



BRAND X

## QUANTITATIVE TRAITS

# Variants dragged down by their neighbours

How does selection shape the genetic variation that influences quantitative traits? Most models assume that selection acts on the specific loci that affect the trait in question. But, according to a recent study in *Caenorhabditis elegans*, selection at neighbouring loci can also have a crucial role.

Rockman and colleagues used variation in the levels of 15,888 *C. elegans* transcripts as model quantitative traits. Mapping variants for each expression trait in 208 intercross lines — genotyping each line for 1,455 SNPs — they identified a total of 2,309 quantitative trait loci (QTLs). The QTLs were not distributed evenly across the genome but were highly enriched on chromosome arms and at their tips compared to chromosome centres. This finding is contrary to what might be expected: in *C. elegans*, the arms of chromosomes have a lower density of genes than do the centres, and so contain fewer potential sites at which variation could have functional effects. So, the expectation would be that chromosome centres harbour more QTLs than other parts of the genome.

Gene-specific variables could potentially account for this unexpected distribution — for example,

the size of a gene or the strength of selection that it experiences might affect the number of variants it contains. However, the authors found that, even in combination, these variables did not account for the observed distribution of QTLs as well as did the chromosomal location alone.

To seek an explanation for these regional effects, the authors considered the high level of self-fertilization in *C. elegans*, which results in low effective rates of recombination between loci. As a result, variants are more likely to be affected by selection at linked sites than in outcrossing species. For example, if a variant is linked to a deleterious mutation that is being selected against, in the absence of recombination its frequency will also be reduced — an effect known as background selection. Under a background selection model, regions of the genome that have higher recombination rates will retain more variation, as mutations under negative selection are less likely to drag neighbouring variants along with them to low frequencies or removal. Although positive selection at a linked gene could, conversely, increase the frequency of a particular variant — and therefore decrease the amount of total variation — previous findings

from a related species suggest that background selection is likely to predominate in *C. elegans*.

In *C. elegans*, levels of recombination are higher in chromosomal arms than at the centres. As a result, background selection should have a weaker effect at chromosome arms, and the arms are therefore expected to retain more variation. Chromosome tips have low recombination rates but these regions are also expected to be enriched in variants compared to centres, as the variants at tips are affected by selection on other loci only on one side. Indeed, the authors found that a background selection model predicted very accurately their observed distribution of genetic variation for expression traits.

These results suggest that the effects of selection on linked loci need serious consideration when assessing the factors that shape the genetic variation that underlies quantitative phenotypes.

Louisa Flintoft

**ORIGINAL RESEARCH PAPER** Rockman, M. V., Skrovaneck, S. S. & Kruglyak, L. Selection at linked sites shapes heritable phenotypic variation in *C. elegans*. *Science* **330**, 372–376 (2010)

**FURTHER READING** Charlesworth, B. Effective population size and patterns of molecular evolution and variation. *Nature Rev. Genet.* **10**, 195–205 (2009)