RESEARCH HIGHLIGHTS

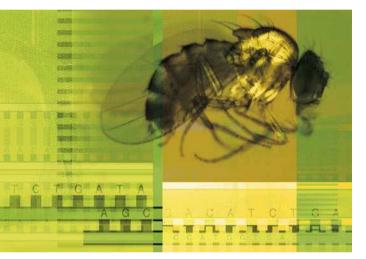
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EVOLUTION

Cis dominates but trans is dominant

Gene expression differences between species may be important in explaining phenotypic divergence, but why do such differences tend to be in *cis* more often than in *trans*? A new study suggests that this could be because *cis* variation is more likely to be additive, whereas *trans* variation is complicated by dominance effects.

Gene expression contributes to morphological phenotypes, but it can also be viewed as a phenotype in itself. As such, its relative simplicity



and the quantitative way in which it can be assayed make it a good phenotype to have its underlying genomic architecture dissected. Lemos and Hartl and colleagues therefore used *Drosophila melanogaster* chromosome substitution lines to assess the relative roles of *cis* and *trans* regulation, and of additive and dominance effects.

The authors used inbred lines that varied only in their second chromosome. There were five different second chromosomes, and they carried out four specific pairwise comparisons: one between two lines that were homozygous for different second chromosomes; and three between heterozygous pairs of lines — each pair sharing a copy of the chromosome that did not feature in the homozygous comparison, and differing on the other copy in the same way that the homozygous pair differed.

Of the 265 genes on the second chromosome that were differentially expressed, nearly twice as many were the result of *cis* regulation than *trans* regulation. The authors then showed that the differences between the homozygous lines were considerably greater than between the heterozygous lines, with more than 70% of the differences being masked in the heterozygote comparisons, an effect that was attributed to recessive variation that had no phenotypic effect. In other words, most of the variation was not additive, but rather was subject to dominance interactions. Most importantly, there was considerable enrichment of *trans* loci among those showing masking.

This result provides a potential explanation for the prevalence of *cis* variation between species and the high levels of *trans* variation within species: *cis* variation is additive and therefore accessible to positive selection, whereas *trans* variation is masked and therefore is not purged by negative selection. This means that *trans* variation could be a significant contributor to genetic load and disease variation.

Patrick Goymer, Associate Editor, Nature

ORIGINAL RESEARCH PAPER Lemos, B. et al. Dominance and the evolutionary accumulation of cis- and trans-effects on gene expression. Proc. Natl Acad. Sci. 105, 14471–14476 (2008)