The genetics of quantitative traits: Challenges and prospects

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For those of us seeking to use genomic tools to clarify the genetic basis of quantitative traits, and inform our plant breeding efforts, this article is a must-read. The authors clearly articulate the remarkably complex nature of the relationship between genotypes and phenotypes and posit that the way forward is through "systems genetics". As the authors point out, despite two decades of intensive efforts at identifying and locating QTL affecting quantitative traits, we have fallen short of explaining genetic variation in terms of underlying genes, effects of segregating alleles in different genetic backgrounds and environments, the molecular basis of functional allelic effects, or the population frequency of causal variants.

The article nicely contrasts the approaches to dissecting complex traits (linkage mapping vs association genetics) in the context of the major components of QTL mapping: detection and localization. The authors conclude that, regardless of approach, what we have learned is that QTL alleles with large effects are rare, most genetic variation for quantitative traits is due to many loci with small to very small effect, and that multiple loci with opposite effects are commonly found in tight linkage. Regarding the molecular basis of quantitative variation, evidence from humans and fruit flies indicates that rare variants and variants with minor allele frequencies less than 5% are frequently associated with variation in quantitative traits.

In detailing challenges to understanding the genetic architecture of complex traits, an excellent treatment is given of context-dependent effects and pleiotropy, issues we typically consider nuisances but are of great importance to our ability to apply what we learn to tree breeding. Context-dependent effects include epistasis (genotype by genotype interactions), genotype by environment, and genotype by sex interactions. The pleiotropy discussion was fascinating. The authors note that genes may have pleiotropic effects, but individual variants likely do not. That is, independent variants (say, SNPs) within a given gene may affect different traits.

The latter half of the paper is an argument for systems genetics or genetical genomics as the way forward in understanding the genetic architecture of complex traits. This basically is a call to large scale use of technologies such as whole-genome transcriptional profiling, proteomics, metabolomics, and organismal phenotypes, all areas now being tested, albeit modestly, by a small cadre of forest geneticists.

As tree breeders what can we take from this paper? First, that we will probably never know everything we want to know about the genetic basis of the traits that interest us, but we probably can know enough to make genetic gains using genomic tools. Secondly, that there is always a need for validation across sites, years, and genetic backgrounds. Finally, more is always better. The more genes/SNPs evaluated, the more likely we are able to explain the variation that interests us.

Reviewed by Nicholas Wheeler