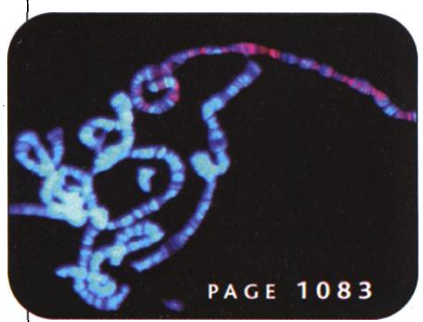
The Evolution of Epigenetics

Epigenetics covers a broad range of effects, and several are discussed in this special issue. But how did epigenetic regulation arise? For RNA-mediated silencing and DNA methylation there is evidence that they have evolved as part of a host defense mechanism against viruses and parasitic DNA.*

The substrate—double-stranded RNA (dsRNA)—for both posttranscriptional gene silencing (PTGS) [or RNA interference (RNAi)] and transcriptional gene silencing (TGS) seen in plants is a common intermediate in the life cycle of many viruses and transposons. Plant viruses are known to be targets and elicitors of PTGS, and suppressors of PTGS have been identified in the genomes of many of these viruses.† These suppressors were previously identified as pathogenicity determinates, indicating that there is ongoing coevolution of plant defense and viral offense. Does RNAi in animals serve a similar function? Possibly: Mutations that impair RNA silencing in *Caenorhabditis elegans* result in the mobilization of transposable elements.†

In TGS in plants, cytoplasmic dsRNA containing promoter sequences is able to direct the silencing, and de novo methylation, of the homologous DNA. Is DNA methylation also used as a means to suppress the invasion of the genome by viruses and transposons?‡ It is true that in plants and filamentous fungi, DNA methylation is mainly restricted to transposons and other repeat sequences. In mammals, coding sequences are also methylated, possibly reflecting the presence of transposons in gene introns. It is also true that *Drosophila melanogaster*, which does not methylate its genome, suffers a very high rate of spontaneous mutations—from 50% to 85%—through the action of transposable elements. The processes of repeat-induced point mutation and methylation induced premeiotically, both found in fungi, and of repeat-induced gene silencing, found in flowering plants, all silence and methylate repeated sequences, a common characteristic of parasitic DNA elements. Further support comes from mutations in the *DDM1* (decrease in DNA methylation) gene in *Arabidopsis*, which results in the reactivation of silent repeat sequences and the activation of a family of transposons.§ Nevertheless, the view that DNA methylation is a host defense mechanism is neither proven nor universal.‖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DDM1 encodes a protein similar to the chromatin remodeling factor SW12/SNF2, and there is other evidence suggesting an intimate link between DNA methylation and chromatin structure¶; thus, if DNA methylation really is part of a host control system, it seems likely that chromatin must be implicated too. Intriguingly, it has been suggested that other epigenetic phenomena, including genomic imprinting in placental mammals and X-chromosome dosage compensation, may themselves have evolved from such host defense mechanisms directed against parasitic DNA.*

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* M. A. Matzke *et al.*, *Genetica* **107**, 271 (1999). † V. Vance, H. Vaucheret, *Science* **292**, 2277 (2001). ‡ J. A. Yoder, C. P. Walsh, T. M. Bestor, *Trends Genet.* **13**, 335 (1997). § A. Miura *et al.*, *Nature* **411**, 212 (2001). ‖ A. Bird, *Trends Genet.* **13**, 469 (1997). ¶ H.-H. Ng and A. Bird, *Curr. Opin. Genet. Dev.* **9**, 158 (1999).

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See also Reports on pp. 1142, 1146, and 1150; www.sciencegenomics.org/resources/res_epigenetics.shtml; and Litt* et al. *in* Science *Express.

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