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REVIEW

Florigen and the Photoperiodic Control of Flowering in Rice

Hiroyuki Tsuji · Shojiro Tamaki · Reina Komiya · Ko Shimamoto

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Abstract Flowering time is a key trait for geographical and seasonal adaptation of plants and is an important consideration for rice breeders. Recently identified genetic factors provide new insights into this complex trait. The list of genes involved in flowering and their functions tells us that the molecular basis of day-length measurement includes both of the evolution of unique factors and the regulatory adaptation of conserved factors in rice. This information helped identify rice florigen, a mobile flowering signal. Our current view of flowering time regulation incorporates the presence of complex layers of gene networks integrated with the synthesis of florigen protein and its subsequent transport and perception.

Keywords Florigen · Flowering time · Genetic pathways

Introduction

Flowering time, often referred to as heading date in cereal crops, is a key agronomical determinant for adaptation to specific cropping locations and growing seasons for current varieties of cultivated rice. Developing early-flowering or photoperiod-insensitive cultivars has been a major objective of rice breeding for several decades. The molecular and developmental determinants of flowering time have thus also particularly important genetic targets for domestication or for breeding new varieties of rice. Flowering time is controlled by many genes, which are expressed or suppressed in close interaction with environmental factors such as day length and temperature. Progress in the molecular genetics has provided a clearer understanding of several pivotal mechanisms regulating flowering time determination in rice, and these studies have been summarized from genetic, molecular biological, or comparative biological perspectives [17, 24, 25, 43, 83]. In this review, we discuss the current understanding of rice flowering, considering the recent finding of a strong candidate for the long sought-after mobile flowering stimulus, florigen [74].

H. Tsuji · S. Tamaki · R. Komiya · K. Shimamoto (✉)
Laboratory of Plant Molecular Genetics,
Nara Institute of Science and Technology (NAIST),
8916-5 Takayama,
Ikoma, Nara 630-0101, Japan
e-mail: simamoto@bs.naist.jp

Hd3a protein as the rice florigen

Heading date 3a (*Hd3a*) was first detected as a quantitative trait locus (QTL), which promotes flowering of rice under short-day (SD) conditions [55, 80]. *Hd3a* encodes an ortholog of *Arabidopsis FLOWRING LOCUS T* (*FT*) [38]. Overexpression of Hd3a protein with the constitutive promoter [38] or vascular-specific promoters [74] results in an early-flowering phenotype, and suppression of *Hd3a* with RNA interference (RNAi) delays flowering [39]. *Hd3a* is a member of a large gene family consisting of at least 13 genes in rice genome [6] and at least two paralogs, *Rice FLOWERING LOCUS T1* (*RFT1*) and *FT-Like* (*FTL*) promote flowering [28, 39]. Hd3a/FT proteins are about 22 kDa in size, and their overall structures are similar to mammalian phosphatidyl ethanolamine-binding proteins or Raf-kinase inhibitor proteins (RKIP) [3], although it is not known whether or not Hd3a/FT binds to phosphatidyl ethanolamine or inhibits kinase.

Recent progress in the molecular genetics of *Arabidopsis* indicates that *FT* has a strong flowering promotion effect downstream of the known photoperiodic flowering pathway

[17, 21, 36]. *Arabidopsis* flowering is promoted by long day (LD), whereas rice flowering is promoted by SD. *FT* is a major floral activator that is expressed in the vascular tissues of leaves under inductive LD in *Arabidopsis* [32, 37, 71]. FT protein interacts with the bZIP transcription factor FLOWERING LOCUS D (FD), which is only expressed in the shoot apical meristem (SAM), and this interaction seems to be necessary for full activation of FT floral promotion [1, 76]. The anatomical separation of expression sites implies that *FT* product is a primary candidate for florigen. If *FT* encodes the florigen, it could act as a mobile agent either via protein or messenger RNA (mRNA), either of which could move to the SAM to interact with FD. Therefore, a major focus was whether transcripts or protein account for the mobile florigenic activity [85].

The question was answered with the introduction of rice as a paradigm for exploring the nature of florigen (Fig. 1) [74]. First, the precise sites of *Hd3a* transcription and mRNA accumulation were determined. The promoter activity of *Hd3a* was detected in transgenic plants expressing *β-glucuronidase* (GUS) under the control of the *Hd3a* promoter in the vascular cells of leaf blades. No GUS activity was detected in the SAM. This is consistent with the tissue specificity of *FT* expression in *Arabidopsis*, although expression is induced by LD for *FT* and by SD for *Hd3a* [32, 37]. *Hd3a* mRNA accumulates in leaf blades but is present at very low levels in leaf sheaths and is four orders of magnitude lower in the shoot apex than in leaf blades under SD conditions. Therefore, it is unlikely that *Hd3a* mRNA moves from leaves to the SAM in any significant amount. *Hd3a* expression is thus limited to the vascular tissues of leaf blades under SD conditions.

Secondly, the tissue localization of Hd3a protein was examined using transgenic rice plants expressing Hd3a-GFP fusion protein driven by the Hd3a promoter. Hd3a-GFP was present in vascular tissue from the leaf blade to the upper part of the stem, the region just below the meristem where nodes are present, and in the inner cone-like region of the SAM. Hd3a-GFP protein is thus synthesized in the vascular tissues of leaf blades and transported through the phloem. Hd3a protein is then unloaded from the end of the vascular tissue and enters the SAM through cells just beneath the SAM [74]. Essentially, the same localization of Hd3a-GFP was observed when other vascular-specific promoters were used to express Hd3a-GFP, confirming that Hd3a-GFP is translocated from leaf and stem vasculature to the SAM. These observations indicate that Hd3a protein is a mobile flowering signal in rice (Fig. 1). The ability of Hd3a/FT protein to move long distances is also suggested from a study of the rice phloem sap proteome [4]. Rice phloem sap contains a member of Hd3a/FT protein family, FT-LIKE12, along with RKIP-like proteins RICE CENTRORADIALIS3 (RCN3) and MOTHER OF FT1. Hd3a itself was not detected, probably because photoperiod conditions and timing of sampling was not suitable for detection of Hd3a. Hd3a/FT proteins, however, have been detected in the phloem sap of other plant species. CmFTL2, a functional ortholog of Hd3a/FT in *Cucurbita maxima*, has also been found in vascular sap and can move through graft unions to promote flowering [47]. Phloem sap obtained from the inflorescence

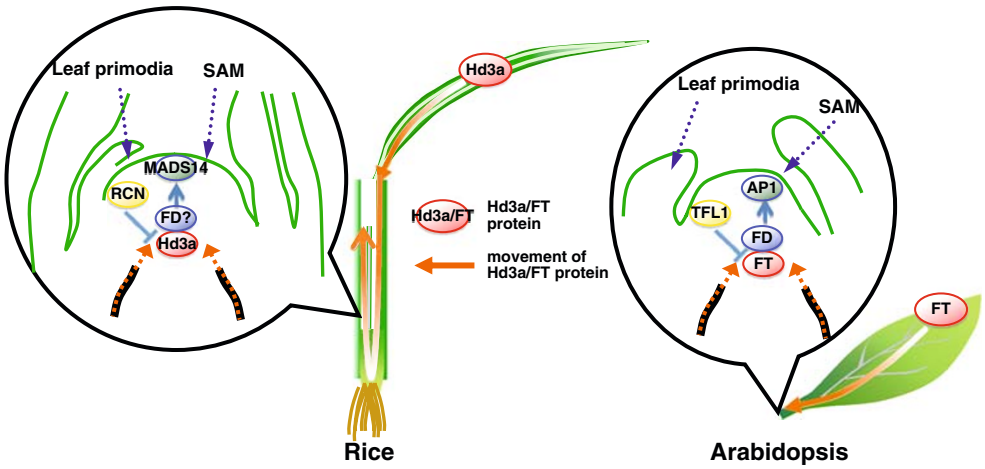

Fig. 1 Model of Hd3a/FT action in rice and *Arabidopsis*. Hd3a/FT protein is synthesized in the vascular tissue of the leaf and transported through phloem tissue. Hd3a/FT protein is unloaded from the end of the vascular tissue and enters into the SAM through the cells just below the SAM. Several lines of evidence suggest that Hd3a/FT protein interacts with the bZIP transcription factor FD, which directly binds promoter region of floral meristem identity gene *AP1*. Hd3a/FT is a strong candidate for florigen.

stems of *Brassica napus* also contained FT protein [14]. These observations provide additional evidence that Hd3a/FT proteins are florigens. Evidence from *Arabidopsis* also supports the florigen activity of FT protein. Phloem-expressed FT-GFP and Myc-tagged FT move to the apex and cause early flowering, but FT protein with nuclear localization signal or 3xYFP do not, probably because of immobilization [8, 29, 52].

RFT1 also promotes flowering in rice

The *RFT1* gene lies adjacent to *Hd3a*, separated by only 11.5 kb on chromosome 6 of rice [26]. *Hd3a* and *RFT1* sequences are very similar, and they were likely produced by a recent tandem duplication event [6]. The corresponding chromosomal regions of the *Hd3a/RFT1* locus in maize or wheat contain only a single *Hd3a* ortholog [10, 82]. *RFT1* tissue-specific expression is similar to that of *Hd3a* in that it is expressed in vascular tissues of leaf blades in response to SD. Thus, *RFT1* could possibly function redundantly with *Hd3a* in promoting rice flowering as another florigen. The interesting involvement of *RFT1* was revealed from a detailed analysis of rice plants with RNAi-suppressed *Hd3a* expression [39]. Flowering of *Hd3a* RNAi plants was delayed by more than 30 days under SD conditions. Although flowering of *RFT1* RNAi plants was normal, suggesting that *RFT1* does not on its own promote flowering under SD conditions, double RNAi plants in which both *Hd3a* and *RFT1* are suppressed did not flower up to 300 days after germination. Both *Hd3a* and *RFT1* are thus involved in the normal regulation of flowering in rice. *RFT1* expression is normally low in wild-type rice plants but is up-regulated in *Hd3a* RNAi plants and is correlated with reproductive transition of the SAM. This up-regulation is also correlated with an increase of histone-3-acetylation of nucleosomes around the transcription initiation site of *RFT1*. These results suggest that *RFT1* expression increases in the absence of Hd3a and that *RFT1* complements *Hd3a* function [39]. RFT1 thus serves as another flowering promotion activity in rice under certain conditions.

Hd3a/FT signaling in the shoot apical meristem

The identification of Hd3a/FT as florigen opens the door to studying the molecular mechanism(s) of Hd3a/FT signaling in the SAM. The current understanding of events downstream of Hd3a/FT activity focuses on FD, MADS-box transcription factors, and CENTRORADIALIS (CEN) / TERMINAL FLOWER1 (TFL1). Corresponding genes of the proteins discussed below are summarized in Table 1.

FD

In the SAM, Hd3a may interact with a bZIP transcription factor orthologous to *Arabidopsis* FD to induce phase transition from vegetative to reproductive states. In *Arabidopsis*, *FD* is expressed on the flanks of the SAM where flower primordia are initiated. *FD* is expressed during the vegetative phase so that it is present when FT arrives. In the presence of FT, FD induces the floral meristem identity gene *APETALA1* (*AP1*) and its paralog *FRUITFULL* (*FUL*) [2, 76]. At present, there are no reports describing FD function in rice, whereas the maize late flowering mutant *delayed flowering 1* (*dlf1*) provides a hint about FD function in rice and other cereals [58]. The *DLF1* gene encodes an ortholog of *FD*. Loss-of-function mutants of maize *DLF1* (*dlf1*) have a late flowering phenotype with some abnormal tassel branches. The most abundant *DLF1* expression is found in the SAM, and it peaks during vegetative-to-reproductive phase transition, decreasing gradually during inflorescence development. DLF1 has also been shown to interact with maize Hd3a/FT. The maize genome contains at least 15 members of the *Hd3a/FT* gene family. Two of them, *Zea mays CENTRORADIALIS 8* (*ZCN8*) and *ZCN14*, interact with DLF1 in yeast two-hybrid assays [10]. *ZCN8* transcripts are present in leaf blades before floral transition, increases just before floral transition, and stays high afterward. Because of its expression pattern and interaction with DLF1, *ZCN8* should be considered as a florigen candidate in maize. *ZCN15*, an ortholog of rice *Hd3a*, which resides in the syntenic chromosome region of rice *Hd3a*, is weakly expressed in leaf blades after phase transition and relatively highly expressed in the developing kernel. The activation of AP1 by Hd3a/FT and FD is operative in cereal crops. The *dlf1* mutation of maize delayed the expression of maize *AP1/FUL* MADS-box gene *ZMM4*, an ortholog of *OsMADS14/RAP1B*, in the SAM [11], and TaFDL2, a wheat FD homolog, can interact with wheat FT protein *VERNALIZATION3* (*VRN3*)/*TaFT* and directly binds the promoter region of wheat *AP1* homologous gene in vitro [45].

There are at least seven orthologs of *FD* in the rice genome [60]. *OsbZIP24* mRNA is relatively abundant in the SAM, and *OsbZIP54* mRNA is distributed throughout the rice plant, including the SAM, whereas transcript accumulation of other FD-like bZIPs is below the microarray detection limit [60]. It is yet to be determined if there is some unresolved functional differentiation among these FD-like proteins of rice.

MADS-box transcription factors

The gene network, which acts downstream of FT in the SAM, involves *MADS-box* genes in *Arabidopsis*. Both FT

Table 1 Genes that are Expected to be Involved in Hd3a/FT Signaling in SAM

Category	Gene name	Accession no.	Organism	Domain	Function	Reference
Hd3a/FT	*Hd3a*	Os06g0157700	Rice	Raf-kinase inhibitor	Florigen; promotion of flowering	[38]
	RFT	Os06g0157500	Rice		Promotion of flowering	[28]
	FTL	Os01g0218500	Rice		Promotion of flowering	[28]
	ZCN8	EU241924	Maize		n.d.	[11]
	ZCN15	EU241930	Maize		n.d.	[11]
	VRN3/TaFT	DQ890165	Wheat		Promotion of flowering	[82]
	FT	At1g65480	*Arabidopsis*		Florigen; Promotion of flowering	[32, 37]
	TSF	AT4g20370	*Arabidopsis*		Promotion of flowering	[78]
CEN/TFL1	*RCN1*	Os11g0152500	Rice	Raf-kinase inhibitor	Inhibition of flowering	[59]
	RCN2	Os02g0531600	Rice		Inhibition of flowering	[59]
	RCN3	Os12g0152000	Rice		Inhibition of flowering	[59, 87]
	OsCEN3	Os04g0411400	Rice		n.d.	[87]
	TFL1	At5g03840	*Arabidopsis*		Inhibition of flowering	[5]
FD	*OsbZIP24*	Os02g0833600	Rice	bZIP	n.d.	[60]
	OsbZIP27	Os03g0306700	Rice		n.d.	[60]
	OsbZIP54	Os06g0719500	Rice		n.d.	[60]
	OsbZIP55	Os06g0720900	Rice		n.d.	[60]
	OsbZIP56	Os06g0724000	Rice		n.d.	[60]
	OsbZIP69	Os08g0549600	Rice		n.d.	[60]
	OsbZIP77	Os09g0540800	Rice		n.d.	[60]
	DLF1	EF093789	Maize		Promotion of flowering	[58]
	TaFDL2	EU307112	Wheat		n.d.	[45]
	FD	At4g35900	*Arabidopsis*		Promotion of flowering	[1, 76]
MADS-box transcription factor (FUL/AP1/CAL)	*OsMADS14/RAP1B*	Os03g0752800	Rice	MADS-box	Promotion of flowering	[41]
	OsMADS15/RAP1A	Os07g0108900	Rice		n.d.	[41]
	ZMM4	AJ430641	Maize		Promotion of flowering	[11]
	WAP1/VRN1	AB007504/AY188331	Wheat		Promotion of flowering	[56, 81]
	FUL	At5g60910	*Arabidopsis*		Promotion of flowering	[15]
	AP1	At1g69120	*Arabidopsis*		n.d.	[51]
	CAL	At1g26310	*Arabidopsis*		n.d.	[33]
MADS-box transcription factor (SOC1)	*OsMADS50/OsSOC1*	Os03g0122600	Rice	MADS-box	Promotion of flowering	[44]
	SOC1	At2g45660	*Arabidopsis*		Promotion of flowering	[65]

n.d. Not functionally determined yet

and FD, together with LEAFY, are required for inducing expression of *AP1* and *FUL* in the SAM [2, 53, 75]. FT-dependent gene regulation is also observed in *Arabidopsis* leaves. Expression of *FUL* and *SEPALATA3* was induced in leaves overexpressing *FT* and was reduced in *ft* and *fd* mutants [75]. Thus, leaves and the SAM may share similar regulatory mechanisms. In rice, the expression of *OsMADS14/RAP1B*, an ortholog of *AP1*, and *OsMADS15/RAP1A* are up-regulated by *Hd3a* in leaf blades under SD conditions [39], suggesting that the same regulatory network is involved in the SAM of rice. *OsMADS14/RAP1B* is expressed in the SAM during the reproductive phase [13, 41], and its ectopic expression strongly promotes rice flowering [31]. Interestingly, a mutant of the *OsMADS14/RAP1B* ortholog in einkorn wheat (*Triticum monococcum*), *maintained vegetative phase* (*mvp*), cannot show transition from vegetative to reproductive phases [67]. The *mvp* phenotype is caused by a deletion of the promoter and coding region of *Wheat AP1* (*WAP1*)/*VERNALIZATION1* (*VRN1*), a gene that lies within the wheat chromosome region corresponding to the region containing *OsMADS14/RAP1B* in rice [81]. Reduced levels of *VRN3/TaFT*, an ortholog of rice *Hd3a*, are associated with lower levels of *VRN1* transcripts, consistent with the observation in rice [82]. Although *AP1* in *Arabidopsis* is unlikely to be the FT target in the SAM for flowering control because *ap1* mutants are not late flowering [62], AP1 MADS-box proteins are likely to function as important mediators of Hd3a/FT activity in flowering of cereals. *OsMADS14/RAP1B* is also an activator of *Hd3a* expression in leaves [34, 43]. Consistent with this, reduced levels of *VRN1* are also correlated with reduced levels of *VRN3* in barley [20].

Suppressor of Overexpression of Constans1 (SOC1) in *Arabidopsis* is a MADS-box protein, and a recent genetic study suggests that FT mediates the activation of *SOC1* downstream of *CONSTANS* (CO) [44]. SOC1 directly interacts with AGAMOUS-LIKE24 (AGL24) MADS-box protein in the shoot apex, and direct binding of the SOC1-AGL24 complex to the promoters of both *SOC1* and *AGL24* upregulates their expression [48]. On the other hand, the regulatory hierarchy and the site of action seem to be different in rice; a T-DNA insertion mutation of *OsMADS50/OsSOC1* results in a reduction of *Hd3a* transcription in leaves, whereas RNAi suppression of *Hd3a* or of both *Hd3a* and *RFT1* does not result in any change in *OsMADS50/OsSOC1* expression. Thus, in rice, *OsMADS50/OsSOC1* acts upstream of *Hd3a* expression in leaf blades [39, 44].

CEN/TFL1

CENTRORADIALIS (CEN)/TERMINAL FLOWER1 (TFL1) proteins provide interesting insights into Hd3a/FT signaling in the SAM. *CEN/TFL1* are homologs of *Hd3a/FT* and encode RKIP proteins, but CEN/TFL1 proteins repress flowering. *Arabidopsis TFL1* mRNA is limited to the central cells of the inflorescence shoot meristem, and the TFL1 protein migrates to outer cells [7]. Repression of flowering has been thoroughly investigated using *Arabidopsis* FT and TFL1 [3, 16]. Proteins carrying replacements of individual residues or specific regions of FT and TFL1 were overexpressed in a *ft tfl1* double mutant to map the residues or regions that confer specific activity on the two proteins. The crystal structures of FT and TFL1 were also compared to map the region of specificity. These analyses suggest that His88 in TFL1 and the corresponding Tyr85 in FT are important for the opposite activities of FT and TFL1 [16] and that the region responsible for the difference is localized in a 14 amino acid segment in the external loop at the C-termini of the proteins [3].

There are at least four *CEN/TFL1*-like genes in the rice genome [6]. *RICE CENTRORADIALS1* (*RCN1*), *RCN2*, and *RCN3/Oscen1* are able to delay flowering and affect panicle architecture when overexpressed [59, 87]. Interestingly, RCN3 protein can be detected in the phloem sap of rice, suggesting that this protein signals to communicate between distant organs, much like Hd3a [4]. An attractive hypothesis to explain the difference between Hd3a/FT and CEN/TFL1 regulatory activity is that the external loops bring different partners to Hd3a/FT or CEN/TFL1, thus defining the function of the complex. Screening for interacting proteins using specific external loop regions may provide further insights into Hd3a/FT signaling for floral promotion.

Molecular-genetic pathways of the photoperiodic flowering in rice

From an understanding of the molecular nature of Hd3a/FT proteins, it can be inferred that the timing of rice flowering is basically determined by the expression levels of the two essential flowering promotion genes, *Hd3a* and *RFT1* in leaf blades, and by the competency of the SAM for Hd3a/FT activity. Recent molecular genetic studies provide important insights into the day-length regulation of *Hd3a* expression. The crucial aspect of this regulation is SD induction and LD repression of *Hd3a* (Fig. 2).

Short-day promotion of Hd3a expression

Under SD conditions, Hd3a expression is induced gradually and peaks at about 30 days before flowering, about the time floral transition occurs [39]. The diurnal peak of *Hd3a* promoter activity and mRNA accumulation coincide at dawn, suggesting the major point of *Hd3a* regulation is transcriptional [23, 38, 74]. The most important factors for this *Hd3a* expression are *Heading date1* (*Hd1*) and *Early heading date1* (*Ehd1*, see below) [24]. *Hd1* was first detected as the major photoperiod-sensitivity QTL, and it encodes a B-box zinc finger protein with a C-terminal CCT (CONSTANS, CONSTANS-LIKE and TIMING OF CAB EXPRESSION1) domain [84]. Under SD conditions, loss-of-function alleles of *Hd1* delay flowering and reduce *Hd3a* mRNA accumulation [23, 28, 38, 84]. Detailed phylogenetic analyses showed that *Hd1* is the sole ortholog of *Arabidopsis CONSTANS* (*CO*), which is also an important activator of *FT* [26]. *Arabidopsis CO* is expressed in leaf phloem tissues [71], and CO protein seems to directly regulate *FT* and its paralog *TWIN SISTER OF FT* (*TSF*) because both *FT* and *TSF* are up-regulated by dexamethasone-induced activation of CO in the presence of the translation inhibitor cycloheximide [65, 78]. Whether Hd1 directly regulates *Hd3a* transcription is not clear, but differences in the temporal patterns of *Hd1* and *Hd3a* mRNA accumulation suggest the involvement of a somewhat more complex regulatory mechanism. *Hd1* mRNA levels peak at midnight, but *Hd3a* mRNA levels peak about 4–6 h after *Hd1* [19, 23, 28].

In addition to transcriptional regulation, Hd1 activity may be regulated by protein stability because *Arabidopsis* CO is subject to the regulation at the protein accumulation level. CO protein is destabilized in darkness by CONSTITUTIVELY PHOTOMORPHOGENIC1, which is counteracted by the blue-light photoreceptor CRYPTOCHROME. A PhyB-mediated signal also destabilizes CO at dawn [30, 42, 49].

Phytochromes also affect the expression of *Hd3a* under SD conditions. *Hd3a* expression under SD conditions is

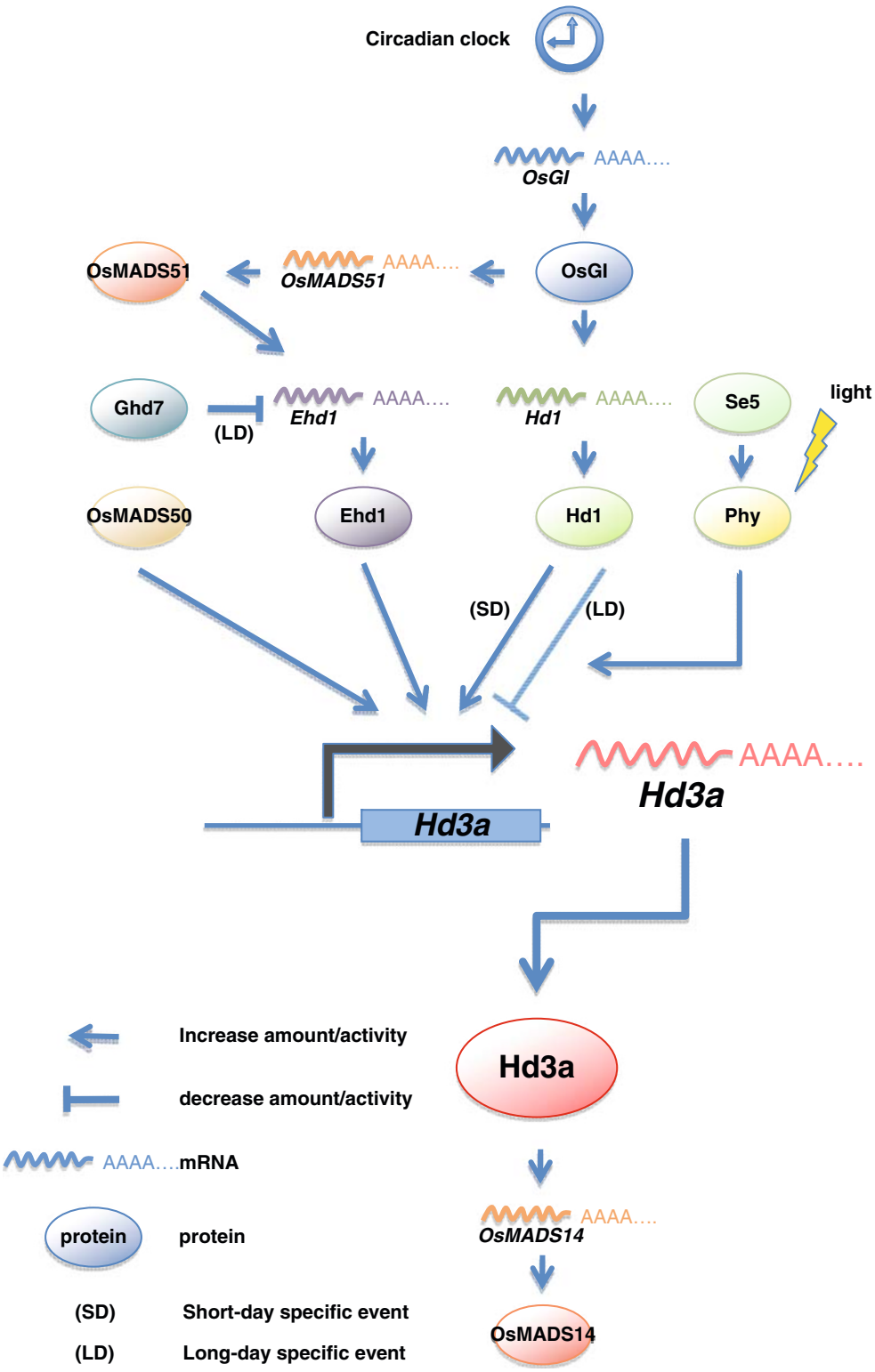

Fig. 2 Regulatory network of rice flowering time. Under short-day conditions, *Hd3a* is mainly up-regulated by Hd1 and Ehd1. *Hd1* is up-regulated by OsGI, and *Ehd1* is up-regulated by OsMADS51, whose expression is up-regulated by OsGI. *OsGI* is regulated by the circadian clock. Under long-day conditions, Hd1 function is converted to repress *Hd3a* in response to a signal from phytochrome. *Ehd1* is repressed by Ghd7, a regulatory component that is up-regulated under long-day conditions, resulting in *Hd3a* repression. SD or LD in *parentheses* indicate short-day- or long-day-specific regulation, respectively.

significantly up-regulated in an early-flowering *photoperiodic sensitivity 5* (*se5*) mutant, which has a mutation in the gene encoding heme oxygenase, which is required for phytochrome chromophore biogenesis [27, 28]. Flowering under SD conditions is also promoted in *phyB* mutants that have loss-of-function alleles in one of the three rice phytochromes[73]. *Hd1* expression is not affected by *se5* or *phyB* mutations [23, 28]; thus, phytochrome represses *Hd3a* expression downstream or independent of *Hd1* expression under SD conditions. These phytochrome

effects may be reminiscent of the activator-to-repressor conversion of a subset of Hd1 proteins that is observed under LD (see below; Izawa et al. [28]).

The primary upstream regulator of *Hd1* expression is *OsGI*, an ortholog of *GIGANTEA* (*GI*) in *Arabidopsis* [18]. OsGI is a large protein that is present in both the nucleus and cytosol of rice cells [1]. Suppression of *OsGI* expression by RNAi or antisense expression caused late flowering and reduced *Hd1* mRNA accumulation under SD conditions [19, 34]. *Arabidopsis* GI plays important roles in *CO* expression through the degradation of a repressor of *CO* transcription [22, 66]. Thus, it is possible that OsGI is part of a similar mechanism in rice, even though the peak in *OsGI* expression at dusk is quite different from the *Hd1* expression peak at midnight, suggesting the intervention of an unknown mechanism, which caused the difference in timing of expression.

OsGI expression shows circadian daily oscillation, implying upstream regulation by the circadian clock [18]. Circadian clock mutants of *Arabidopsis* have aberrant *GI* expression [54, 61], and GI itself is also considered to be a clock-associated protein [35, 50, 86].

Another major *Hd3a* activator, *Ehd1*, was identified from a QTL of a cross between the cultivar T65 and Nipponbare [12]. *Ehd1* encodes a B-type response regulator, and a functional mutation is found in the GARP (maize GOLDEN2, the ARR B-class proteins from *Arabidopsis*, and *Chlamydomonas Psr1*) domain, which decreased affinity to the target DNA sequence. Mutations or RNAi suppression of *Ehd1* decreased *Hd3a* expression under SD conditions, indicating that *Ehd1* is the upstream regulator of *Hd3a* expression [12, 34]. *Ehd1* is preferentially expressed under SD conditions, peaking twice, before and after dawn, and *Hd3a* expression is essentially the same as *Ehd1* in the absence of functional *Hd1* [12].

Ehd1 is regulated by at least two factors, *OsMADS51* and *Ghd7* (for grain number, plant height, and heading date 7) [34, 77]. *OsMADS51* acts as the activator of *Ehd1* expression under both SD and LD, while *Ghd7* mainly acts as a suppressor of *Ehd1* under LD (see below). An *osmads51* T-DNA insertion mutation reduced *Ehd1* expression under both SD and LD. *OsMADS51* expression is also up-regulated by *OsGI* because *OsGI* antisense repression reduced *OsMADS51* and *Ehd1* expression. *OsGI* and *OsMADS51* show similar daily expression oscillation, peaking at dusk in SD.

Long-day suppression of Hd3a expression

Under LD conditions, *Hd3a* expression is very low in any developmental stage [39]. Diurnal expression is also lower than under inductive SD conditions [38]. Hd1 also has an important role in this suppression, although it works as activator of *Hd3a* expression under SD. Before the molecular cloning of *Hd1*, it was demonstrated that near-isogenic lines containing *hd1* mutant alleles exhibited not only delayed flowering under SD conditions but also early flowering under LD conditions, indicating that Hd1 could repress flowering under LD and that Hd1 function is modified depending on day length [46]. Phytochrome signaling affects this day-length-dependent conversion of Hd1 activity because this conversion is not observed in the phytochrome-deficient mutant; flowering of the double mutant *se5 hd1* (which lacks both phytochrome and functional *Hd1*) was slightly later than that of the *se5* single mutant (which lacks only phytochrome) [28]. Consistent with this observation, *Hd3a* mRNA accumulation is lower in *se5 hd1* than in *se5* mutant lines. The involvement of functional modification of Hd1 by day length is further supported by the direct manipulation of *OsGI* expression and the resulting change in *Hd1* and *Hd3a* expression levels [19]. Overexpression of *OsGI* delays flowering under both SD and LD, indicating that *OsGI* can act as a suppressor of flowering signals when it is constitutively expressed. In *OsGI* overexpressing plants, *Hd1* mRNA levels increase under both SD and LD, whereas *Hd3a* mRNA levels are negatively correlated with *Hd1* mRNA, indicating that *Hd1* can act as a suppressor of *Hd3a* when it is highly induced by *OsGI* constitutive expression. *OsGI* overexpression could also be expected to increase *Hd3a* expression through *Ehd1* up-regulation by the *OsGI-OsMADS51* pathway (see above, Kim et al. [34]), but this effect was not observed, probably because of strong Hd1 suppressive activity. A comparison of daily temporal expression patterns of *Hd1* and *Hd3a* indicate that higher expression levels of *Hd1* during light periods might suppress *Hd3a*. Under SD conditions, wild-type *Hd1* expression starts to increase at the beginning of the dark period, thus keeping Hd1 as an activator. *OsGI* overexpressors, however, express a significant level of *Hd1* during light periods, thus converting Hd1 into a repressor. Under LD, wild-type *Hd1* expression starts to increase in the light, resulting in the conversion of Hd1 into a suppressor [19]. Thus, the external coincidence model could be applied to rice: Circadian clock-regulated *Hd1* expression and an external light signal mediated by phytochrome generate the specific response to day length [25].

The repressor function of Hd1 is not observed in connection with *Arabidopsis* CO, indicating that there is a different mechanism that provides this function. The photoperiod-sensitivity QTL *Hd2* may provide information for understanding this mechanism. *Hd2* is detected as a QTL in crosses between *japonica* cultivar Nipponbare and *indica* cultivar Kasalath [80]. A functional allele of *Hd1* is required for Nipponbare allele of *Hd2* to delay flowering in response to LD [46]. In addition, this *Hd2* allele is required

for *Hd6*, another photoperiod-sensitivity QTL, to delay flowering under LD [79]. Map-based cloning of this QTL revealed that it encodes an α-subunit of casein kinase II (CK2α) [72]. Plant CK2 is composed of two catalytic (α) subunits and two regulatory (β) subunits. CK2α is mainly localized in nucleus in maize [64], and several nuclear proteins are identified as substrates of CK2α in maize and barley [40, 68], suggesting that rice Hd6 also functions in nucleus. In *Arabidopsis*, CK2 activity affects the timing of floral transition through phosphorylation of CIRCADIAN CLOCK ASSOCIATED1 (CCA1) and LATE ELONGATED HYPOCOTYL (LHY) proteins, which are the components of central oscillators of plant circadian clock [9, 63, 69, 70]. Thus, the functional interaction between rice LHY and Hd6 will be an interesting issue. Rice genome contains a single ortholog of *CCA1* and *LHY*, *OsLHY* [26]. When overexpressed in *Arabidopsis*, both OsLHY and Arabidosps CCA1 delay flowering. However, *OsLHY* overexpression showed only subtle effect on the rhythmic expression of *PRR1* compared with the dramatic effect of *CCA1* overexpression, suggesting functional difference between them [57].

Ehd1 expression is suppressed under LD, which also results in reduced Hd3a expression. *Ghd7* is responsible for the suppression of *Ehd1* [77]. Ghd7 protein contains a CCT domain with about 60% identity to Hd1, but Ghd7 lacks the zinc finger motif, which is present in Hd1. *Ghd7* expression is significantly higher under LD in leaf vascular tissue, and its diurnal expression peaks at dusk. *Ghd7* expression does not affect *Hd1* expression, but it strongly suppresses *Ehd1*.

Night-break suppression of Hd3a expression

A short light exposure during the dark period can significantly delay flowering of SD plants. This night-break effect has long been discussed in the context of day-length measurement in SD plants, but detailed understanding of the molecular mechanism of night break has been very limited. Like other SD plants, rice shows significant response to night break [23]. Night break suppresses *Hd3a* at the transcription level without affecting the expression patterns of *Hd1* and *OsGI*. The effect of illumination varies depending on its timing within the dark period. The night-break effect is most significant in the middle of the dark period. This night-break effect dependence on timing is correlated with the expression pattern of *Hd1*. Because *Hd3a* expression is mainly governed by the activity of *Hd1* and *Ehd1*, the night-break signal may affect both of the activities, which repress *Hd3a* transcription. The night-break effect on *Hd3a* expression was abolished by mutations of *phyB*, thus the night-break signal is mediated by phyB, which probably acts via the activities of Hd1 and Ehd1 [23].

Perspectives

Research on flowering time regulation in rice expands the field of mobile molecular signaling in plants. Florigen is also referred to as a flowering hormone because of its mobile nature and the universality of its flowering promotion activity. Using the analogy of the canonical plant hormone studies, the next step in florigen research would be understanding Hd3a/FT synthesis, transport, identification of receptors, and subsequent cellular signaling. Virtually nothing is known about Hd3a long-distance trafficking. How Hd3a in companion cells is transferred to sieve element systems, how the direction of movement in phloem is determined, and how Hd3a targets the SAM after unloading from the upper end of the phloem are all open questions. Flowering time research has also identified many important genes as resources for breeding. The genetic basis of natural variation or artificial selection in flowering time genes, including genes that are or were lost through the process of domestication, should contribute not only to a further understanding of the mechanism of flowering but also to future breeding applications.

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