

# Ethanol resistance in *Drosophila melanogaster* has increased in parallel cold-adapted populations and shows a variable genetic architecture within and between populations

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## Abstract

Understanding the genetic properties of adaptive trait evolution is a fundamental crux of biological inquiry that links molecular processes to biological diversity. Important uncertainties persist regarding the genetic predictability of adaptive trait change, the role of standing variation, and whether adaptation tends to result in the fixation of favored variants. Here, we use the recurrent evolution of enhanced ethanol resistance in *Drosophila melanogaster* during this species' worldwide expansion as a promising system to add to our understanding of the genetics of adaptation. We find that elevated ethanol resistance has evolved at least three times in different cooler regions of the species' modern range - not only at high latitude but also in two African high altitude regions - and that ethanol and cold resistance may have a partially shared genetic basis. Applying a bulk segregant mapping framework, we find that the genetic architecture of ethanol resistance evolution differs substantially not only between our three resistant populations, but also between two crosses involving the same European population. We then apply population genetic scans for local adaptation within our quantitative trait locus regions, and we find potential contributions of genes with annotated roles in spindle localization, membrane composition, sterol and alcohol metabolism, and other processes. We also apply simulation-based analyses that confirm the variable genetic basis of ethanol resistance and hint at a moderately polygenic architecture. However, these simulations indicate that larger-scale studies will be needed to more clearly quantify the genetic architecture of adaptive evolution, and to firmly connect trait evolution to specific causative loci.

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