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Silencing paradox resolved

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The paradoxical involvement of RNA-mediated gene silencing in the maintenance of some DNA silencing is bridged in *Arabidopsis* plants by an RNA polymerase that acts as a liaison between both pathways, UK researchers report in the February 3 issue of *Science*.

Alan Herr, from the John Innes Centre, Norwich, and colleagues from there and elsewhere show that an RNA polymerase connects RNA and DNA silencing pathways. They found that mutants in RNA polymerase IV (Pol IV, also called RPD1), part of a new clade of polymerases in plants, were defective in both pathways.

"The finding of a new silencing-specific RNA polymerase is a surprising twist in the evolution of RNA polymerases," Herr wrote *The Scientist* in an E-mail. "Even though Pol IV is plant specific, the function of Pol IV may be performed by another RNA polymerase in other programs. Silencing of a locus does not mean that it is not transcribed."

RNA silencing occurs through the multiprotein RNA-induced silencing complex that cleaves double stranded RNA, producing short interfering RNAs (siRNA), which then amplify the cycle. Conversely, DNA silencing occurs through chromatin-mediated mechanisms that can include DNA methylation and histone modifications to form transcriptionally inactive heterochromatic regions. In the Pol IV mutant, both siRNA formation and DNA methylation are decreased at heterochromatic regions, Herr and colleagues found.

"Pol IV works together with a different type of RNA polymerase previously implicated in gene-silencing mechanisms called RNA-dependent RNA polymerase to produce double-stranded RNA that is then processed into small RNAs by a dicer enzyme," Herr wrote in his E-mail. "These small RNAs then act as the specificity determinant for the establishment and maintenance of the silenced state."

The new report is consistent with a general silencing model that Shiv Grewal of the National Institutes of Health calls "a self-enforcing loop." According to the model, siRNA is targeted to heterochromatin, and "heterochromatic regions recruit the RNAi machinery through the interactions of chromodomains," Grewal,, who was not involved in the study, told *The Scientist*. This in turn reinforces the complex by producing more siRNA transcripts. Polymerase IV may allow just enough transcription in heterochromatic regions to kick-start the loop, Grewal said.

Steve Jacobsen, of the University of California, Los Angeles, described the research as a case in which plants "use transcription to keep a locus silent. Methylation shuts genes off, but too strong of a shutoff is not good for maintaining siRNA-mediated silencing. Shut off all transcription, and siRNA can't work.

Jerzy Paszkowski at the University of Geneva, Switzerland, said the model raises "he chicken and egg problem" about which part of the loop comes first. Grewal suggested that "bidirectional transcription may be the initial trigger," like that found in transposable elements and other repetitive sequences.

In the battle between transposable elements overtaking a genome and a genome completely quiescing these parasites, Pol IV may be playing both sides, allowing transcription and silencing. According to Grewal, "Transposable elements have evolved to transcribe in the presence of heterochromatin, an adaptive response to overcome the heterochromatic machinery to silence them." While heterochromatin bodyguards this incomplete silencing, Pol IV allows transposable elements to "sneak past the door," says Grewal.

Herr and colleagues found that Pol IV is a plant-specific polymerase that groups outside of the usual polymerases I, II, and III. "The phylogenetic restriction of Pol IV suggests that it has an evolutionarily derived function rather than an evolutionary basal one," according to Jim Birchler at the University of Missouri, Columbia. Consistently, a predicted subunit of the new polymerase IV machine, RPD2, controls silencing in *Arabidopsis*.

Though Pol IV has a genetic function in silencing, Birchler noted that "Pol IV could have a role in silencing in the plant kingdom that is not understood at all. Determining the conditions under which Pol IV performs transcription is an important next step."

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