

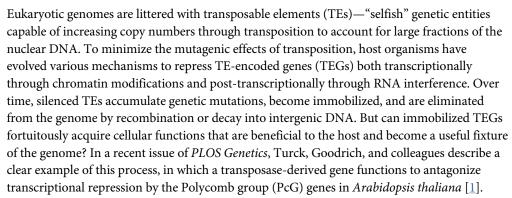
**PERSPECTIVE** 

## Public Service by a Selfish Gene: A Domesticated Transposase Antagonizes Polycomb Function

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PcG genes play critically important roles in regulating plant development by targeting thousands of genes for transcriptional repression through trimethylation of lysine 27 on histone H3 (H3K27me3) [2]. In Arabidopsis, PcG function requires two classes of protein complexes: Polycomb Repressive Complexes 1 and 2 (PRC1 and PRC2, respectively). The enzymatic complex PRC2 contains one of the three H3K27 trimethyltransferases, MEDEA (MEA), CURLY LEAF (CLF), and SWINGER (SWN), whereas the PRC1 complex includes the H3K27me3-binding protein LIKE HETEROCHROMATIN PROTEIN 1 (LHP1). To better understand the mechanisms that may counteract PcG repression, two independent suppressor screens were performed to identify mutants that could revert the developmental and transcriptional defects of the CLF and LHP1 mutants, respectively [1,3]. One gene named ANTAGONIST OF LIKE HETEROCHROMATIN PROTEIN 1 (ALP1) was isolated from both screens, indicating that it likely functions broadly in antagonizing PcG repression [1,3]. This notion is supported by several lines of evidence: (1) alp1 suppresses the developmental phenotypes of clf; (2) a significant faction of genes overexpressed in clf are no longer overexpressed in alp1 clf; (3) ALP1 functions upstream of PcG-repressed genes (e.g., AGAMOUS); (4) many PcG-target genes are down-regulated in alp1 when normal PcG activity is present; (5) alp1 enhances the defects of several mutants of trithorax group (trxG) genes involved in counteracting PcG repression; and (6) ALP1 physically interacts with PRC2 in planta. Taken together, these results strongly indicate that ALP1 is generally required to antagonize PcG repression at a large number of developmentally important genes [1].

Interestingly, ALP1 encodes a protein that is highly similar to the transposases (TPases) of the PIF/Harbinger superfamily of DNA TEs  $[\underline{1,3}]$ . The first active member of the superfamily, PInstability Factor (PIF), was identified in maize as repeated mutagenic insertions into the





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anthocyanin regulatory gene R and was later found to be similar to the *Harbinger* elements computationally identified from Arabidopsis [4-6]. The PIF/Harbinger superfamily is distantly related to the bacterial IS5 elements and includes five major groups in eukaryotes: two separate plant-specific groups (PIF- and Pong-like groups), an animal-specific group, and two fungal groups [7]. Members of the PIF/Harbinger superfamily share several characteristics: they have short terminal inverted repeats (TIRs), prefer to insert into 3-bp target sites embedded in longer palindromic sequences, and encode two proteins (a Myb-like DNA-binding protein and a TPase) that are both required for transposition [8,9]. ALP1 shares extensive homology with PIF-like TPases. However, there are several important differences: (1) PIF- and Pong-like elements are present at moderate-to-high copy numbers in plant genomes (from dozens in Arabidopsis to ~1,000 in Brassica oleracea), whereas ALP1-like genes are present at single copy in land plants; (2) the DDE catalytic motif in PIF-like TPases is mutated in ALP1 and its homologues in angiosperms (but not in gymnosperms, ferns, bryophtyes, and green algae) and the Myb-like gene and TIRs are missing from ALP1 flanking sequences; and (3) the majority of PIF-like elements are transcriptionally silent and have accumulated missense or nonsense mutations, whereas ALP1 is broadly expressed in Arabidopsis leaves, stems, flowers, and roots, and its coding capacity is well preserved in land plants [1]. Taken together, these results suggest that ALP1 likely originated from a PIF-like TPase gene and acquired an important cellular function in the common ancestor of angiosperms.

In addition to *ALP1*, a number of TPase-derived genes have been described in eukaryotes (for excellent recent reviews, see [10,11]). The majority of such genes were computationally identified based on the set of characteristics that distinguish *ALP1* from *PIF* TPases, including loss of catalytic activity for transposition, high degree of evolutionary conservation, being present at low copy number, and evidence for transcriptional activity. Importantly, several TPase-derived genes have been shown to provide vital functions for the hosts. For example, the SET-MAR protein—created from a fusion between a *Mariner* TPase and a SET histone methyltransferase domain—is required for the maintenance of genome integrity in primates [12,13]. In plants, the *Arabidopsis DAYSLEEPER* gene encodes a DNA-binding protein derived from a TPase of the *hAT* superfamily. DAYSLEEPER binds to a *cis*-regulatory motif upstream of multiple genes and the *daysleeper* mutant displays severe and pleiotropic developmental phenotypes [14]. As another example, *FHY3* and *FAR1* are derived from the *MURA* TPase gene encoded by Mutator-like elements (MULEs) [15]. However, both *FHY3* and *FAR1* function as transcription factors that activate gene expression under far-red light.

How ALP1 antagonizes PcG repression and how a TPase acquired such a function remain open questions. Based on the observation that the interactions of PRC1 and ALP1 with PRC2 appeared to be mutually exclusive, Liang et al. proposed that ALP1 may compete with PRC1 for binding to PRC2 and thereby alleviate PcG repression [1]. In this regard, it is interesting to note that, during *PIF* transposition, the TPase is recruited to TEs by interacting with the Mybdomain protein, which in turn binds specific DNA sequences at TE ends [9]. It is therefore possible that a catalytically inactive mutant TPase with altered preference for protein–protein interactions might have fortuitously acquired PRC2-binding activity. It is also possible that, considering the role of PcG as a "backup system" to repress TE activity (behind DNA methylation) [16], the interaction of a TPase with PRC2 may have originally evolved as an anti-repression mechanism by the TE. Future work should address these questions, for example, by determining whether the same domain is involved in ALP1–PRC2 and TPase–Myb-protein interactions. With the rapid advances of genomic resources and reverse-genetic tools, *ALP1* should serve as harbinger of the identification and functional characterization of many more selfish genes that have evolved to serve their hosts.



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