

Studies whereas,  
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negatively



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Studies have revealed that > 99% of the methylome within a species is conserved (Li et al., 2015b).

It is the remaining 1% which holds the subtle and profound variations within the accessions of same species. The 1% epigenetic variation includes several thousands of differentially methylated regions (DMRs). Mostly, the genes nearby the DMRs do not exhibit any change in gene expression (Eichten et al., 2013, Schmitz et al., 2013a), whereas, ~10-20% of DMRs are negatively associated with gene expression. Subtle variations in the methylated regions are not associated with any significant change in gene expression.

Many of the DMRs among the genotypes of a same species are due to misdirected RdDM or altered targeting of heterochromatin (Schmitz et al., 2013a, Schmitz et al., 2013b). Higher levels of DMRs in specific accessions of a species that are associated with functional variation of genes are reckoned to be responsible for maintenance of epigenetic regulation in these accessions (Dubin et al., 2015, Shen et al., 2014). Qualitatively expressed genes (0 or 1 expression) rather than the quantitatively expressed genes have higher chances to be associated with DMRs (Li et al.

, 2015b). Variations in DNA methylation levels are attributed to epialleles and have been reported to affect traits like, fruit ripening (Manning et al., 2006), floral morphology (Cubas et al., 1999) and anthocyanin component (Chandler, 2007). Quantitative nature of DNA methylation in plants has been further substantiated by analysis of epigenetic recombinant inbred line (epiRIL) populations in Arabidopsis (Johannes et al.

, 2009, Reinders et al., 2009). EpiRILs can bring out the cryptic information within the genome that has been silenced due to DNA methylation in a portion of the progeny and these variations which otherwise were hidden could be mapped to genomic regions with altered methylation, if accounts for phenotypic variation (Cortijo et al., 2014, Kooke et al., 2015). Efforts to create such epiRILs in crop plants have not been successful because of the lethality of parental DNA methylation mutants with severe effects on crop methylomes (Hu et al.

, 2014, Li et al., 2014). Epialleles resulting from epigenetic variations can arise either due to non-genetic or genetic sources (Richards, 2006, Taudt et al., 2016). Non-genetic sources accounts to failure to properly maintain methylation states or off-target sRNA effects. Non-genetic sources involve DNA methylation due to developmental and environmental factors. Genetic sources of epialleles on the other hand can be transposon insertions that changes the chromatin conformation and brings about structural rearrangements (Hollister and Gaut, 2009).

Cis or trans arrangements of TE insertions brings changes in methylation through siRNA production via RdDM. Tapping epigenetic variations for crop improvement depends upon the stability of its transmittance. Stable epigenetic inheritance would have high degree of linkage disequilibrium of epialleles with nearby genetic polymorphisms (Springer and Schmitz, 2017). Association mapping or genomic selection studies using high-density single nucleotide polymorphisms (SNP) maps can thus help in mapping DMRs and using it for crop improvement even in the absence of specific causative SNP linked to phenotypic variation (Springer and Schmitz, 2017). Studies

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in Arabidopsis have shown that genetic variations like SNPs are more stably inherited than single cytosine methylation across generations. However, DMRs at several hundred of regions (regional methylation) were found to have greater stable inheritance than individual modifications across generations (Becker et al.

, 2011, Ossowski et al., 2010, Schmitz et al., 2011). Environmental conditions also influence the stability of inheritance of DNA methylation as confirmed by a study in Arabidopsis plants grown for ~100 years in natural environment showed stable methylome inheritance across generations even in varying environment conditions (Hagmann et al., 2015). However, other studies in Arabidopsis and rice showed severe stress may result in unstable methylation inheritance (Jiang et al., 2014, Zheng et al., 2017).

DMRs having significant associations with local SNPs or small insertions and deletions (Indels) have been found to have stable inheritance (Schmitz et al., 2013b). In maize, 50% of DMRs were significantly associated with local SNPs suggesting stable epigenetic inheritance (Eichten et al., 2013). These studies also imply that genotypes with greater genetic variations also have more variations in terms of DNA methylation. TEs have a significant role in defining the size and structure of plant genomes.

Crops with complex genomes have developed chromatin-based mechanisms to withstand the presence of silenced TEs near the actively expressed genes. Better understanding of chromatin regulation and diversity in crop species can help to select and engineer crops with stable performance (Springer et al., 2016). Increase in the copy number of TE puts the genome integrity in

jeopardy. However, eukaryotes have natural ability to combat such threat by deploying siRNAs derived from TEs for their transcriptional silencing and heritable epigenetic modifications (Slotkin and Martienssen, 2007).

Methylation of TE and gene expression is inversely correlated and if the suppressed gene expression has deleterious effects, then it undergoes purifying selection with stronger impact on methylated TEs proximal to genes (Figure 3). Expression of long terminal repeat (LTR) retrotransposons, which acts via RNA as intermediate for its mobility often result in double stranded RNA, which is a source of siRNAs, ultimately leading to the heterochromatin state in eukaryotes (Grewal, 2010). TEs like other target genes are silenced by association of sRNAs with AGO proteins and forming the RNA-induced silencing complex (Fang and Qi, 2016). The regulation and roles of different TEs, in chromosome architecture and gene regulation, depends on location of TEs on the chromosomes: near a gene, within a gene, in a pericentromere/TE island, or at the centromere core. TEs contained in these regions are silenced by the chromatin-remodeling protein DDM1, and the size of TE islands is correlated with the plant genome size (Sigman and Slotkin, 2016). In another study, where a high copy number of TEs pose a concern to plant genome's health, a concept of 'zombies' (aberrant transcripts capable of instigating silencing in trans) has been well described to counteract the situation (Lisch and Bennetzen, 2011).

In *Arabidopsis*, where Tnt1 retrotransposon from tobacco was transferred, and despite its transcriptional silencing via RdDM mediated by siRNAs an increase in its copy number was observed (Perez-Hormaeche et al., 2008). These findings suggest the possibility of LTR retrotransposons to escape the

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active silencing surveillance mechanisms present in host genome. However, an increase in siRNAs from Athila retrotransposons in sperm and pollen indicated that transcriptional activation of transposons in vegetative nuclei imposed silencing in male gamete (Slotkin et al., 2009). RdDM is not a preferred choice in the regions like pericentromere rich heterochromatin enriched with larger transposons (Schoft et al., 2009, Zemach et al., 2013). Methylation at such loci is mediated by siRNA-independent pathway, which rely on DDM1; the DNA (cytosine-5)-methyltransferase 1 (DNMT1) class enzyme MET1, CMT2, CMT3. More than 2000 transposons were found to be reactivated in *ddm1* mutant compared to ~40 in a RdDM-defective mutant (Zemach et al., 2013). The methylated endogenous transposons in a RdDM crippled system are thought to be due to maintenance of CG and CHG methylation independent of RdDM. This implies additional roles of RdDM associated siRNAs in genome defense which not only includes TGS.