis*. *Cell* 106 (4), 477–487. doi: 10.1016/s0092-8674(01)00460-3

Ietswaart, R., Wu, Z., and Dean, C. (2012). Flowering time control: another window to the connection between antisense RNA and chromatin. *Trends Genet.* 28 (9), 445–453. doi: 10.1016/j.tig.2012.06.002

Izaurralde, E., Lewis, J., McGuigan, C., Jankowska, M., Darzynkiewicz, E., and Mattaj, I. W. (1994). A nuclear cap binding protein complex involved in pre-mRNA splicing. *Cell* 78 (4), 657–668. doi: 10.1016/0092-8674(94)90530-4

Jang, Y. H., Park, H. Y., Lee, K. C., Thu, M. P., Kim, S. K., and Suh, M. C. (2014). A homolog of splicing factor SF1 is essential for development and is involved in the alternative splicing of pre-mRNA in *Arabidopsis thaliana*. *Plant J.* 78 (4), 591–603. doi: 10.1111/tpj.12491

Jurica, M. S., and Moore, M. J. (2003). Pre-mRNA splicing: awash in a sea of proteins. *Mol. Cell.* 12 (1), 5–14. doi: 10.1016/s1097-2765(03)00270-3

Kuhn, J. M., Breton, G., and Schroeder, J. I. (2007). mRNA metabolism of flowering-time regulators in wild-type *Arabidopsis* revealed by a nuclear cap binding protein mutant, *abh1*. *Plant J.* 50 (6), 1049–1062. doi: 10.1111/j.1365-313X.2007.03110.x

Kwak, J. S., Son, G. H., Song, J. T., and Seo, H. S. (2017). Post-translational modifications of FLOWERING LOCUS C modulate its activity. *J. Exp. Bot.* 68 (3), 383–389. doi: 10.1093/jxb/erw431

Laloum, T., Martin, G., and Duque, P. (2018). Alternative splicing control of abiotic stress responses. *Trends Plant Sci.* 23 (2), 140–150. doi: 10.1016/j.tplants.2017.09.019

Laubinger, S., Sachsenberg, T., Zeller, G., Busch, W., Lohmann, J. U., Rätsch, G., et al. (2008). Dual roles of the nuclear cap-binding complex and SERRATE in pre-mRNA splicing and microRNA processing in *Arabidopsis thaliana*. *Proc. Natl. Acad. Sci. U.S.A.* 105 (25), 8795–8800. doi: 10.1073/pnas.0802493105

Lempe, J., Balasubramanian, S., Sureshkumar, S., Singh, A., Schmid, M., and Weigel, D. (2005). Diversity of flowering responses in wild *Arabidopsis thaliana* strains. *PloS Genet.* 1 (1), 109–118. doi: 10.1371/journal.pgen.0010006

Lewis, J. D., Izaurralde, E., Jarmolowski, A., McGuigan, C., and Mattaj, I. W. (1996). A nuclear cap-binding complex facilitates association of U1 snRNP with the cap-proximal 5' splice site. *Genes Dev.* 10 (13), 1683–1698. doi: 10.1101/gad.10.13.1683

Li, P., Tao, Z., and Dean, C. (2015). Phenotypic evolution through variation in splicing of the noncoding RNA *COOLAIR*. *Genes Dev.* 29 (7), 696–701. doi: 10.1101/gad.258814.115

Li, S., Yamada, M., Han, X., Ohler, U., and Benfey, P. N. (2016). High-resolution expression map of the *Arabidopsis* root reveals alternative splicing and lincrna regulation. *Dev. Cell* 39 (4), 508–522. doi: 10.1016/j.devcel.2016.10.012

Liu, F., Quesada, V., Crevillen, P., Baurle, I., Swiezewski, S., et al. (2007). The *Arabidopsis* RNA-binding protein FCA requires a lysine-specific demethylase 1 homolog to downregulate FLC. *Mol. Cell* 28 (3), 398–407. doi: 10.1016/j.molcel.2007.10.018

Liu, F., Marquardt, S., Lister, C., Swiezewski, S., and Dean, C. (2010). Targeted 3' processing of antisense transcripts triggers *Arabidopsis* FLC chromatin silencing. *Science* 327 (5961), 94–97. doi: 10.1126/science.1180278

Liu, L., Wu, F., and Zhang, W. (2016). A conserved interaction between SKIP and SMP1/2 aids in recruiting the second-step splicing factors to the spliceosome in *Arabidopsis*. *Mol. Plant* 9 (12), 1660–1663. doi: 10.1016/j.molp.2016.09.007

Lockhart, J. (2018). Fresh as an Exitron: a flower-specific splice variant of *AUXIN RESPONSE FACTOR8* helps shape the stamen. *Plant Cell* 30 (3), 518–519. doi: 10.1105/tpc.18.00208

Long, Y., Sou, W. H., Yung, K. W. Y., Liu, H., Wan, S. W. C., et al. (2019). Distinct mechanisms govern the phosphorylation of different SR protein splicing factors. *J. Biol. Chem.* 294 (4), 1312–1327. doi: 10.1074/jbc.RA118.003392

Luo, X., Chen, T., Zeng, X., He, D., and He, Y. (2019). Feedback regulation of *FLC* by FLOWERING LOCUS T (FT) and FD through a 5' promoter region in *Arabidopsis*. *Mol. Plant* 12 (3), 285–288. doi: 10.1016/j.molp.2019.01.013

Lyons, R., and Kazan, K. (2016). The link between flowering time and stress tolerance. *J. Exp. Bot.* 67 (1), 47–60. doi: 10.1093/jxb/erv441

Mahrez, W., Shin, J., Muñoz-Viana, R., Figueiredo, D. D., Trejo-Arellano, M. S., Exner, V., et al. (2016). BRR2a affects flowering time *via FLC* splicing. *PloS Genet.* 12 (4), e1005924. doi: 10.1371/journal.pgen.1005924

Marquardt, S., Raitskin, O., Wu, Z., Liu, F., and Sun, Q. (2014). Dean, CFunctional consequences of splicing of the antisense transcript *COOLAIR* on *FLC* transcription. *Mol. Cell* 54 (1), 156–165. doi: 10.1016/j.molcel.2014.03.026

Matera, A. G., and Wang, Z. (2014). A day in the life of the spliceosome. *Nat. Rev. Mol. Cell Biol.* 15 (2), 108–121. doi: 10.1038/nrm3742

Mei, W., Liu, S., Schnable, J. C., Yeh, C. T., Springer, N. M., Schnable, P. S., et al. (2017). A comprehensive analysis of alternative splicing in paleopolyploid maize. *Front. Plant Sci.* 8, 694. doi: 10.3389/fpls.2017.00694

Melzer, R. (2017). Regulation of flowering time: a splicy business. *J. Exp. Bot.* 68 (18), 5017–5020. doi: 10.1093/jxb/erx353

Michaels, S. D., and Amasino, R. M. (1999). *FLOWERING LOCUS C* encodes a novel MADS domain protein that acts as a repressor of flowering. *Plant Cell* 11 (5), 949–956. doi: 10.1105/tpc.11.5.949

Michaels, S. D., He, Y., Scortecci, K. C., and Amasino, R. M. (2003). Attenuation of FLOWERING LOCUS C activity as a mechanism for the evolution of summer-annual flowering behavior in *Arabidopsis*. *Proc. Natl. Acad. Sci. U.S.A.* 100 (17), 10102–10107. doi: 10.1073/pnas.1531467100

Okumoto, K., Ono, T., Toyama, R., Shimomura, A., Nagata, A., and Fujiki, Y. (2018). New splicing variants of mitochondrial Rho GTPase-1 (Miro1) transport peroxisomes. *J. Cell Biol.* 217 (2), 619–633. doi: 10.1083/jcb.201708122

Pajoro, A., Severing, E., Angenent, G., and Immink, R. (2017). Histone H3 lysine 36 methylation affects temperature-induced alternative splicing and flowering in plants. *Genome Biol.* 18 (1), 102. doi: 10.1186/s13059-017-1235-x

Park, H. Y., Lee, H. T., Lee, J. H., and Kim, J. K. (2019a). *Arabidopsis* U2AF65 regulates flowering time and the growth of pollen tubes. *Front. Plant Sci.* 10, 569. doi: 10.3389/fpls.2019.00569

Park, Y. J., Lee, J. H., Kim, J. Y., and Park, C. M. (2019b). Alternative RNA splicing expands the developmental plasticity of flowering transition. *Front. Plant Sci.* 10, 606. doi: 10.3389/fpls.2019.00606

Raghunathan, P. L., and Guthrie, C. (1998). RNA unwinding in U4/U6 snRNPs requires ATP hydrolysis and the DEIH-box splicing factor Brr2. *Curr. Biol.* 8 (15), 847–855. doi: 10.1016/s0960-9822(07)00345-4

Reeves, P. A., He, Y., Schmitz, R. J., Amasino, R. M., Panella, L. W., and Richards, C. M. (2007). Evolutionary conservation of the FLOWERING LOCUS C-mediated vernalization response: evidence from the sugar beet (Beta vulgaris). *Genetics* 176 (1), 295–307. doi: 10.1534/genetics.106.069336

Richter, R., Kinoshita, A., Vincent, C., Martinez-Gallegos, R., Gao, H., van Driel, A. D., et al. (2019). Floral regulators FLC and SOC1 directly regulate expression of the B3-type transcription factor TARGET OF FLC AND SVP 1 at the *Arabidopsis* shoot apex *via* antagonistic chromatin modifications. *PloS Genet.* 15 (4), e1008065. doi: 10.1371/journal.pgen.1008065

Rodríguez-Cazorla, E., Ortuño-Miquel, S., Candela, H., Bailey-Steinitz, L. J., Yanofsky, M. F., Martínez-Laborda, A., et al. (2018). Ovule identity mediated by pre-mRNA processing in *Arabidopsis*. *PloS Genet.* 14 (1), e1007182. doi: 10.1371/journal.pgen.1007182

Rosa, S., Duncan, S., and Dean, C. (2016). Mutually exclusive sense-antisense transcription at FLC facilitates environmentally induced generepression. *Nat. Commun.* 7, 13031. doi: 10.1038/ncomms13031

Samach, A., Melamed-Bessudo, C., Avivi-Ragolski, N., Pietrokovski, S., and Levy, A. A. (2011). Identification of plant RAD52 homologs and characterization of

the *Arabidopsis thaliana RAD52-like* genes. *Plant Cell* 23 (12), 4266–4279. doi: 10.1105/tpc.111.091744

Searle, I., He, Y., Turck, F., Vincent, C., Fornara, F., Kröber, S., et al. (2006). The transcription factor FLC confers a flowering response to vernalization by repressing meristem competence and systemic signaling in *Arabidopsis*. *Genes Dev.* 20 (7), 898–912. doi: 10.1101/gad.373506

Severing, E. I., van Dijk, A. D., Morabito, G., Busscher-Lange, J., Immink, R. G., and van Ham, R. C. (2012). Predicting the impact of alternative splicing on plant MADS domain protein function. *PloS One* 7 (1), e30524. doi: 10.1371/journal.pone.0030524

Shang, X., Cao, Y., and Ma, L. (2017). Alternative splicing in plant genes: a means of regulating the environmental fitness of plants. *Int. J. Mol. Sci.* 18 (2). doi: 10.3390/ijms18020432

Shao, C., Yang, B., Wu, T., Huang, J., Tang, P., Zhou, Y., et al. (2014). Mechanisms for U2AF to define 3' splice sites and regulate alternative splicing in the human genome. *Nat. Struct. Mol. Biol.* 21 (11), 997–1005. doi: 10.1038/nsmb2906

Sheldon, C. C., Burn, J. E., Perez, P. P., Metzger, J., Edwards, J. A., Peacock, W. J., et al. (1999). The FLF MADS box gene: a repressor of flowering in *Arabidopsis* regulated by vernalization and methylation. *Plant Cell* 11 (3), 445–458. doi: 10.1105/tpc.11.3.445

Sheldon, C. C., Rouse, D. T., Finnegan, E. J., Peacock, W. J., and Dennis, E. S. (2000). The molecular basis of vernalization: the central role of FLOWERING LOCUS C (FLC). *Proc. Natl. Acad. Sci.* 97 (7), 3753–3758. doi: 10.1073/pnas.060023597

Slotte, T., Huang, H.-R., Holm, K., Ceplitis, A., Onge, K. S., Chen, J., et al. (2009). Splicing variation at a *FLOWERING LOCUS C* homolog is associated with flowering time variation in the tetraploid *Capsella bursa-pastoris*. *Genetics* 183 (1), 337–345. doi: 10.1534/genetics.109.103705

Streitner, C., Danisman, S., Wehrle, F., Schöning, J. C., Alfano, J. R., and Staiger, D. (2008). The small glycine-rich RNA binding protein AtGRP7 promotes floral transition in *Arabidopsis thaliana*. *Plant J.* 56 (2), 239–250. doi: 10.1111/j.1365-313X.2008.03591.x

Streitner, C., Köster, T., Simpson, C. G., Shaw, P., Danisman, S., and Brown, J. (2012). WAn hnRNP-like RNA-binding protein affects alternative splicing by *in vivo* interaction with transcripts in *Arabidopsis thaliana*. *Nucleic. Acids Res.* 40 (22), 11240–11255. doi: 10.1093/nar/gks873

Swiezewski, S., Crevillen, P., Liu, F., Ecker, J. R., Jerzmanowski, A., and Dean, C. (2007). Small RNA-mediated chromatin silencing directed to the 3' region of the *Arabidopsis* gene encoding the developmental regulator, FLC. *Proc. Natl. Acad. Sci. U.S.A.* 104 (9), 3633–3638. doi: 10.1073/pnas.0611459104

Swiezewski, S., Liu, F., Magusin, A., and Dean, C. (2009). Cold-induced silencing by long antisense transcripts of an *Arabidopsis* Polycomb target. *Nature* 462 (7274), 799–802. doi: 10.1038/nature08618

Tian, Y., Zheng, H., Zhang, F., Wang, S., Ji, X., Xu, C., et al. (2019). PRC2 recruitment and H3K27me3 deposition at *FLC* require FCA binding of *COOLAIR*. *Sci. Adv.* 5 (4), eaau7246. doi: 10.1126/sciadv.aau7246

Valcárcel, J., and Green, M. R. (1996). The SR protein family: pleiotropic functions in pre-mRNA splicing. *Trends Biochem. Sci.* 21 (8), 296–301. doi: 10.1016/S0968-0004(96)10039-6

Verhage, L., Severing, E., Bucher, J., Lammers, M., Busscher-Lange, J., Bonnema, G., et al. (2017). Splicing-related genes are alternatively spliced upon changes in ambient temperatures in plants. *PLoS One* 12 (3), e0172950. doi: 10.1371/journal.pone.0172950

Vosseberg, J., and Snel, B. (2017). Domestication of self-splicing introns during eukaryogenesis: the rise of the complexspliceosomal machinery. *Biol. Direct.* 12 (1), 30. doi: 10.1186/s13062-017-0201-6

Wahl, M. C., Will, C. L., and Lührmann, R. (2009). The spliceosome: design principles of a dynamic RNP machine. *Cell* 136 (4), 701–718. doi: 10.1016/j.cell.2009.02.009

Wang, H., You, C., Chang, F., Wang, Y., Wang, L., Qi, J., et al. (2014). Alternative splicing during *Arabidopsis* flower development results in constitutive and stage-regulated isoforms. *Front. Genet.* 5, 25. doi: 10.3389/fgene.2014.00025

Wang, Q., Zhang, L., Lynn, B., and Rymond, B. C. (2008). A BBP-Mud2p heterodimer mediates branchpoint recognition and influences splicing substrate abundance in budding yeast. *Nucleic Acids Res.* 36 (8), 2787–2798. doi: 10.1093/nar/gkn144

Wang, Z., Ji, H., Yuan, B., Wang, S., Su, C., Yao, B., et al. (2015). ABA signalling is fine-tuned by antagonistic *HAB1* variants. *Nat. Commun.* 6, 8138. doi: 10.1038/ncomms9138

Wang, Y. Y., Xiong, F., Ren, Q. P., and Wang, X. L. (2019). Regulation of flowering transition by alternative splicing: the role of the U2 auxiliary factors. *J. Exp. Bot.* doi: 10.1093/jxb/erz416

Werner, J. D., Borevitz, J. O., Uhlenhaut, N. H., Ecker, J. R., Chory, J., and Weigel, D. (2005). FRIGIDA-independent variation in flowering time of natural *Arabidopsis thaliana* accessions. *Genetics* 170 (3), 1197–1207. doi: 10.1534/genetics.104.036533

Whittaker, C., and Dean, C. (2017). The *FLC* locus: a platform for discoveries in epigenetics and adaptation. *Annu. Rev. Cell. Dev. Biol.* 33, 555–575. doi: 10.1146/annurev-cellbio-100616-060546

Will, C. L., and Lührmann, R. (2011). Spliceosome structure and function. *Cold Spring Harb. Perspect. Biol.* doi: 10.1101/cshperspect.a003707

Wu, J., Wei, K., Cheng, F., Li, S., Wang, Q., Zhao, J., et al. (2012). A naturally occurring InDel variation in *BraA.FLC.b* (*BrFLC2*) associated with flowering time variation in *Brassica rapa*. *BMC Plant Biol.* 12, 151. doi: 10.1186/1471-2229-12-151

Wu, Z., Zhu, D., Lin, X., Miao, J., Gu, L., Deng, X., et al. (2016). RNA binding proteins RZ-1B and RZ-1C play critical roles in regulating pre-mRNA splicing and gene expression during development in *Arabidopsis*. *Plant Cell* 28 (1), 55–73. doi: 10.1105/tpc.15.00949

Xiao, J., Li, C., Xu, S., Xing, L., Xu, Y., and Chong, K. (2015). JACALIN-LECTIN LIKE1 Regulates the Nuclear Accumulation of GLYCINE-RICH RNA-BINDING PROTEIN7, influencing the RNA processing of FLOWERING LOCUS C antisense transcripts and flowering time in *Arabidopsis*. *Plant Physiol.* 169 (3), 2102–2117. doi: 10.1104/pp.15.00801

Xiong, F., Ren, J. J., Yu, Q., Wang, Y. Y., Lu, C. C., Kong, L. J., et al. (2019a). AtU2AF65b functions in ABA-mediated flowering *via* regulating the pre-mRNA splicing of *ABI5* and *FLC* in Arabidopsis. *New Phytol.* 223 (1), 277–292. doi: 10.1111/nph.15756

Xiong, F., Ren, J. J., Yu, Q., Wang, Y. Y., Kong, L. J., Otegui, M. S., et al. (2019b). *AtBUD13* affects pre-mRNA splicing and is essential for embryo development in *Arabidopsis*. *Plant J.* 98 (4), 714–726. doi: 10.1111/tpj.14268

Yan, Q., Xia, X., Sun, Z., and Fang, Y. (2017). Depletion of *Arabidopsis* SC35 and SC35-like serine/arginine-rich proteins affects the transcription and splicing of a subset of genes. *PloS Genet.* 13 (3), e1006663. doi: 10.1371/journal.pgen.1006663

Yan, Z., Shi, H., Liu, Y., Jing, M., and Han, Y. (2019). KHZ1 and KHZ2, novel members of the autonomous pathway, repress the splicing efficiency of *FLC* pre-mRNA in *Arabidopsis*. *J. Exp. Bot.* erz499. doi: 10.1093/jxb/erz499

Yuan, Y. X., Wu, J., Sun, R. F., Zhang, X. W., Xu, D. H., Bonnema, G., et al. (2009). A naturally occurring splicing site mutation in the *Brassica rapa FLC1* gene is associated with variation in flowering time. *J. Exp. Bot.* 60 (4), 1299–1308. doi: 10.1093/jxb/erp010

Zhang, J. Z., Li, Z. M., Mei, L., Yao, J. L., and Hu, C. G. (2009). *PtFLC* homolog from trifoliate orange (*Poncirus trifoliata*) is regulated by alternative splicing and experiences seasonal fluctuation in expression level. *Planta.* 229 (4), 847–859. doi: 10.1007/s00425-008-0885-z

Zhao, J., Kulkarni, V., Liu, N., Del Carpio, D. P., Bucher, J., and Bonnema, G. (2010). *BrFLC2* (*FLOWERING LOCUS C*) as a candidate gene for a vernalization response QTL in *Brassica rapa*. *J. Exp. Bot.* 61 (6), 1817–1825. doi: 10.1093/jxb/erq048

Zhu, F. Y., Fan, T., Liu, Y. G., Zhu, F. Y., Chen, M. X., Shi, L. et al. (2017). Proteogenomic analysis reveals alternative splicing and translation as part of the abscisic acid response in *Arabidopsis* seedlings. *Plant J.* 91 (3), 518–533. doi: 10.1111/tpj.13571

Zou, X., Suppanz, I., Raman, H., Hou, J., Wang, J., Long, Y., et al. (2012). Comparative analysis of *FLC* homologues in *Brassicaceae* provides insight into their role in the evolution of oilseed rape. *PloS One* 7 (9), e45751. doi: 10.1371/journal.pone.0045751