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How transposable elements are recognized and epigenetically silenced in plants?

Beibei Liu[1] and Meixia Zhao[2]

Abstract

Plant genomes are littered with transposable elements (TEs). Because TEs are potentially highly mutagenic, host organisms have evolved a set of defense mechanisms to recognize and epigenetically silence them. Although the maintenance of TE silencing is well studied, our understanding of the initiation of TE silencing is limited, but it clearly involves small RNAs and DNA methylation. Once TEs are silent, the silent state can be maintained to subsequent generations. However, under some circumstances, such inheritance is unstable, leading to the escape of TEs to the silencing machinery, resulting in the transcriptional activation of TEs. Epigenetic control of TEs has been found to be closely linked to many other epigenetic phenomena, such as genomic imprinting, and is known to contribute to regulation of genes, especially those near TEs. Here we review and discuss the current models of TE silencing, its unstable inheritance after hybridization, and the effects of epigenetic regulation of TEs on genomic imprinting.

Addresses

[1] Department of Biology, Miami University, Oxford, OH 45056, USA
[2] Department of Microbiology and Cell Science, University of Florida, Gainesville, FL 32611, USA

Corresponding author: Zhao, Meixia (meixiazhao@ufl.edu)

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Introduction

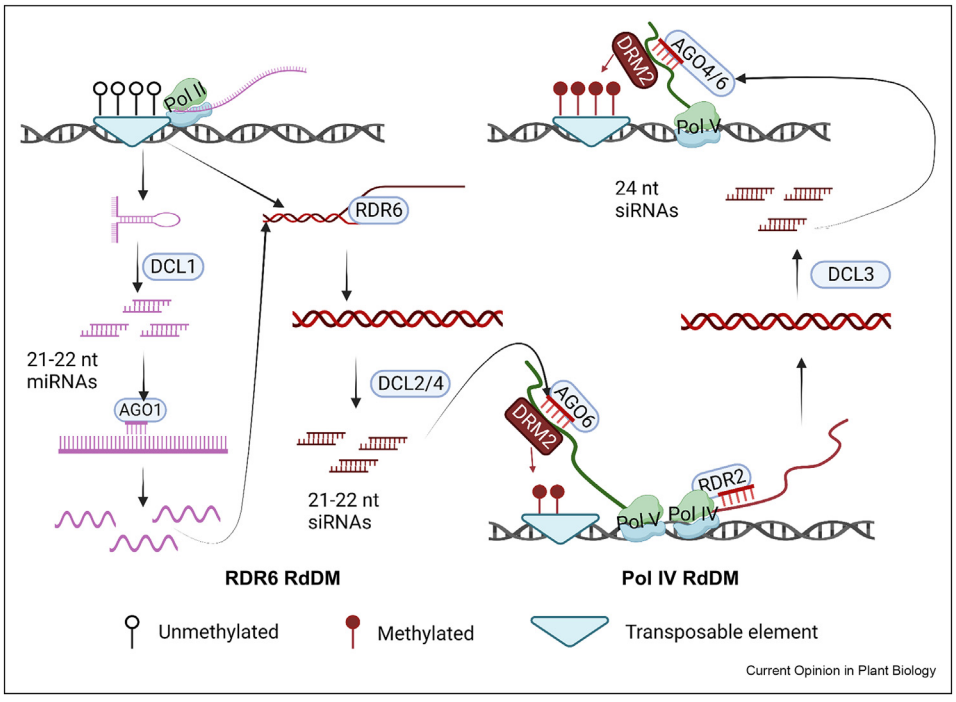
In the past three decades, sequencing of hundreds of thousands of eukaryotic genomes has revealed that transposable elements (TEs) or transposons, also known as "jumping genes", are the major components of most eukaryotic genomes [1]. For example, TEs make up nearly half of our human genome and up to 85% of the maize genome [2,3]. TEs can be classified into two major classes: Class I elements, also known as retrotransposons, which transpose via an RNA intermediate and through the "copy-and-paste" mechanism, and Class II elements or DNA transposons that employ the "cut-and-paste" transposition mechanism [4,5]. Although TEs have the ability to make copies of themselves and move to new sites in genomes, most of them are silenced by epigenetic pathways that involve small RNAs (specially small interfering RNAs in plants and piwi-interacting RNAs in mammals), DNA methylation, and histone modifications [6,7]. While much is known about how TE silencing is maintained and reinforced, relatively little is known about how TE silencing is initiated in the first place. It has been demonstrated that when a TE is transcriptionally activated, it can generate small interfering RNAs (siRNAs), which can initiate DNA methylation through the non-canonical RNA-directed DNA methylation (RdDM) pathway (Figure 1) [8,9]. Once the initial methylation of the TE is established, this TE is subject to canonical RdDM to reinforce its silencing [10,11].

The silenced state of TEs can be heritably transmitted over mitotic cell divisions and multiple generations. However, in certain situations, TEs can switch to a transcriptionally active state, which can lead to transposition. Epigenetics is believed to be both heritable and reversible. The stability of TE silencing depends on various factors, including the location of the TE sequence, cytosine sequence context, and environmental conditions [12–14]. Numerous examples demonstrate that the genetic and epigenetic effects of TEs contribute to gene expression, phenotypic variation, and genome evolution [15]. In this review, we present recent findings of the initiation and maintenance of TE silencing. We also discuss the unstable inheritance of DNA methylation particularly at the CHH (where H = A, C or T) cytosine context, using hybridization as an example. Additionally, we focus on the role of TEs in genomic imprinting to understand how the epigenetic control of TEs affects nearby gene expression.

Initiation and establishment of epigenetic silencing of TEs

An active TE is often subject to silencing machinery to prevent it from either causing deleterious mutations or

Figure 1



Initiation and establishment of TE silencing through RDR6 and Pol IV RdDM pathways. Active TEs can be transcribed by Pol II and copied into double-stranded RNA by RDR6, which are then cleaved into 21 or 22-nt siRNAs by DCL2/4. These 21 or 22- nt siRNAs target Pol V scaffolding transcripts in the nucleus, initiating RdDM [8,9]. Once a low level of methylation is established at the TE, Pol IV is recruited to generate 24-nt siRNAs to establish canonical RdDM [10,11,17].

accumulation to a high copy number. In plants, the mechanisms underlying the initiation of TE silencing are not well understood, but it clearly involves the triggering and reinforcement of DNA methylation. As insightfully summarized in several reviews [10,11,16–18], canonical RNA-directed DNA methylation (RdDM), which is centered on two plant specific RNA polymerases IV and V (Pol IV and Pol V), plays an important role in silencing TEs. In plant genomes, previously silenced TEs can be used to target active homologous TEs through the RdDM pathway. These silenced TEs can be recognized and transcribed by Pol IV into 30 to 40- nucleotide (nt) short single-stranded RNAs, which are copied into double-stranded RNAs (dsRNAs) by RNA DEPENDENT RNA POLYMERASE 2 (RDR2). These dsRNAs are then processed by DICER-LIKE 3 (DCL3) into 24-nt small interfering RNAs (siRNAs) [19], which can be incorporated into ARGONAUTE 4 (AGO4) or AGO6 to target the scaffold transcripts generated from Pol V. This leads to the recruitment of the *de novo* DNA methyltransferase DOMAINS REARRANGED METHYLTRANSFERASE 2 (DRM2) to the original or homologous sequences to trigger methylation in all of the three cytosine contexts (CG, CHG, and CHH) (Figure 1) [11,17]. Canonical RdDM primarily targets short TEs and TE edges, where the chromatin is more accessible, rather than deeply inaccessible heterochromatin primarily consisting of long terminal repeat (LTR) retrotransposons farther from genes. The methylation of these longer TEs is catalyzed by METHYTRANSFERASE 1 (MET1) for CG, CHROMOMETHYLASE 3 (CMT3) for CHG, and CHROMOMETHYLASE 2 (CMT2) for CHH, and usually relies on DECREASE IN DNA METHYLATION 1 (DDM1) [20–22]. RdDM is proposed to serve as the boundaries between deeply silenced heterochromatin and more active euchromatin, promoting and reinforcing TE silencing near genes to prevent the spread of euchromatin from genes into neighboring TEs. In Arabidopsis and maize, short TEs near more highly expressed genes frequently recruit RdDM activities [20–22].

One poorly understood question is how TEs are precisely recognized by Pol IV or in other words, how Pol IV is recruited to target TE sequences while avoiding genes. Pol IV is believed to be recruited to a subset of RdDM targets by its interacting protein SAWADEE HOMEODOMAIN HOMOLOG 1 (SHH1). SHH1 adopts a unique tandem Tudor-like fold and binds to the methylated histone 3 lysine 9 dimethylation (H3K9me2) and unmethylated histone 3 lysine 4 (H3K4me0) [23,24]. The chromatin remodeler

CLASSY (CLSY) family proteins are required for siRNA generation at nearly all Pol IV target loci, presumably via easing the passage of Pol IV in a locus-specific manner at different genomic regions [25,26]. Besides the known Pol IV-associated proteins, including RDR2, SHH1, and CLSY, recent research has identified another Pol IV interacting protein, ZMP (zinc finger, mouse double-minute/switching complex B, Plus-3 protein), which also can recruit Pol IV to a subset of genomic sites that are independent of SHH1. ZMP prefers to bind to H3K4me-depleted regions flanked by regions with H3K4me3. Interestingly, ZMP has a dual role as it also prevents Pol IV from targeting a specific set of genes that are lowly expressed with fewer exons and tend to be located near TEs [27].

The recruitment of Pol IV to TEs requires a pre-existing low level of DNA methylation [23,28], which raises the question of how DNA methylation is initially established at a naïve locus. Several research findings have demonstrated that non-canonical RdDM also termed RNA DEPENDENT RNA POLYMERASE 6 (RDR6) RdDM can establish DNA methylation at naïve loci [8,9,29,30]. In non-canonical RdDM, RNA polymerase II (Pol II) transcripts of TEs can be processed by RDR6 and DICER-LIKE *2* (DCL*2*) or DICER-LIKE 4 (DCL4) into 21 or 22-nt siRNAs, which are then loaded onto AGO6 through a Pol V scaffolding transcript to trigger the initial establishment of DNA methylation (Figure 1) [8,9,18,31]. Once the initial methylation is established, canonical RdDM takes over to achieve complete methylation and silencing of TEs. Because the major role of 21 or 22-nt siRNAs is involved in post-transcriptional gene silencing [9], why some of them are loaded onto AGO6 and how Pol V is recruited to active TEs for *de novo* methylation remain enigmatic. Recent research has found that these Pol II siRNAs can guide AGO4-clade proteins (AGO4, AGO6 or AGO9) to new target loci independent of pre-existing DNA methylation, which is necessary for the recruitment of Pol V to trigger the initial establishment of DNA methylation. Furthermore, they have discovered that the raw transcripts produced by Pol II can be processed by any DCL protein into 21-24-nt siRNAs, which are capable of targeting the first round of RdDM [32].

RDR6 RdDM acts on many long and autonomous TEs when they are transcriptionally active and plays a critical role in the initiation and establishment of TE silencing [8,30]. Another important question is how TE mRNAs, not gene mRNAs, are recognized and selected to produce 21 or 22-nt siRNAs. A recent publication also suggests that TE mRNAs undergo frequent ribosome stalling caused by unfavorable codon usage, resulting in subsequent inefficient translation that induces RNA truncation [33]. These truncated TE mRNAs might be prone to being targeted by RDR6 given its preference for aberrant, less polyadenylated RNAs to produce secondary siRNAs [34]. Recent research has revealed that ribosome stalling is not a prerequisite for the biogenesis of microRNA-triggered secondary siRNAs [35]. However, it is still uncertain whether ribosome stalling is essential for TEs to generate 21 or 22-nt siRNAs to establish DNA methylation at naïve loci.

Small RNAs can also be produced independently of RDR activities. For example, some inverted repeats, transcribed by Pol II, can be processed into siRNAs to introduce DNA methylation in *cis* or in *trans* [18]. During transposition, some TEs generate derivative copies. In some cases, these derivative elements, sometimes referred to as "*killers*" trigger epigenetic silencing of the entire TE family. A well-characterized example is "*Mu killer*" in maize, which consists of an inverted duplication of the 5' terminal inverted repeat and a portion of the *mudrA* genes from the autonomous element *MuDR* [36,37]. *Mu killer* expresses a long hairpin transcript that is further processed into siRNAs. These siRNAs act to target the transposase gene of *MuDR* resulting in the transcriptional silencing of all the other *Mutator* elements in the family [38]. This silencing can be inherited to the progeny and maintained in a silenced state even without the presence of the trigger *Mu killer*. A similar killer has also been described in the active maize *Ac/Ds* transposon system [39]. Similar to *Mu killer*, *Ac killer* is also initiated from naturally occurring inverted duplications of partial *Ac* transposon sequences. These duplicated sequences are transcribed by nearby promoters, which are further processed into small RNAs that trigger heritable silencing of the active elements [39]. These fundings suggest another general mechanism for initiating the silencing of active transposons.

Maintenance and establishment of epigenetic silencing of TEs

Once the initiation of TE silencing is established, the silenced state of TEs such as DNA methylation and H3K9me2, can be maintained in subsequent generations [18,31,40]. In plants, DNA methylation at CG, CHG and CHH sequence contexts is maintained by different pathways and methyltransferases. Because methylation in the CG and CHG contexts are symmetric, their methylation can be easily propagated during DNA replication using the methylated strand as a template to synthesize the newly methylated strand [31,41]. CG cytosine methylation (mCG) is maintained by MET1, which recognizes hemi-methylated CG dinucleotides through VARIANT IN METHYLATION (VIM) proteins [10,11,42]. Maintenance of CHG methylation (mCHG) is catalyzed by CMT3, a DNA methyltransferase that contains a chromodomain that recognizes H3K9me2 through a self-reinforcing loop between DNA methylation and H3K9me2 [23,43,44]. Methylation of TEs leads to the further deposition of H3K9me2 by histone methyltransferase KRYPTONITE

(KYP, also known as SUVH4, SUPPRESSOR OF VARIEGATION 3−9 HOMOLOG 4), or SUVH5 or SUVH6, which in turn promotes mCHG and CHH methylation (mCHH) [31,41]. mCHH is maintained by persistent *de novo* methylation of DRM2 via the RdDM pathway. This process requires the presence of small RNAs and relatively open chromatin, particularly on young and short transposons and the edges of long transposons. In addition, mCHH can also be maintained by CMT2 in conjunction with H3K9me2 in internal regions of long TEs that are in deep heterochromatic regions [45,46], similar as mCHG. Structural and functional characterizations of DRM2 and Arabidopsis CMT3/maize ZMET2 (the ortholog of Arabidopsis CMT3) have demonstrated that DNA deformation in conjunction with histone readout influences the cytosine substrate specificity and activity of these methyltransferases [47,48]. Although DMR2-induced substrate deformation occurs for all cytosine sequence contexts, DRM2 demonstrates a preference for substrate recognition with AT-rich nucleotides at the +1-flanking site against CG sites, thereby reinforcing methylation of CHH sequence contexts [47]. Additionally, the readout of H3K9me2 and H3K18 by ZMET2/CMT3-mediated leads to allosteric activation of ZMET2, which in turn stimulates the binding of ZMET2 to mCHG substrates [48]. These data may also explain the over-representation of mCAA and mCAT or mCTA compared to other CHH subcontexts, as well as the over-representation of mCAG or mCTG compared to other CHG subcontexts [49]. These findings indicate that the recognition of substrates, underpinned by DNA deformation, has strong implications in the establishment and maintenance of sequence-specific DNA methylation in plants [47,48].

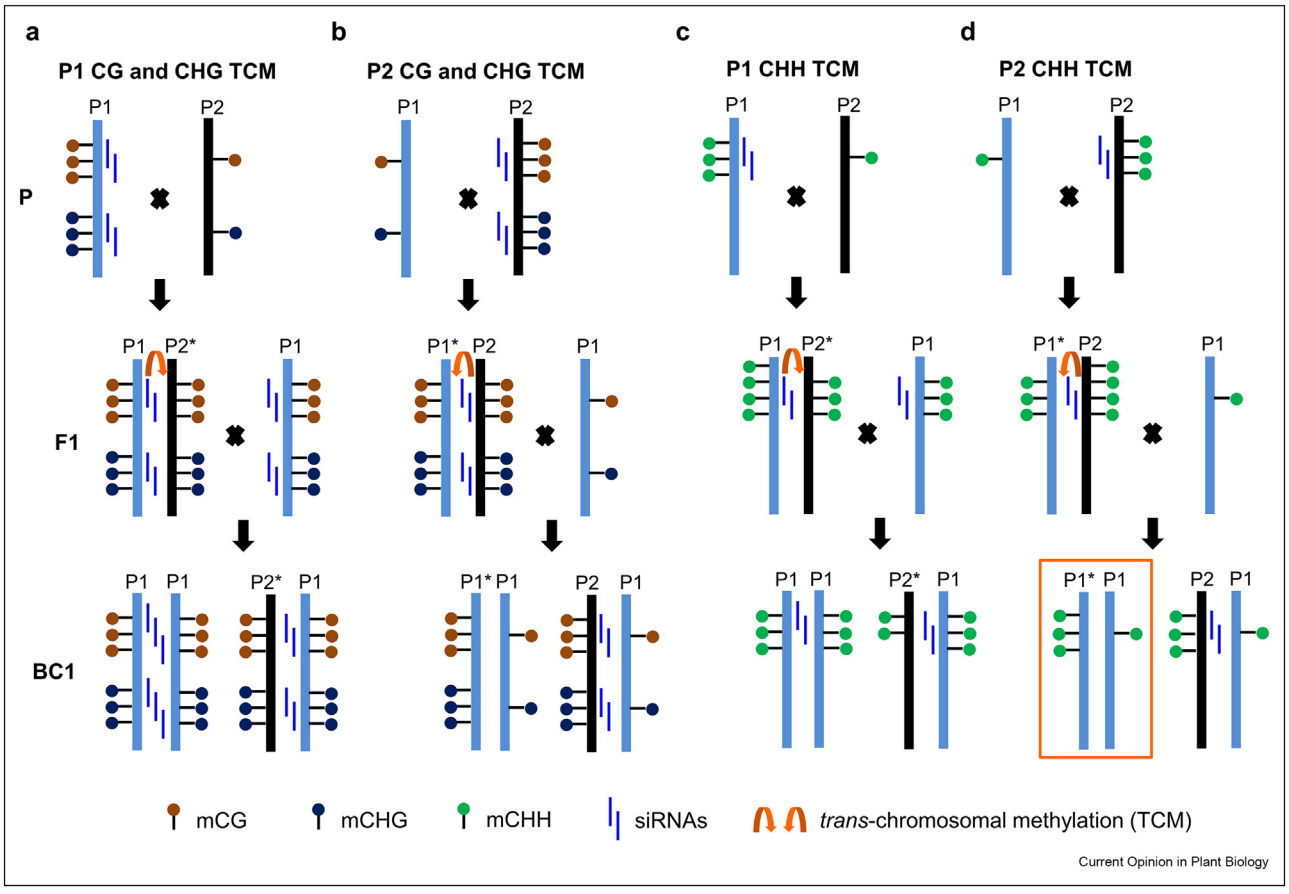
While mCG and H3K9me2/mCHG(H) are maintained almost independently, recent studies have revealed local and global crosstalk between DNA methylation and heterochromatic marks by investigating *de novo* methylation of TEs after the loss of these silent marks [46,50]. The recovery of H3K9me2/mCHG(H) is generally efficient and precise in most TE genes (coding regions within TEs) after reintroduction of the wild type alleles, and this process is independent of the RdDM pathway. However, the efficiency of this recovery diminishes when mCG is lost, as observed in the *ddm1* mutants, indicating a facilitative role for mCG in the establishment of mCHG(H) [46]. Further investigation of a subset of TE genes that do not undergo successful recovery demonstrates a notable substitution of H2A.W with H2A.Z within these TE genes. This replacement of H2A.Z leads to the loss of mCG, consequently impeding the recovery process for these TE genes. It is proposed that the presence of H2A.W in most TE genes may enable cells to retain a memory of where to reintroduce H3K9me2 and mCHG(H) [46,50]. Intriguingly, recent findings indicate that DDM1 possesses two conserved domains that can bind to H2A.W. This interaction plays a crucial role in initiating and maintaining transcriptional silencing of potentially mobile TEs within heterochromatin [51]. Taken together, these studies suggest that maintenance and establishment of TE silencing require coordinated interactions between DNA methylation and histone modifications.

Unstable inheritance of epialleles

Although efficient silencing of TEs is double guarded by DNA methylation and histone modifications, there are situations, such as tissue culture [52], biotic and abiotic stresses [13,14,53,54], hybridization [55−57] and inbreeding [58], in which the stability of silencing can be perturbed. Transcripts from silenced TEs have been detected in Arabidopsis mutants defective in DNA methylation. However, transposition of TEs has been observed for only a few transposons in these mutants [59−61]. Recent research in Arabidopsis has identified a large number of TEs that are upregulated in DNA methylation-free mutants, but only a dozen of them transpose in the genome [62−64]. In a subset of TEs, the removal of high levels of DNA methylation causes a complete loss of H3K9me2, but recruits histone 3 lysine 27 trimethylation (H3K27me3) to the TEs, which keeps them silent [64]. This suggests that DNA methylation and histone modifications serve as complement defense mechanisms to maintain TE silencing and preserve genome integrity.

DNA methylation undergoes changes during hybridization, leading to heritable transfer of the silent states of epigenetic alleles (epialleles). *Trans*-chromosomal methylation (TCM) in F1 hybrids relies on RdDM, in which small RNAs particularly 24-nt siRNAs from one allele trigger methylation of the other allele [65−71]. A reduction in 24-nt siNRAs has been reported in Arabidopsis F1 hybrids of C24 and Ler ecotypes [72]. However, another study did not observe significant changes in siRNA abundance in different Arabidopsis F1 hybrids [67], suggesting that genotypes play an important role in *trans*-chromosomal interaction. Recent research using maize hybrids of B73 and Mo17 has also shown that in 63% of the *trans*-chromosomal differentially methylated regions (DMRs), siRNAs from one allele are sufficient to trigger methylation without triggering siRNA biogenesis from the other allele in F1 hybrid plants. This is particularly observed in regions where the abundance of parental siRNAs differs (Figure 2) [73]. These studies suggest that Pol IV is exclusively active at the allele that produces small RNAs, even though both alleles are methylated in hybrids. However, it remains unclear why Pol IV fails to recognize the newly methylated allele. The role of small RNAs alone appears insufficient in explaining all cases. For example, in hybrids, there are multiple regions where methylation decreases following hybridization compared to the parents, despite the production of small RNAs [73].

Figure 2

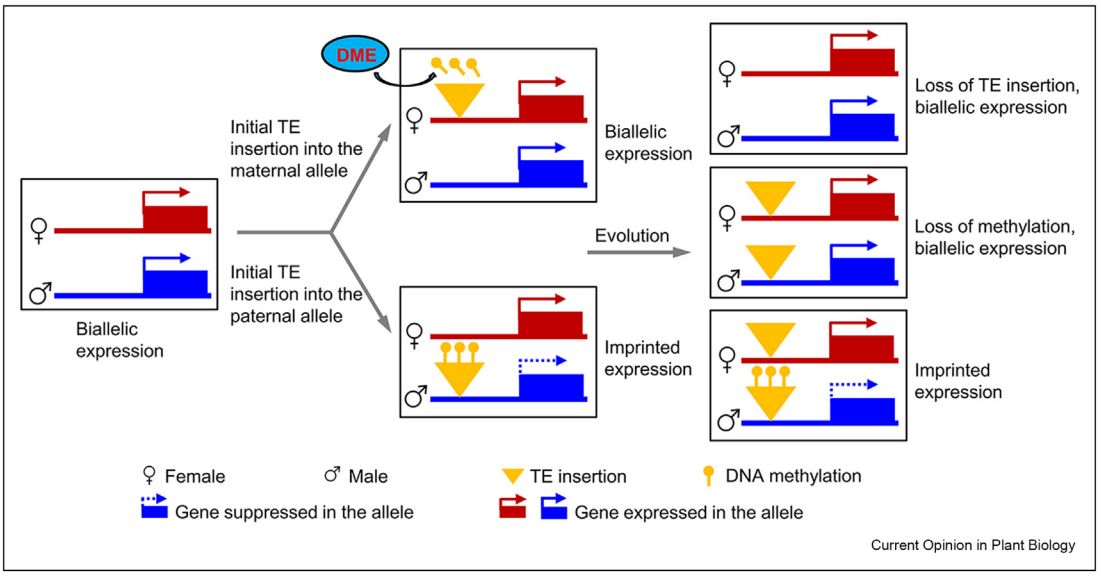


Initiation and maintenance of DNA methylation through hybridization. **(a)** P1 CG and CHG *trans*-chromosomal methylation (TCM) differentially methylated regions (DMRs). For P1 CG and CHG TCM DMRs, the P1 derived siRNAs establish *de novo* methylation of the hypomethylated P2 allele in F1 (P2*). Subsequently, through backcrossing, this newly induced methylation at both CG and CHG sequence contexts remains stable in both homozygous (P1/P1) and heterozygous (P2*/P1) regions of BC1 plants. **(b)** P2 CG and CHG TCM DMRs. For P2 CG and CHG TCM DMRs, the P2 derived siRNAs establish *de novo* methylation of the hypomethylated P1 allele in F1 (P1*). Subsequently, in both homozygous (P1*/P1) and heterozygous (P2/P1) regions of BC1 plants, the methylation levels are observed to be at the mid-parent value. **(c)** P1 CHH TCM DMRs. **(d)** P2 CHH TCM DMRs. For both P1 and P2 CHH TCM DMRs, the levels of mCHH from both the high- and low-parent (parents with the higher and lower methylation levels) alleles are increased in F1. However, the additional mCHH that is added in the F1 generation is not transmitted to the next generation. Intriguingly, in homozygous (P1*/P1) regions of BC1 plants, mCHH is reestablished at P2 CHH TCM DMRs, even in the absence of small RNAs (as indicated by the orange box). These models are proposed based on the major results from Ref. [73]. P1, parent 1; P2, parent 2; F1, filial 1; BC1, backcrossed 1. Asterisks denote the newly converted (methylated) allele. Only TCM DMRs following hybridization are shown here.

Histone modifications such as histone H2A variants could potentially offer an explanation [46], as differences in these modifications between the two hybrid alleles may impede the recruitment of Pol IV to the newly methylated allele.

The stability of transgenerational inheritance of epialleles varies at different loci and is largely determined by the DNA sequence itself [74]. While methylation changes in CG and CHG are stably inherited in recombinant inbred lines over multiple generations, epiallelic switching frequently occurs at many loci, a broad spectrum of which are TEs [74—76]. A recent study in maize identified thousands of loci change methylation in F1 hybrids. However, only approximately 3% of these changes are transmitted through six generations of backcrossing and three generations of selfing [70]. The stability of DRM2-dependent mCHH is particularly unstable, given that it requires small RNAs to persistently trigger methylation through the RdDM pathway. A recent report using F1 hybrids, along with their parents and backcrossed progeny has proving compelling evidence with respect to the heritable transmission of acquired methylation in both CG and CHG sequence contexts in the next generation (Figure 2a and b). In contrast, the overall increase in mCHH observed in F1 is diminished in BC1 progeny (Figure 2c and d), suggesting that the elevated mCHH in F1 heterozygotes is likely a result of hybridization rather than a simple interaction between alleles. Notably, once the hypomethylated

Figure 3



Model depicting the role of transposons in the formation of imprinted genes. Initially, a TE is inserted near a gene on either the maternal or paternal allele. Subsequently, the TE undergoes epigenetic silencing through methylation. Because DME only removes methylation from the maternal allele, the gene exhibits imprinted expression exclusively when the TE insertion occurs on the paternal allele. Over several generations, the TE insertion may undergo purging via natural selection or lose DNA methylation, resulting in restoration of biallelic expression of the gene. The maintenance of imprinted expression patterns occurs only when both the TE insertion and its associated methylation are inherited.

allele has encountered the hypermethylated allele, the epigenetic state of the former retains the information to reestablish methylation in BC1 progeny even in the absence of small RNAs (indicated by the orange box in Figure 2d). Moreover, through the utilization of *mop1* mutants (*mediator of paramutation1*, the ortholog of Arabidopsis *rdr2*), this study has demonstrated that although increased mCHH in the TCM DMRs in F1 plants relies on RdDM, initiation of the epigenetic state in those regions can be triggered in the absence of DNA methylation [73]. These epialleles via DNA methylation can give rise to novel phenotypes. However, the extent to which methylation epialleles are stably inherited across multiple generations remains to be explored.

The role of TE silencing in genomic imprinting

The epigenetic silencing of TEs near genes has various effects on gene expression, including genomic imprinting. Genomic imprinting is an epigenetic phenomenon where the expression of maternal and paternal alleles differs depend on their parent-of-origin [77,78]. DNA methylation and H3K27me3 are believed to be the two major epigenetic marks known to contribute to imprinting in flowering plants [77,78]. Site specific hypomethylation of the maternally inherited DNA in endosperms is introduced by DEMETER (DME), a 5-methylcytosine DNA glycosylase capable of actively removing methyl groups from cytosines. DME is highly active in the central cell of the female gametophyte and the vegetative cell of the male gametophyte [79–82]. In these cells, DME demethylates TEs and other repeats [82–85], resulting in maternally specific expression of genes in the endosperm that are located near these TEs (Figure 3). One of the imprinted genes in plants is *FLOWERING WAGENINGEN* (*FWA*). The imprinted expression of *FWA* depends on the maternal DNA hypomethylation in its promoter region, which contains two direct repeats related to a SINE retroelement [86,87]. It has been proposed that DME-mediated demethylation of transposons in the central and vegetative cells serves as a genome defense mechanism to reinforce the silencing of transposons in the gametes [88,89]. Demethylation of TEs leads to their transcriptional activation, resulting in the production of siRNAs in the central cell and vegetative nucleus. These siRNAs are hypothesized to be transported to the eggs and sperms to promote methylation of TE sequences there, thereby enforcing their silencing in the gametes [78,89,90].

A significant number of imprinted genes have been found to contain TEs in their flanking regions [83,91,92], indicating a potential relationship between TEs and genomic imprinting. Given that TE insertions are random and highly polymorphic, this may also explain why imprinting of genes is poorly conserved even among closely related species, and many imprinted genes have undergone relaxed selection [93–96]. It is important to note that the primary role of these TEs is not to generate imprinted gene expression. Instead, gene imprinting

arises as a byproduct of the transient release of TE silencing mediated by DME in specific cells. While there is strong evidence showing that the establishment of imprinting is closely linked to TEs, it remains unclear whether TEs are the underlying cause of the imprinted status of these genes. Interestingly, a recent study using *de novo Mutator* (*Mu*) transposon insertions have led to the creation of two potentially novel imprinted genes. These genes do not exhibit imprinting when the *Mu* insertions are segregated away [97], indicating that TE insertions can be one of the causes introducing genomic imprinting. It would be intriguing to investigate whether the imprinted expression of these two genes can be stably inherited into subsequent generations, and if heritable, whether such inheritance is tightly linked to the presence or absence of the *Mu* insertions and their corresponding epigenetic modifications.

Conclusion and perspectives

To counter the threat posed by TEs to genome integrity, host organisms have evolved a set of defense mechanisms to suppress TE activity. In most cases, the silencing machinery is highly efficient to silence the vast majority of TEs. However, there are specific circumstances where transposons can evade such silencing mechanisms [13,14,53]. While the reactivation of transposons has been observed under a variety of biotic and abiotic stresses, little is known about why and how silencing mechanisms are not functional for a subset of transposons while remaining active for other TEs in the genome. We propose that the transposon sequence itself (e.g. TE type), its location as well as time (e.g. developmental stage and cell type) are important factors that can influence the initiation, maintenance, and reactivation of TE silencing. In most plant genomes, TEs particularly LTR retrotransposons are enriched in condensed heterochromatic regions with lower recombination rates and fewer genes compared to euchromatic regions. TEs in these regions are heavily methylated and modified with repressive histones, meaning that they are deeply silenced. The maintenance of silencing for these TEs is highly stable, even in the presence of stress or mutation in genes involved in DNA methylation, and does not rely on RdDM. On the other hand, TEs located in relatively open chromatin regions, such as those near genes, are frequent targets of RdDM and are more susceptible to transcriptional activation upon stress, hybridization, or other conditions [17,22,98]. In maize, many of these TEs are DNA elements, and elevated mCHH at their edges reinforces their silencing [21].

In addition to TE location and sequence, we believe that time is also an important component of the epigenetic regulation of TEs [16]. Here time can be related but not limited to different developmental stages, tissues, cell types, and plant generations. It appears that silencing pressure in shoot apical meristems, central cells of the female gametophyte and vegetative nuclei of the male gametophyte is weaker compared to that in leaves. Single-cell experiments would be a useful technique to investigate the dynamics of TE silencing in different cells.

The impacts of TEs on the genome also depend on the location of TEs and time. TEs residing in heterochromatic regions tend to have less effects on the genome compared to those in euchromatic regions. When TEs insert into or near genes, they have the potential to introduce new epigenetic regulations, which may be beneficial to the organism. Investigating how organisms have evolved strategies to balance the detrimental and beneficial aspects of TEs, as well as exploring the co-evolution of TEs and genes within the genomic ecosystem would be intriguing areas to explore in future TE research.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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