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SHORT COMMUNICATION

Miniature Inverted-repeat Transposable Elements (MITEs) and their effects on the regulation of major genes in cereal grass genomes

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Abstract Various chemical modifications to non-coding DNA sequences can alter the regulation of gene expression. Although the mechanisms governing these pathways are still unclear, and non-coding regions were previously referred to as junk DNA, the evidence accumulated to date shows that these unknown processes are becoming more understandable and, in addition, that these sequences (Transposable Elements, repeat sequences) play critical roles in gene regulation. Consequently, this study aims to understand how Miniature Inverted-repeat Transposable Elements (MITEs) and chromatin remodeling complexes are involved in regulating the gene expression of *Rht-1* and *tb1*, key developmental loci from bread wheat (*Triticum aestivum*) and maize (*Zea mays*), respectively. At present, the transcription regulation functions of MITEs in crop genomes are rather undefined, therefore it becomes important to focus on these issues in order to improve current molecular breeding methods. Moreover, this study will attempt to shed light on historical and conspicuous phenotypic changes undergone by both crops, which have been previously considered to be a consequence of the overexpression of these master regulators involved in their development.

Keywords Plant development · Crop epigenetics · Miniature Inverted-repeat Transposable Elements · Chromatin remodeling complexes

Whereas Transposable Elements (TEs) have long been considered as selfish 'junk DNA without function', the data accumulated recently have supported the idea that they are essential components of the genome organization and key players in genome evolution (Contreras et al. 2015). Crop genomes are largely populated with TEs that are efficiently targeted by epigenetic markers, and part of the epigenetic diversity observed might be explained by TE polymorphisms (Mirouze and Vitte 2014). Indeed, it has been suggested that multi-protein chromatin remodeling complexes can bind to TEs inserted in AT-rich sequences of high affinity, named Matrix Attachment Regions (MARs), and thus control the expression of major proteins involved in gene regulatory networks critical for development (Xu et al. 2013).

According to their transposing intermediates, TEs are classified into two types, class I (RNA) and class II

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(DNA). The genome size of a plant species is largely determined by its class I TEs; however, a plant genome may also harbor a large number of short class II TEs, called Miniature Inverted-repeat Transposable Elements (MITEs) (Chen et al. 2014). MITEs consist of 100–800 DNA base-pair sequences, which display conserved inverted repeats (TIRs) flanked by target site duplications (TSDs). These elements are often associated with the regulatory regions of the genes of angiosperms and they are also predicted to play important roles in plant genome evolution (Lu et al. 2012). There are many studies showing the role of MITEs in the regulation of cereal grass genomes. For example, in bread wheat (*Triticum aestivum*), it has been demonstrated that a *Tourist* MITE insertion into the 3′ untranslated region upregulates the transcription of the small heat shock protein gene *TaHSP16.9-3A* (Li et al. 2014), and that small non-coding RNAs (sRNAs) perfectly match MITEs (Cantu et al. 2010). Moreover, it has been recently shown that conserved sequences located tens of kilobases upstream of the maize (*Zea mays*) *tb1* and bread wheat *Rht-B1/D1* genes contain this class of TEs (Clark et al. 2006; Studer et al. 2011; Zhou et al. 2011; Wilhelm et al. 2013; Wu et al. 2013). This is an important issue, because it has been shown that the overexpression of *tb1* and *Rht-B1/D1* genes are associated with domestication and improvement processes for both crops (Hedden 2003; Clark et al. 2006; Tsiantis 2011; Vaschetto 2015). Consequently, since it is known that MITEs may affect (either upregulate or downregulate) the expression of nearby genes (Chen et al. 2014), *tb1* and *Rht-1* MITE insertions might play different roles:

(a) In the first place, as suggested by Avramova et al. (1998), MITEs may act as MARs, where chromatin remodeling complexes can associate in order to mark them epigenetically, involving the control of higher-order chromatin structure and thus regulating the locus-specific expression. Consistent with this, chromatin immunoprecipitation experiments indicate that the acetylation of histones at enhancer-distal nucleosomes is enhanced tenfold in the presence of MARs, showing that these regions mediate long-range chromatin accessibility and transcriptional activation (Fernández et al. 2001). Coordinated spatial and temporal control of eukaryotic gene expression involves numerous regulatory elements and many of these are involved in long-range intra- or interchromosomal interactions; i.e., the 3D chromosome structure is a key component of gene expression regulation (Comet et al. 2011). Both the *Rht-1* and *Zinc Finger-1* (*ZnF-1*) conserved genes found in wheat homoeologous regions are also localized in a orthologue region of the maize *tb1* gene (Wilhelm et al. 2013), suggesting that transcriptional control should be produced by chromatin organization of these linkage blocks. Chromatin remodeling complexes can be also involved in the establishment of epigenetic modifications at sequences surrounding the MARs, resulting eventually in the overexpression of nearby genes by the spread and encouragement of epigenetic remodelling. In this regard, Tsiantis (2011) indicated that the insertion of a *Hopscotch* retrotransposon flanking the *Tourist* MITE located 60 kb upstream of the maize *tb1* gene was a target of human selection, and it would have triggered major changes in shoot branching by upregulation of *tb1* expression.

(b) Moreover, *tb1* and *Rht-1* MITE insertions should also be involved in the control of transcription through RNA interference (RNAi) pathways, since it is known that MITE-derived small RNAs may be produced by microRNA (miRNA) or small interfering RNA (siRNA) biogenesis (Yan et al. 2011; Lu et al. 2012; Chen et al. 2014). MITEs can generate miRNA-like repeat-associated siRNAs (ra-siRNAs) that have roles during plant stress responses and hormone signaling (Yan et al. 2011), and might represent the evolutionary link between miRNA and siRNAs (Ortiz-Morea et al. 2013). Once transcribed, long TIRs of some MITEs have the potential to form stem–loop structures comparable to those obtained from miRNA genes. However, most MITEs have short or no TIR sequences and therefore small RNAs from such MITE sequences are unlikely to be generated through the miRNA biogenesis pathway. It is for this reason that the factors determining the abundance of MITE-derived small RNAs remain unclear (Chen et al. 2014).

In addition, knowledge of MITE functions would allow better understanding of the regulation mechanisms involved in epigenetic phenomena such as genomic imprinting or paramutation. Regulation of gene expression involves long-distance communication between regulatory elements, but how this is achieved remains unknown (Comet et al. 2011). By using bioinformatic tools, Stam et al. (2002) suggested that sequences involved in paramutation and enhancer activity on the maize *b1* alleles display similarity to a hypothetical MAR. Interestingly, MITE and MAR regions show sequence similarities, such as a high AT content or repeat sequence patterns, whereby structure–function analyses will shed light on how these sequences act to regulate gene expression. Moreover, it has been shown that, as for the *b1* gene (Belele et al. 2013), specific tandem repeat sequences in the *Arabidopsis pheres1* (*phe1*) imprinted gene are also required for epigenetic silencing (Villar et al. 2009), thus indicating that there are resemblances in the mode of functioning of both processes.

Even though plant developmental genetics was left out of breeders' thinking in the past, the data provide ample support for the role of genetic and epigenetic mechanisms operating mainly in critical regulatory areas of the genome to generate an adaptive phenotypic change (Tsaftaris et al. 2008). Likewise, *tb1* and *Rht-B1/D1* loci have been shown to be involved in the control of diverse and critical developmental processes. Further molecular and in silico characterization of these essential factors in development should contribute to our understanding of phenotypic modifications that were found to be positively related to higher agronomic yields. Subsequently, manipulation of the *tb1* and *Rht-B1/D1* loci might enable the production of new high-yielding maize and bread wheat varieties, respectively, this being a challenge that should be taken up by molecular breeders. In conclusion, the next few years will be fundamental to our knowledge and application of these emerging issues of crop molecular biology.

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Compliance with ethical standards

Conflict of interest The author declares that he has no conflict of interest.

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