

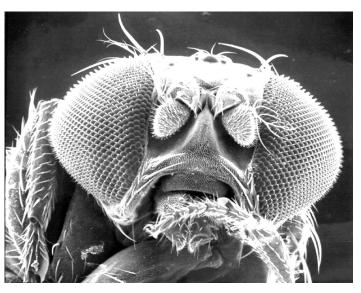




Context-Dependent Effects and the Genetic Architecture of Quantitative Traits: Lessons From Drosophila

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A major challenge of modern biology is to understand the genetic and environmental factors causing variation in quantitative traits, such as susceptibility to common diseases, height and blood pressure in humans. This is required for predicting phenotypes from genetic and genomic data, the goal of precision medicine. Although intense efforts have been devoted to genome wide association studies for many diseases and quantitative traits in humans in the past decade, relatively few causal genes have been identified, in part due to extensive local linkage disequilibrium in human populations. The Drosophila melanogaster Genetic Reference Panel (DGRP) consists of 205 sequenced inbred strains derived from the Raleigh, NC population. The DGRP is a community resource for genome wide association (GWA) analyses for genetically complex traits, in a scenario where all molecular variants are known. The large amount of quantitative genetic variation, lack of population structure and rapid local decay of linkage disequilibrium in the DGRP present a favourable scenario for identifying candidate causal genes and even polymorphisms affecting complex traits. I will present the lessons we have learned about the genetic architecture of quantitative traits from studies on the DGRP and outbred populations derived from it with a focus on context-dependent allelic effects, and the implications of the Drosophila data for genotype-phenotype mapping for complex traits in other species, including humans.



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