GENE REGULATION

Grouped in silence

Nuclear subdomains that contain Polycomb group (PcG) bodies are known to silence gene activity — but do they do so directly, by binding of PcG proteins to target promoters, or indirectly, by compartmentalizing the target genes into the repressive subdomain? A study in flies shows that the epigenetic silencing of Hox genes by PcG proteins is mediated by the genes' three-dimensional proximity in the nucleus.

The identity of anterior–posterior fly body segments is maintained by the repression of particular Hox genes by PcG proteins in spatially distinct domains. Using fluorescent *in situ* hybridization and immunostaining to Polycomb, Bantignies and colleagues found that Hox genes colocalize in PcG bodies, but only in those regions of the embryo or larva in which the Hox genes are repressed. Colocalization depends on PcG proteins and involves target genes — for example, Antennapedia (*Antp*) and Abdominal-B (*AbdB*) — that are up to 10 Mb apart.

Chromosome conformation capture on chip experiments confirmed the presence of long-range interactions: the chromosomal contact between *Antp* and *AbdB* was mediated by two *AbdB* PcG response elements (PREs), *Fab7* and *Mcp*. When *Fab7* is mutated, the expression of several genes, including *Antp*, is derepressed. This interaction between *Antp* and *AbdB* PREs is also physiologically relevant: target PREs have a PcG-dependent epigenetic mark and, *in vivo*, *Fab7* or *Mcp* mutations enhance the homeotic phenotype of a sensitized *Antp* allele.

The long-range interactions seen in PcG bodies may be a new form of regulatory mechanism that depends on nuclear positioning. It remains to be seen whether the PREs of other genes show similar relationships.

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