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Abdullatif Azab
Department of Microbiology, Quaid-i-Azam University Islamabad, 45320, Pakistan

Subrina Jesmin
Department of Microbiology, Quaid-i-Azam University Islamabad, 45320, Pakistan

Farzana Sohael
Department of Microbiology, Quaid-i-Azam University Islamabad, 45320, Pakistan

Rabia bangash
Department of Microbiology, Quaid-i-Azam University Islamabad, 45320, Pakistan

Corresponding Author:
Abdullatif Azab
Department of Microbiology, Quaid-i-Azam University Islamabad, 45320, Pakistan

Epigenetic regulation of the genome through transposable elements and its related non-coding small RNA

Abdullatif Azab, Subrina Jesmin, Farzana Sohael and Rabia Bangash

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Abstract
Transposons are mobile DNA sequences abundant in eukaryotic genomes. Non-coding small RNAs have various biological functions and affect gene expression at different levels. Transposons are an important source of non-coding small RNAs in many eukaryotic genomes. Some recent studies have found that transposons and their derived non-coding small RNAs participate important roles in gene regulation, but few relevant reviews exist in China. Therefore, this paper reviews the current research achievements on transposons and non-coding small RNAs from two aspects: the relationship between transposons and their derived non-coding small RNAs and their role in the genome and biological evolution.

Keywords: Transposon, non-coding small RNA, small RNA

Introduction
Transposable elements (TEs) are DNA sequences that copy themselves and move around the host genome, inserting themselves into other regions of the chromosome. Transposons were first discovered in 1950 in MCCLINTOCK [1]'s study of grain color changes in maize. The concept of transposons was not widely accepted until 1967 when SHAPIRO [2] discovered transposon insertion sequences in his study of galactose operons in Escherichia coli. With sequencing technology development, researchers have found transposable and transposon-like sequences in more and more eukaryotic genomes. Transposons have been found in plants such as snapdragon, petunia, delphinium and sweet pea [3]. Transposon sequences have also been found in the genomes of many mammals, fish and birds. With the deepening of research on transposons, evidence shows that transposons have an important impact on genes' evolution, expression, and function [4]. According to their transposon mechanism, transposons can be roughly divided into classes I and II. Class I transposons, also known as retrotransposons, are catalyzed by reverse transcriptase to make cDNA, then inserted into the genome. Class I transposons can be divided into long terminal repeat (LTR) and no-long terminal repeat (non-LTR) according to whether they have long terminal repeat sequences or not. Whether they can encode reverse transcriptase, LTR retrotransposons can be divided into autonomous retrotransposons and non-autonomous retrotransposons. According to their structure, the non-LTR class of retrotransposons can be divided into long interspersed repetitive elements. LINE) Furthermore, short interspersed nuclear element, SINE.
Class II transposons, also known as DNA transposons in DNA-DNA mode, are catalyzed by transcriptase, using two mechanisms of shear-stick and fall-stick. The two ends of the Inverted terminal repeats (ITR) of class II transposons are inverted terminal repeats (ITR) and usually contain the gene sequences that can encode transposases. Self-encoded transposase can recognize the ITR sequences at both ends of transposons, thus mediating the transposon translocation of DNA. insert it into other positions on the chromosome. Class II transposons can be divided into autonomous DNA transposons and non-autonomous DNA transposons according to whether they can carry out autonomous transposons. Non-autonomous DNA transposons can be transposed only with the help of autonomous DNA transposons [5].

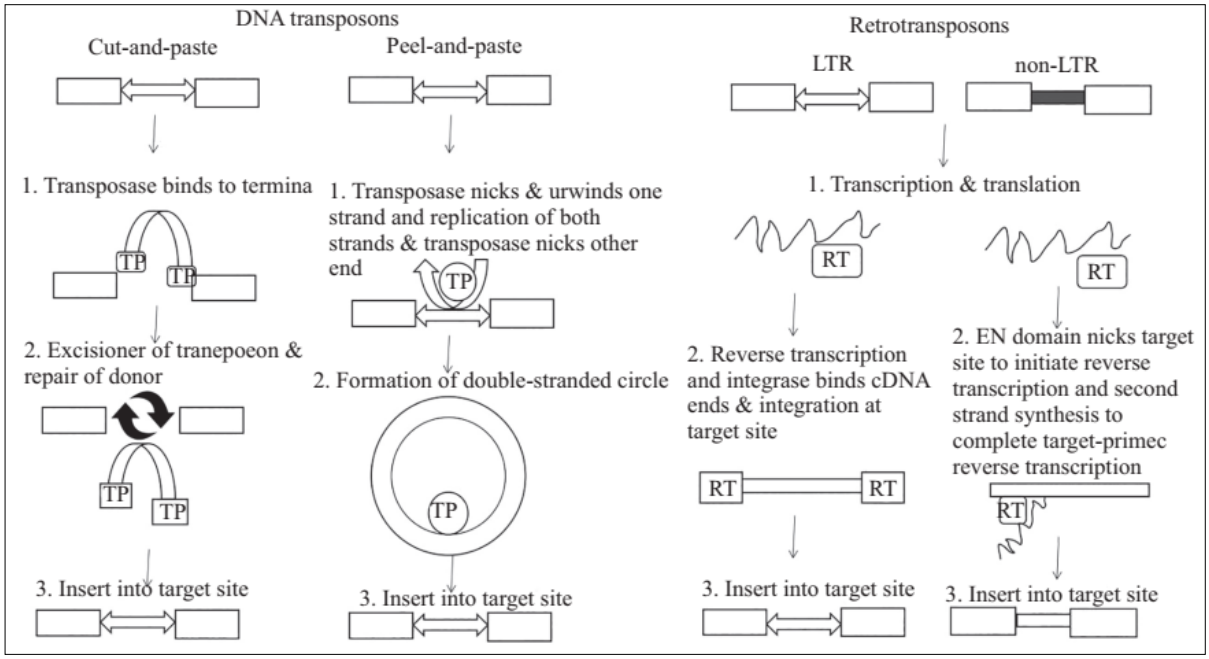

Fig 1: Transposition process of two types of Transposons

The approximate transposable process of the two types of transposons is shown in Figure 1. Non-coding RNA is an RNA molecule that does not code for a protein. It has a very wide range of biological functions. Gene transcription, post-transcription, and gene translation are all aided by non-coding regulatory RNAs [6]. By looking at whether the length is greater than or less than 200 nucleotides, we can classify long and short non-coding RNA as either long or short. MicroRNA (miRNA), small interfering RNA (siRNA), and PIWI protein-interacting RNA (piRNA) are examples. These non-coding RNA molecules are engaged in gene expression and regulation on various levels and areas of the process. More recent research shows the connection between transposons and non-coding regulatory RNAs. Most of the small RNAs abundant in eukaryotes, such as siRNA, miRNA and piRNA, are derived from transposons.

In plants, these small RNAs derived from transposons regulate the expression of motifs by regulating the methylation process of DNA. In animals, transposon-derived piRNA can induce mRNA degradation in sperm cells, thus affecting the process of sperm becoming mature sperm. TEs expression in mice is also silenced due to the piRNA-mediated ping-pong cycle. This paper focuses on the relationship between transposons and miRNA, piRNA and siRNA, and the expression regulation mechanism of host factors.

Regulation of gene expression by transposons and their miRNA sources

miRNA is a kind of non-coding endogenous single-stranded RNA with a length of 20-24 nt, which plays an important role in the biological gene regulation network. First, miRNA can complement target mRNA in reverse pairing, thus inhibiting mRNA expression at both transcriptional and post-transcriptional levels [7-8]. In animals, miRNA and mRNA's low base complementary pairing inhibits mRNA translation. In plants, miRNA has a high degree of base pairing and matching with mRNA, and miRNA mediates degradation of target mRNA [7, 9]. Secondly, many studies have proved that miRNA can target to encode many regulatory proteins and transposons and participate in plants' response to heat stress, playing an important role in plant growth and development and stress resistance [10]. The maturation and functional progression of miRNA requires the participation of two protein families, namely the DICER protein family and the Argonaute protein family. DICER protein is an endonuclease, and its homologous protein is called DCL(Dicer-like) protein. MiRNAs of 21 nt size are produced by dCL1/4 (Dicer-like 1/4) protein addition to miRNA precursors, which have a stem-ring structure [11-12]. Argonaute protein exists widely in various organisms and is the core RNA Interference (RNAi) pathway in eukaryotes. After processing by DCL endonuclease, small RNAs such as siRNA. An RNA-induced silencing complex (RISC) is formed when miRNA and piRNA bind to the Argonaute protein, and this complex regulates gene expression both during transcription and post-transcription. [13].

Many miRNAs are derived from transposon sequences [14]. In mammals, many miRNAs are TEs or derivatives of TEs, which are involved in forming miRNA stem ring structures. 20% of known miRNAs in the human genome are derived from MITE (Miniature Inverted -repeat transposable Elements) [15]. MiRNAs with reversed TEs sequences were mainly from SINE and LINE transposons, while miRNAs partially overlapped with non-inverted TEs sequences were mainly from SINE, LINE and DNA transposons. The miRNAs derived from TEs were mainly from DNA transposon and SINE sequences. Among other animals, Researcher [16] conducted high-throughput sequencing of all small RNAs in half of the gastrula of embryos at three development time points of tropical African Xenopus laevis and discovered a new miRNA named siRNA. The newly discovered miRNA is derived from transposon sequences remaining in introns. Transposons are an important source of miRNA in plants. Researcher [17] proved that miRNA evolved from TEs in some plants to study original target genes related to the CDS region and TEs homologous sequence, and TEs can form folding in the non-coding region the transcript finally form miRNA. Researcher [18] used deep sequencing data sets to study two typical miRNA pathways in Rice, the DCL1/4 pathway and the Argonaute 1(AGO1) mediated pathway. It was found that the miRNA

hairpin structure was specifically enriched in AGO1 immunoprecipitation samples, while the miRNA hairpin structure was relatively less in dCL1/4 knockout genotypes. These miRNA hairpin structures have significant homology with MITE transposons, a rich DNA transposon in Rice. This indicates that TEs also form miRNA hairpin structures in some plants. 2297 miRNAs were identified in the fast-growing roots, stems and leaves of bamboo [19-20]. Other research group found that 29.1% of these identified miRNAs came from MITE-related sequences, among which MITE contributed the most to the hAT transposon superfamily. These studies indicate that MITE transposon is one of the main sources of miRNA [21].

miRNA can maintain genomic stability by inhibiting TEs transposition. An example is miRNA translation inhibition of L1(LINE1) transposons. L1 is the most abundant autonomic transposable element in mammals, accounting for 20% of mammalian genomes. Studies have found that miRNA induces L1 transposon silencing and plays an important role in the genomic stability and plasticity of the L1 transposon. miRNAs have evolved L1 functional regulation mechanisms in some somatic cells to compensate for piRNA deficiency in non-germ cells [22]. In these cells, miRNA-induced silence complexes were guided by Mir-128 and directly bound to L1 target ORF2 RNA. This interaction would lead to instability of L1 transcripts, resulting in transcriptional inhibition of L1 transposons, thus reducing the probability of L1-mediated mutagenesis. Another study also demonstrated a possible link between L1 transposable and miRNA expression. Studies [23] conducted deep sequencing and global analysis on breast cancer cells with L1 active and L1 silenced and found that miRNA expression would increase when L1 was silenced. This indicates that L1 may be associated with miRNA expression activation. Mir-845 is a highly conserved miRNA in plants. In Arabidopsis pollen, Mir-845 can bind to the PRIMER binding site (PBS) of LTR retrotransposon and stimulate the accumulation of 21-22 nt small RNA through RNA polymerase V, which can mediate the dose-response of the arabidopsis gene set [24].

According to the research on the origin of miRNA and miRNA regulation on genes and transposons, it can be inferred that TEs in some organisms can regulate the expression of themselves and other genes through self-derived miRNAs. Some studies provide evidence for this hypothesis, miR820 is a TEs derived miRNA in wheat that targets DRM2(Domains rearranged methyltransferase) transcripts, Its inhibition of the DRM2 gene will lead to a decrease in DNA methylation and an increase in the expression of TEs transcription products [25]. This is an example of TE-derived miRNA modulating plant DNA methylation. Many miRNAs are derived from L2(LINE2) transposons in human brain tissue. These TEs-derived miRNAs are located on introns of protein-coding genes. L2 elements in the human genome lack promoters of their own, and lncRNAs have been found to use their promoters to force transcription of pri-miRNA transcripts of inserted L2 fragments [26]. This is an example of transcription of TEs derived miRNA driven by lncRNA. In the human genome, some target genes of TEs transcription derived miRNA are identified as TEs sequences embedded in the 3 ‘UTR (3' Untranslated Region), which can regulate gene expression by combining with TEs sequences in the 3 'UTR [27-28]. For example, the target of functional miRNA associated with AGO2 protein is the L2 transposon sequence in 3 'UTR [29].

Regulation of gene expression by transposon and piRNA

piRNA is a small non-coding RNA with a length of 24~31 nt. Such small non-coding RNAs are abundant in germ cells and can interact with the regulatory protein PIWI protein in germ cells to influence organisms' reproductive development and epigenetic regulation [30-31]. piRNA's regulatory effect is mainly reflected in mRNA degradation and transcriptional inhibition of TEs. Its interaction with PIWI protein can guide the degradation of PIWI protein to target mRNA and promote DNA methylation to silence TEs expression. The main idea is that small piRNA precursor are produced by endonuclease zucchini (endonuclease zucchini) after endonuclease cleavage of long precursor transcripts. After cutting, the 5 'end of piRNA binds to the PIWI protein. According to how organisms produce it, piRNA can be divided into primary piRNA and secondary piRNA. Primary piRNAs are derived from the transcription of single-stranded piRNA precursor molecules catalyzed by RNA polymerase II. This precursor molecule is also known as an RNA cluster. It was then transported into the cytoplasm by a protein MAEL (Maelstrom, MAEL) with RNA binding activity and containing a conserved HMG-box (High Mobility group box) domain [31-32]. After entering the cytoplasm, piRNA generates the 5 'end of primary piRNA through the interaction between MAEL protein and PLD6 endonuclease [33-34]. The piRNA body preferentially binds to PIWI protein to achieve stability, and then the Piwi-piRNA complex is produced and modified at the 3 'end to produce primary piRNA[35-36]. Primary piRNA can lead to 11~12 nt secondary piRNA through PIWI protein-mediated antisense transcription cleavage, and this process of secondary piRNA production is known as the ping-pong cycle. Secondary piRNA can, in turn, promote the generation of primary piRNA. Scientist [37] studied the evolutionary interaction of TEs and piRNA in dogs, horses and bats with statistical methods and found that the TEs subfamily with the most transcribed times could trigger the most intense ping-pong cycle. This indicates that piRNA production has an important relationship with TE transcription. In some eukaryotes, TEs are the main source of piRNA. GAN *et al*. [38] found that TEs were one of the main sources of piRNA in the first two cell periods after deep sequencing and bioinformatics analysis of type A spermatogonial cells, coarse embryonic spermatogonial cells and round spermatogonial cells of mice. Three kinds of retrotransposons, LTRs, LINEs and SINEs, abundant in mice, produced large piRNA. Researchers have come to similar conclusions in studies involving humans and fruit flies.

At the transcriptional and post-transcriptional stages, piRNA can mute TEs. piRNA similarly mediates inhibition of post-transcriptional transposons by the ping pong cycle. piRNA recognizes transposon targets, and PIWI proteins cut transposon domains to silence them while generating a new piRNA in the opposite direction. These newly generated piRNA then bind AGO3 proteins and undergo a series of modifications involving ZUC endonucleases and some unknown nucleoids to form an aug-piRNA complex. AUGpiRNA complex can recognize and slice more clustering transcripts and generate more antisense piRNA [39-40]. Similar mechanisms have been found in many species. For example, the ping-pong cycle function has been identified as an effective means of transposon transcriptional degradation and small RNA amplification in

black-belted mice and mice [41-42]. Human testicles may go through a ping-pong cycle mediated by piRNA, according to Scientist [28], who used high-throughput sequencing to identify piRNA from three adult testicular samples. piRNA can also silence TEs before transcription. After binding with piRNA, nuclear PIWI protein will be induced to transfer into the nucleus and then bind with newborn RNA through piRNA base pairing. This process will lead to DNA methylation and histone modification, thus inhibiting the transcription of TEs. Many studies have provided evidence. For the first time, it has been shown that the piRNA-PIwi system silences L1(line-1) transposons at the same chromosomal sites as piRNA clusters, thereby exposing the regional mechanism of L1(line-1) silences. Male germ cell transcriptional activation was observed in mice lacking the PIWI family proteins MILI or MIWI2, which were deficient in the methylation of L1 transposons and intracellular LTR-retrotransposons [44]. Mice lacking MILI interacting proteins showed DNA methylation loss and L1 expression reactivation [45].

piRNA also resulted in TEs silencing at the shear level. In drosophila, P transposon is a DNA transposon that can induce hybrid sterility. piRNA can inhibit the transposon activity of P transposon by shearing the last intron of p transposon. Pirna-mediated transcriptional suppression of P transposons occurs at the shearing stage, which may be completed during chromosome remodeling [30]. The regulation of piRNA on mRNA in drosophila is a typical example of TEs and its derivative piRNA affecting mRNA expression. In the early embryos of fruit flies, TE-derived piRNA can bind to the UTR (Untranslated Region) of Nanos mRNA and regulate its expression (Figure 1). In early embryos, the vegetative cells deposit cytoplasmic contents into the egg, activating TEs transcripts in the egg and vegetative cells. Activated TEs transcripts were processed into piRNA by egg whites of PIWI, AUB(Aubergine) and dmAGO3(Drosophila melanogaster Argonaute 3) (Figure 2). piRNA derived from TEs is maternally inherited in embryos at fertilization. In early embryos, piRNA derived from roO and 412 lines transposons binds to AUB protein and dmAGO3 protein to inhibit maternal Nanos mRNA [46]. The Smaug protein and piRNA binding to this mRNA are conducive to attracting cCR4-NOT (Recruitment of the C-C Chemokine receptor Type 4-negative on TATA) inactivated enzyme complex. Resulting in subsequent translation inhibition (FIG. 2) [47-48].

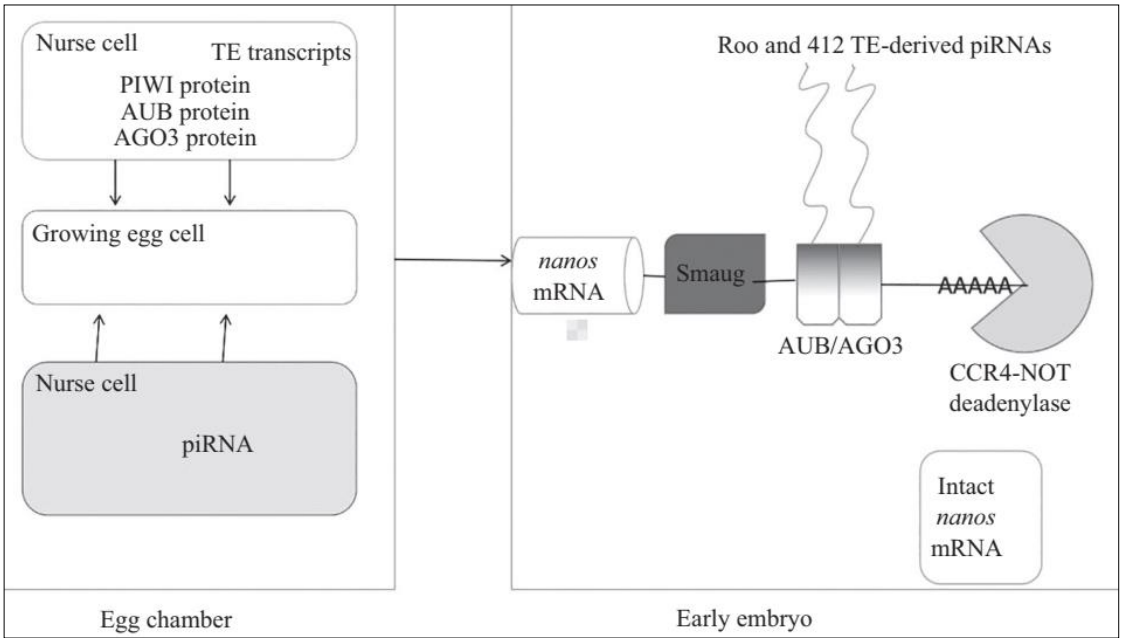

Fig 2: Gene regulation of TEs derived piRNA in Drosophila

piRNA mediated TEs regulation of mRNA also exists in the process of sperm production in mice. Scientist [49] found that piRNA-mediated mRNA decay is necessary for round sperm cells to become mature sperm. Prepachytene piRNA (pre-pachytene piRNAs) derived from TEs is abundant in the germ cells of the gonads of unborn and newborn male mice. This piRNA can be loaded into the MIWI2 egg white and MILI proteins of the mouse PIWI protein family, and the MIWI2 protein and MILI protein mutants can block the spermatogenesis of the fine line, pabulinear line and divine phase, respectively, accompanied by the up-regulation of TEs. Some studies have also found that piRNA can indirectly affect miRNA translation activation during spermatogenesis [50]. In round sperm cells, many MIWI proteins were found to bind endogenous mRNAs, and signal sites of the ping-pong cycle were identified in the cleavage sites of MIWI protein-bound mRNAs. Meanwhile, we also found that the shear activity of MIWI protein, which mediates mRNA decay, plays an important role in this process.

This indicates that the mechanism of piRNA production in the decay process of mRNA may be the ping pong cycle and also indicates that TES-related piRNA plays an important role in the process of round sperm becoming mature sperm. In the process of sperm cell elongation, many Pectinea piRNA can target mRNA in the round and elongated sperm cells during sperm formation, resulting in enrichment of CHROmatin Assembly Fact-1 nuclease and cleavage of MIWI protein. Finally, mRNA degradation was caused [51]. In general, during animal spermatogenesis, TEs derived piRNA can affect the degradation of related mRNA to regulate spermatogenesis.

Effects of transposons and their siRNA on gene expression

SiRNA, a double-stranded RNA fragment with a 20-25 nt, regulates gene expression and maintains genomic stability. It has three main functions: first, it cuts the mRNA transcript through RNA interference (RNAi) to prevent its translation; second, it participates in DNA methylation through the RdDM process; third, it participates in the response of plants to heat stress. TEs are the major source of siRNA in plants and animals. Endogenous Short RNA (Endogenous Short RNA) is a siRNA found in non-gonad cells. TEs have been proved to be one of the important sources of Endo-SiRNA in non-gonadal cells of drosophila [52]. In our study on LTR sequences of Phyllum Piniculata, 15% of 21 nt siRNA and 18% of 24 NT siRNA were fully matched with LTR reverse transcription factor related sequences, and 21 NT siRNA was mainly derived from THE Tat and Oryco lines of LTR transposons. 24 NT RNA was mainly derived from Tat and Reina lines of LTR transposons [21]. In another research on the bamboo genome, researchers identified 23 154 siRNA in bamboo internodes, 67% from MITE transposons [53]. It is worth noting that many TEs related to siRNA affect gene expression in animals and plants to some extent. In plants, TEs and their derived siRNA can participate in THE DNA methylation process through the plant RdDM pathway, thus affecting gene expression. RNAi in plants refers to siRNAs of 21~25 nt that are cleaved by double-stranded RNA (dsRNA) family members.

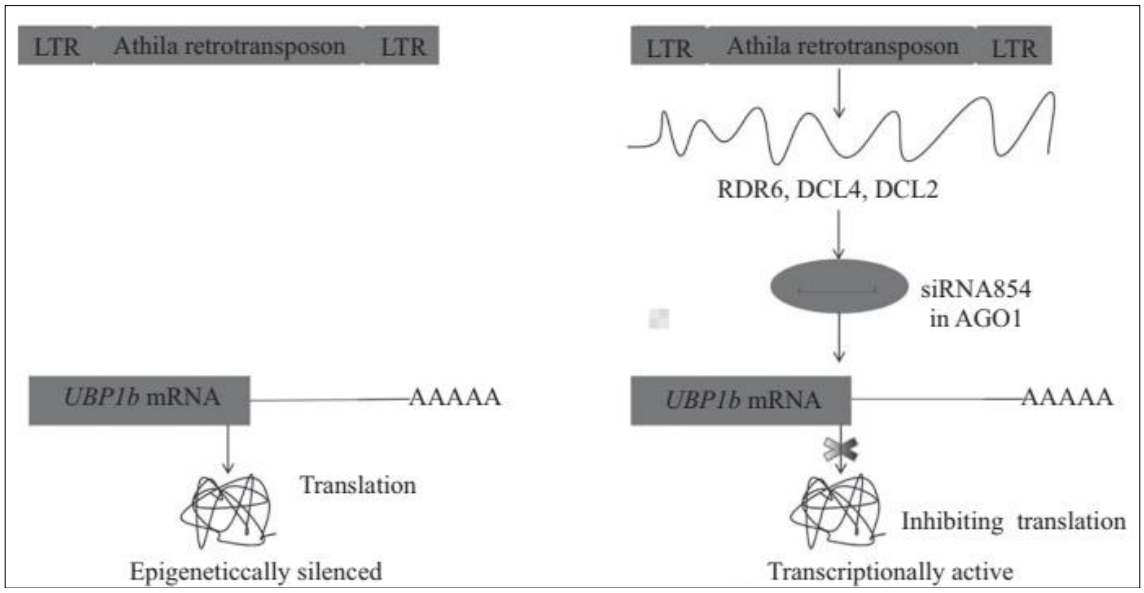

Fig 3: Gene regulation of TEs derived siRNA in *Arabidopsis*

This siRNA can be introduced into different pathways to regulate post-transcriptional gene expression in plants or animals. In plants, siRNA plays a role in gene silencing by directing cytosine methylation activity of complementary DNA sequences. This nuclear regulatory system is called RNA-directed DNA methylation (RdDM). One example is the flowering locus C (FLC) gene regulation. FLC gene is the main inhibiting gene of flowering, and the vernalization mechanism negatively regulates it. This phenotypic mechanism is associated with the insertion of 1 224 bp involuntary mutator-like transposons into the first intron of FLC, which inhibits the expression of allelic Moines of FLC. At the same time, the FLC gene is subject to siRNA-mediated inhibitory chromatin modification by homologous transposons from other locations in the genome [54-55]. One example is the flowering imprinting gene (FWA), which is expressed specifically in the endosperm but not in the vegetative tissues of Arabidopsis thaliana.

The expression of tissue specificity of FWA depended on the demethylation of the FWA promoter, which was composed of two direct repeating sequences, one of which was related to SINE retrotransposon. Methylation of the FWA promoter leads to the formation of local heterochromatin, which leads to the generation of transcriptional silencing and SINE transposon-related siRNA. This siRNA can also generate new silences in unmethylated FWA genes through the RdDM pathway [56].

In another example, when an epigenetic gene activates the Athila retrotransposon in Arabidopsis, its transcript is processed into siRNA. It directly binds to UBP1b (3 'UTR of the GENIC Oligouridylate binding protein 1B) mRNA and affects the expression of UBP1b mRNA (Figure 2) [57-58]. When the wild-type epigenome is silenced by DNA methylation, the LTR retrotransposon will not produce Athila retrotransposon derived siRNA so that Athila transposon does not affect UBP1B mRNA function (Figure 3) [59-60]. When epigenetic silencing from Athila transposon is removed, the transposon generates 21-22 nt endo-SIRNAs via RDR6(RNAdependent RNA Polymerase 6) enzyme and DCL1/4 protein. Athila siRNAs and siRNA854 of these siRNAs bind to the protein AtAGO1(Arabidopsis Thaliana AGO1) and regulate UBP1b mRNA through four binding sites in its 3 'UTR. Inhibition of UBP1b translation [57, 60] (FIG. 3). In plant gamete production and embryo development, transposons and siRNA regulate genes by RNA interference and RdDM. The mechanism of transposon activity inhibition in gametes is an important defense against mutation to ensure the stability of the host genome. DME(Demeter) is a helical hairpin DNA glycosylation enzyme that removes methylated cytosines, leading to overall hypomethylation of the endosperm [61]. DME's active demethylation activates transposon expression and introduces transposon transcripts into the RNAi pathway to generate siRNAs that induce DNA methylation

[62]. siRNAs produced in the endosperm enter the egg cell and guide DNA methylation, leading to the silencing of the germ cell interlock [63].

This mechanism may be one of the mechanisms that inhibit transposon activity in embryos. In addition, Scientist [64] found that siRNA obtained from RNAi degraded mRNA and TEs directly binds to AGO6 protein, which then binds to TE chromatin, enabling siRNA to play a role in the process of RdDM. In Arabidopsis, mutants encode mutations in ATP-dependent chromatin remodeling genes, whole-body DNA methylation levels are reduced and associated TEs are activated. Activation of these TEs are accompanied by the production of endogenous small RNAs, called epigenetically activated siRNAs. These siRNAs can cleat TEs transcripts, resulting in TEs silencing [65]. In the study of Rice TEs derived siRNA by Scientist [66], TEs derived siRNA815 can induce DNA methylation of target gene loci through the RdDM pathway. In conclusion, TEs related siRNA plays an important role in the DNA methylation of plants. In Arabidopsis thaliana seedlings under heat stress, a type Copia retrotransposon named ONSEN is transcriptionally active and capable of synthesizing extratrosomal DNA copies [67-69]. During siRNAs generation, heat-induced ONSEN accumulation is activated. After stress, ONSEN transcripts and *in vitro* extrachromosomal DNA were gradually reduced, and a high frequency of new ONSEN insertion was observed in siRNA deficient progenies of stressed plants. It was also found that in mutant plants unable to produce siRNA, if ONSEN transposition were induced during organ differentiation, the stress mechanism would be maintained during the development of the mutant plants, indicating that the siRNA pathway can regulate the transposition of retrotransposons induced by the environment, thus regulating the environmental stress gene network in plants.

SiRNA silenced TEs expression. In drosophila, endo siRNA can bind to AGO2 protein, and AGO2 protein bound to these small RNAs can mediate the cleavage of TEs transcript complementary to endo-siRNA sequence, resulting in TEs transcript degradation and expression suppression [70-72]. Sterility in mice appears to be caused by the silencing of TEs in the germ cells through the Endo-siRNA route [73-75]. When the endo-siRNA-mediated silence is disturbed, the expression levels of Endo-siRNAs and their related retrotransposons are altered by the ectopically expressed protein TDB-43 (TAR DNA binding protein 43), which is linked to ALS, as was discovered in a drosophila model study [76-82]. These studies suggest that siRNA in animal cells plays a role in TEs silencing. In arabidopsis DDM1(Decrease in DNA methylation1) mutant, DNA methylation level is reduced, and many transposons are reactivated. Activation of these transposons is accompanied by the production of small RNAs of 21 to 22 nT called epigenetically activated siRNAs; These esaiRNAs can cleat TEs transcripts and silence TEs expression. It is noteworthy that some of these esaiRNAs can act on mRNA and reduce its expression level. For example, siRNA854 can act on the 3 'UTR region of the transcription of UBP1(Upstream Binding protein 1) gene encoding stress particle protein.

Conclusion

The effects of TEs on the genome can be roughly divided into three categories: first, the insertion of TEs changes the reading frame and splicing pattern of the coding region, resulting in the loss of gene function and the change of expression pattern; Second, the insertion of TEs induced the emergence of new regulatory elements; Third, TEs silences gene expression by changing chromosomal state. The effect of TEs related non-coding RNAs on the genome also follows these rules. First of all, from the relationship between evolution and origin, TEs are the main source of small RNA in organisms. Secondly, from the perspective of function and expression, some regulation of the TEs gene set is completed by its small derivative RNA. As in plants, TEs derived siRNA regulates GENE expression by regulating DNA methylation through the RDdM pathway. Tes-derived piRNA in mice and drosophila could affect mRNA degradation during spermatogenesis. Finally, transposons and non-coding RNAs also interact and regulate each other. SiRNA leads to TEs silencing in flies and mice. piRNA can silence TEs expression at both transcriptional and post-transcriptional levels. These indicate an important and close relationship between transposons and non-coding RNAs (Table 1).

The rapid development of sequencing technology and bioinformatics is the key to the rapid development of transposon and non-coding RNA research. The combination of high-throughput sequencing technology and microRNA-SEP technology can better analyze the relationship between miRNA family members, identify the specific biological behavior of miRNA under the target species, and identify new miRNA fractions, which has also become a good tool for studying the relationship between miRNA and transposons. Further application of RNA-SEP technology has made it possible to detect transcripts with low abundance. RNA molecules bound to proteins were sequenced using RIP (RNA Binding Protein Immunoprecipitation Assay) and CHIP (Chromatin Immunoprecipitation assay). The specific binding information of protein and RNA can be obtained. RIP technology and CHIP technology can better study the RNA-induced silencing complex and reveal the binding relationship between small RNA and its target gene.

Table 1: Regulation of genes by TEs derived microRNAs and their relationship with TEs

Small RNA	Relationship with TEs	Silencing effect on TEs	Regulation of animal gene	Regulation of plant genes
miRNA	TEs are involved in the formation of miRNA hair- pin structure. Many miRNAs are TE or derivatives of TE	Transcriptional inhibition of L1 transposon by miRNA	The target site of L2 transposon is TEs sequence	Affect DNA methylation level
piRNA	TEs are the main source of piRNA in some special cell stages In some mammals, the TEs subfamily with the most transcription times can trigger the most intense ping-pong cycle	Regulation of LTR trans poson by Pingong cycle Inhibition of TEs transcription by DNA methylation and histone modification Inhibition of p transposon transposable activity by piRNA silencing mechanism of Zebrafish L1 transposon	piRNA in *Drosophila* affects sperm formation	
siRNA	Endo-siRNA is derived from TEs sequence, and 24 nt siRNA is also derived from TEs siRNA in Phyllostachys heterocycla genome comes from LTR TEs	EasiRNA silences the expression of TEs Inhibition mechanism of transposable activity in gametes	Endo-siRNA induces infertility in mice	Inhibition of FLC gene and FWA gene expression Inhibition of transposons in plant gamete and embryonic development. It is involved in the response of plants to heat stress

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