

Silencing: new faces of Morpheus' molecule

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Eukaryotic genomes contain large numbers of transposable elements that not only pose a threat to genome integrity but also regulate expression of certain protein-coding genes. The molecular mechanisms of transposon silencing are still not very well understood. Two papers in this issue of *The EMBO Journal* shed new light on the function of Morpheus' molecule (MOM1), one of the most mysterious components of the silencing systems in plants.

Transcriptional gene silencing is a process that controls expression of transposons and repetitive DNA elements. It is involved not only in maintaining genome integrity but also in regulating expression of genes that harbor transposons in their promoters. The core mechanism of transcriptional gene silencing involves establishment of DNA methylation and/or certain covalent modifications of histone tails, which block transcription by RNA Polymerases I, II or III.

One of the most mysterious components of transcriptional gene silencing system in *Arabidopsis thaliana* is MOM1, named after the Greek god of dreams (Amedeo *et al*, 2000). It is distinct from most known components of transcriptional silencing pathways in plants, in that it silences transcription, but is not required to maintain DNA methylation associated with the silent state (Amedeo *et al*, 2000; Habu *et al*, 2006; Vaillant *et al*, 2006). Although based on sequence similarities MOM1 seemed to be a chromatin remodeling factor (Amedeo *et al*, 2000), the recent discovery that 87% of its sequence, including the SNF2 domain, is dispensable for silencing showed how little we know about the molecular mechanism of MOM1 function (Caikovski *et al*, 2008). Two papers in this issue of *The EMBO Journal* (Numa *et al*, 2009; Yokthongwattana *et al*, 2009) address the question of how MOM1 works.

Yokthongwattana *et al* started with a clever forward genetic screen designed to find mutants in genes encoding proteins that are functionally related to MOM1. They identified a mutant in NRPE1, the largest subunit of RNA Polymerase V (Pol V), a specialized plant-specific RNA Polymerase. The *mom1 nrpe1* double mutant displayed a dramatic loss of transcriptional gene silencing compared with the subtler effects of single *mom1* or *nrpe1* mutants. This suggested that both MOM1 and Pol V contribute to transcriptional silencing but that they work in parallel, non-redundant pathways.

Pol V is known to function in an RNA-dependent DNA methylation (RdDM) pathway, where short interfering RNAs guide DNA methylation and transcriptional silencing to

transposons and other repetitive DNA elements (Wierzbicki *et al*, 2008, 2009; Matzke *et al*, 2009). Thus, Yokthongwattana *et al* extended their genetic analysis to other components of the RdDM pathway and concluded that, at least for a subset of loci, MOM1 functions in a pathway parallel to RdDM.

To determine whether this functional interaction between MOM1 and RdDM is of general importance, Yokthongwattana *et al* carried out an extensive transcriptome analysis. Genetic interactions between MOM1 and Pol V turned out to be quite complex and locus-specific (Figure 1). At some loci, double mutants showed disruption of silencing that was considerably stronger than in either individual mutant, thus confirming that MOM1 and Pol V can work in parallel. Surprisingly, at a different subset of loci the effects of *mom1*, *nrpe1* and *mom1 nrpe1* were very similar, suggesting that in these cases MOM1 and Pol V work in the same silencing pathway. At yet a third subset of loci, the silencing defects observed in *nrpe1* were reversed in *nrpe1 mom1* double mutants, suggesting that

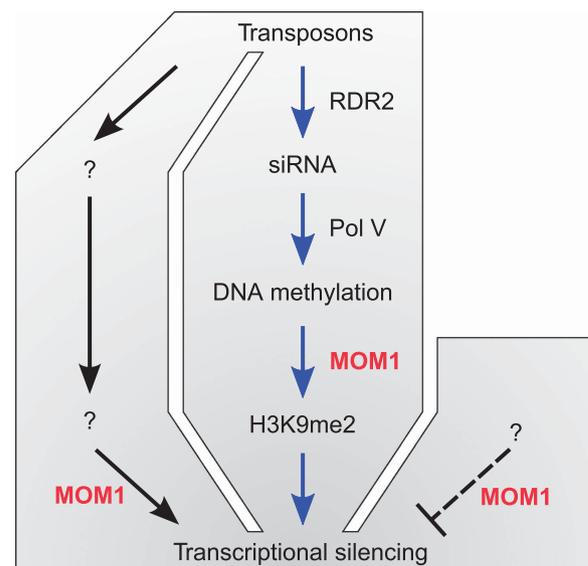


Figure 1 Model for multiple, locus-specific functions of MOM1 in transcriptional silencing. At certain loci MOM1 works as a part of the RdDM pathway (center pathway with blue arrows), where it mediates transduction of the silencing signals from DNA methylation to dimethylation of lysine 9 of histone H3 (H3K9me2). At other loci, MOM1 contributes to transcriptional silencing in an unknown pathway that is parallel and non-redundant to RdDM (left pathway). At a third subset of loci, MOM1 directly or indirectly counteracts silencing by RdDM (right pathway).

MOM1 may directly or indirectly counteract Pol V. This shows that depending on the locus, MOM1 and Pol V may genetically interact in at least three distinct manners (Figure 1).

A similar transcriptome analysis was carried out by Numa *et al.* However, instead of comparing multiple genetic backgrounds, Numa *et al.* identified loci that were derepressed in *mom1* mutants and compared them with previously published small RNA deep sequencing data sets. MOM1 targets turned out to be significantly enriched in 24 nt small RNA dependent on RDR2, an RNA-dependent RNA polymerase involved in RdDM. This led Numa *et al.* to a similar conclusion as Yokthongwattana *et al.* that MOM1 shares a subset of target loci with the RdDM pathway.

Numa *et al.* identified several loci at which *mom1* has effects similar to RdDM pathway mutations. This is consistent with the results of Yokthongwattana *et al.* that MOM1 may work in the RdDM pathway (Figure 1). However, the particular design of transcriptome analysis did not allow Numa *et al.* to identify alternative types of genetic interactions. Instead, they studied the mechanism of MOM1 function at the loci where it acts in the RdDM pathway. They found

that MOM1 is needed for the establishment of dimethylation at lysine 9 of histone H3 (H3K9me₂), which is a mark associated with silent chromatin. As DNA methylation is also needed for the establishment of H3K9me₂, whereas MOM1 is not needed for the establishment of DNA methylation, Numa *et al.* concluded that at these loci, MOM1 is involved in transmission of the silencing signal from DNA methylation to histone modifications (Figure 1).

Collectively, the two papers show that MOM1 has multiple locus-specific functions in transcriptional gene silencing. One of these functions is transduction of silencing signals from DNA methylation to repressive histone modifications. Other functions that are defined genetically still await mechanistic explanation. Most importantly, these papers raise the question of how the various different functions of MOM1 are selectively employed at specific loci.

Conflict of interest

The author declares that he has no conflict of interest.

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