⮕ COMPLEX TRAITS

Using genetic architecture to improve predictions

The future phenotypes of organisms can be predicted using SNP genotypes, and this information has applications in fields such as medicine, forensics and agriculture. The accuracy of genomic predictions depends on various factors, including the genetic architecture of the trait, particularly the number of loci that affect the trait and the distribution of their effects. A recent study in cows applies knowledge of the genetic architecture of traits to assess and improve the accuracy of genomic predictions.

Hayes *et al.* used genome-wide association studies to investigate the distributions of effect sizes for loci affecting three model complex traits in Holstein cattle: coat colour, fat content of milk and 'overall type' (which is made up of several aspects of cow conformation). They found that three SNPs explained 24% of the variation in the proportion of black coat colour (one in *KIT*, one

in *MITF* and one on chromosome 8) and a large number of loci with small effects contributed to the remaining variation. Similarly, percentage of milk fat had one locus of large effect (*DGAT1*) and many with very small effects. By contrast, the overall type trait showed a distribution of a large number of loci with small effects. Therefore, there are substantial differences in the underlying genetic architecture of these three traits, suggesting that this is likely to be the case for other complex traits.

How does knowledge of the architecture of these complex traits affect predictions of breeding value (the genetic merit of an individual which would be passed on to future progeny)? The authors used the SNP effects for each trait to estimate quantitative breeding values and found that the accuracy of predictions was higher for traits with loci of large effects than for traits with only loci of small effects.

They then showed that the accuracy of genomic predictions can be improved by using information about the distribution of the effect sizes, so that the assumed distribution matches the true distribution. For example, the effect sizes for overall type have a normal distribution, so the genomic prediction is improved by modelling using a normal distribution.

Can these results in cattle be extrapolated to complex traits in humans and other species? Interestingly, most complex traits seem to be like overall type in their genetic architecture, with little evidence for loci with large effects. Cattle have advantages for studying complex traits as large quantities of data are available through pedigreed breeding programmes. However, the linkage disequilibrium blocks are larger than in humans, particularly within a cattle breed, and cattle domestication may have affected patterns of genetic diversity, which could limit how generally observations from cattle can be applied.

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