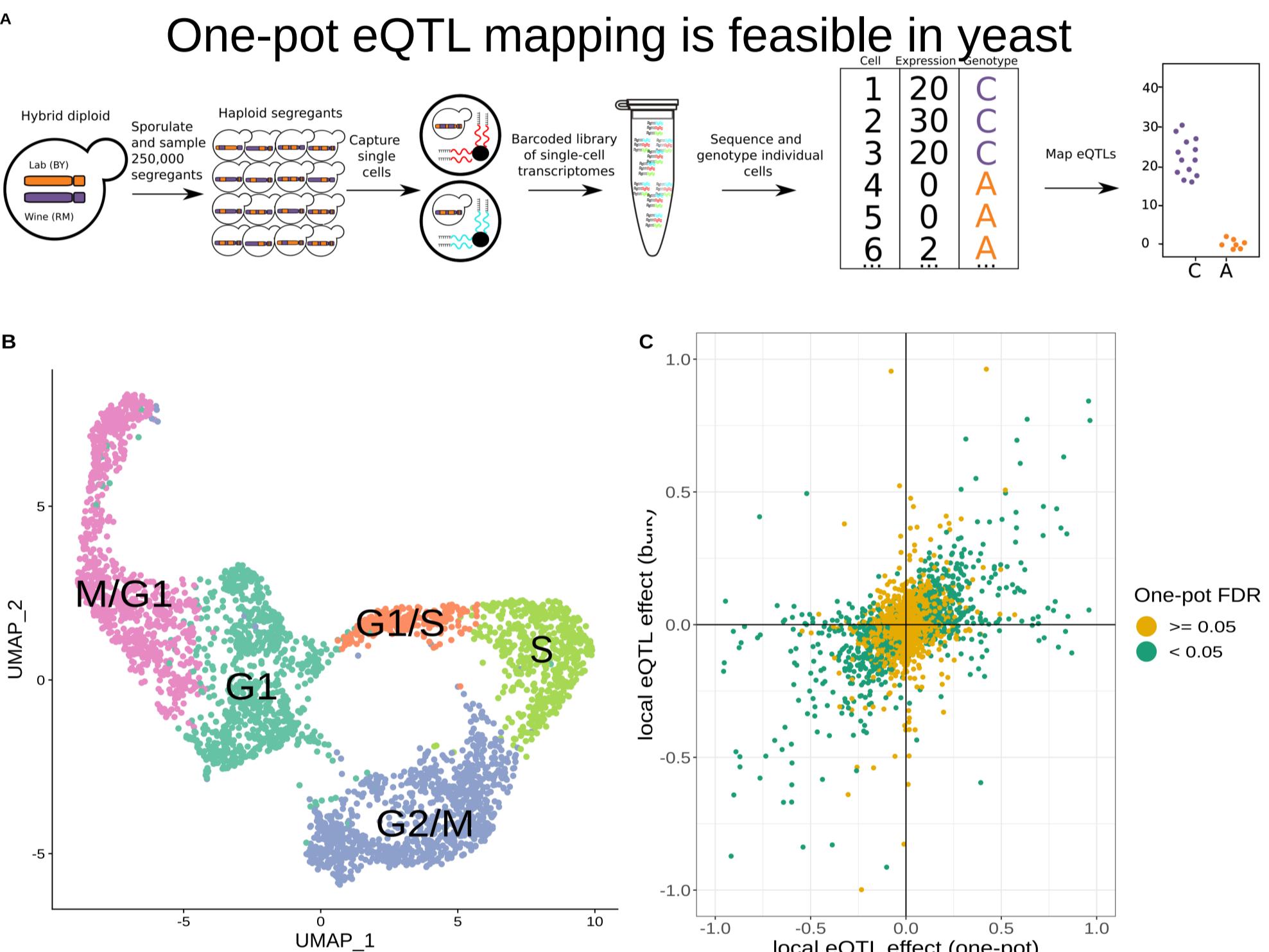


# Single-cell eQTL mapping in yeast reveals a tradeoff between growth and reproduction

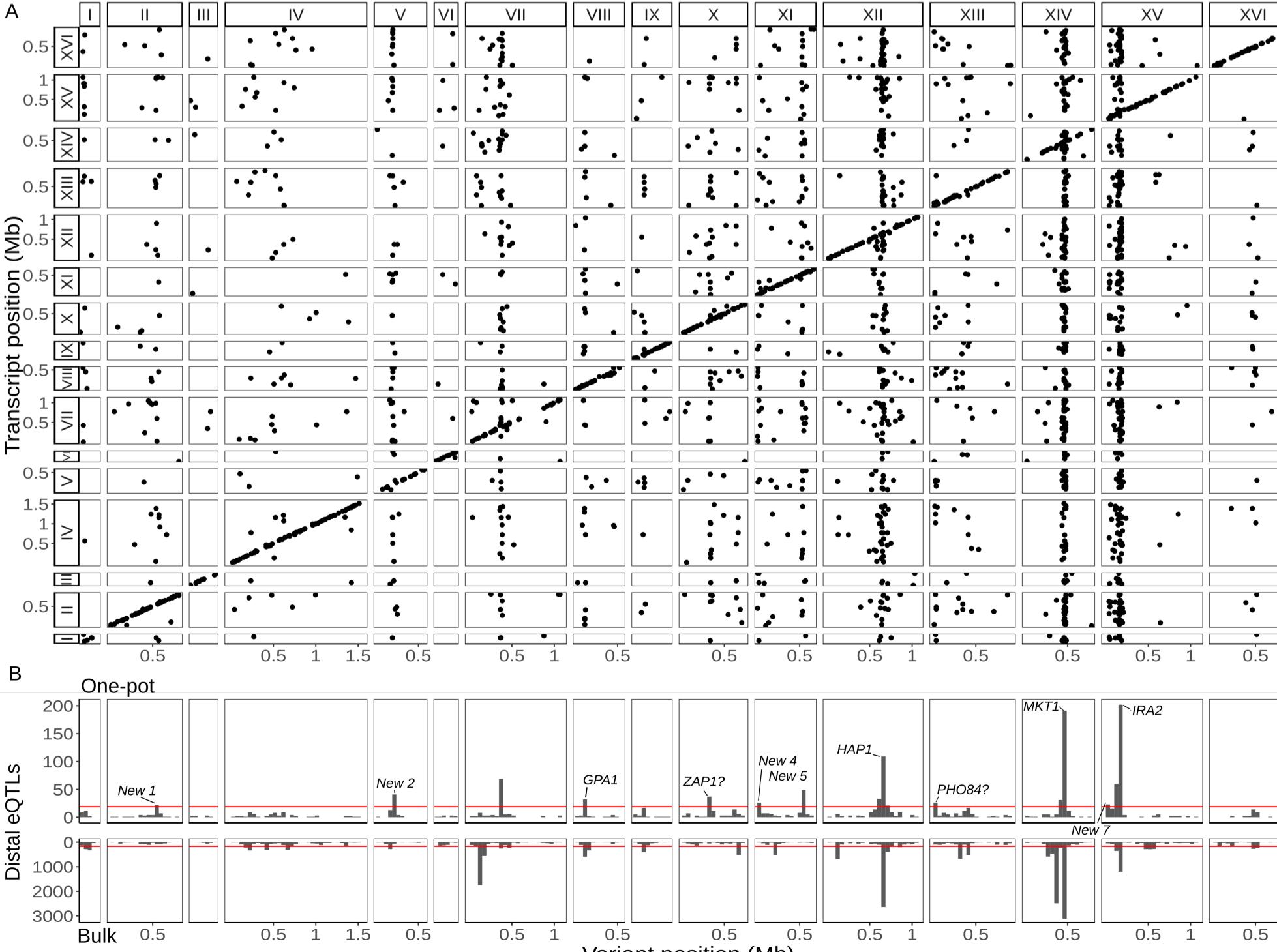
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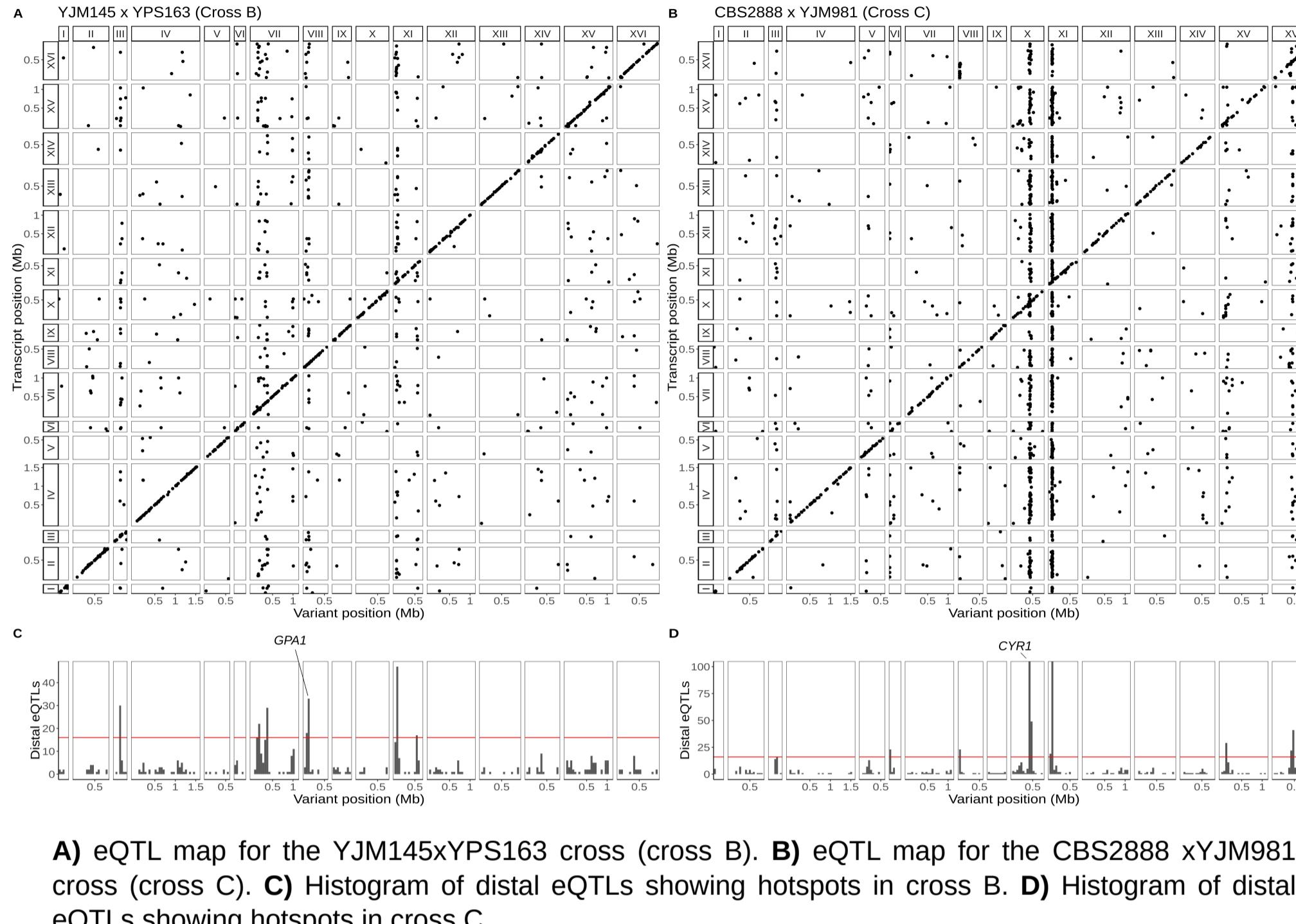
**Abstract:** Expression quantitative trait loci (eQTLs) provide a key bridge between noncoding DNA sequence variants and organismal traits. The effects of eQTLs can differ among tissues, cell types, and cellular states, but these differences are obscured by gene expression measurements in bulk populations. We developed a one-pot approach to map eQTLs in *Saccharomyces cerevisiae* by single-cell RNA sequencing (scRNA-seq) and applied it to over 100,000 single cells from three crosses. We used scRNA-seq data to genotype each cell, measure gene expression, and classify the cells by cell-cycle stage. We mapped thousands of local and distant eQTLs and identified interactions between eQTL effects and cell-cycle stages. We took advantage of single-cell expression information to identify hundreds of genes with allele-specific effects on expression noise. We used cell-cycle stage classification to map 20 loci that influence cell-cycle progression. One of these loci influenced the expression of genes involved in the mating response. We showed that the effects of this locus arise from a common variant (W82R) in the gene *GPA1*, which encodes a signaling protein that negatively regulates the mating pathway. The 82R allele increases mating efficiency at the cost of slower cell-cycle progression and is associated with a higher rate of outcrossing in nature. Our results provide a more granular picture of the effects of genetic variants on gene expression and downstream traits.



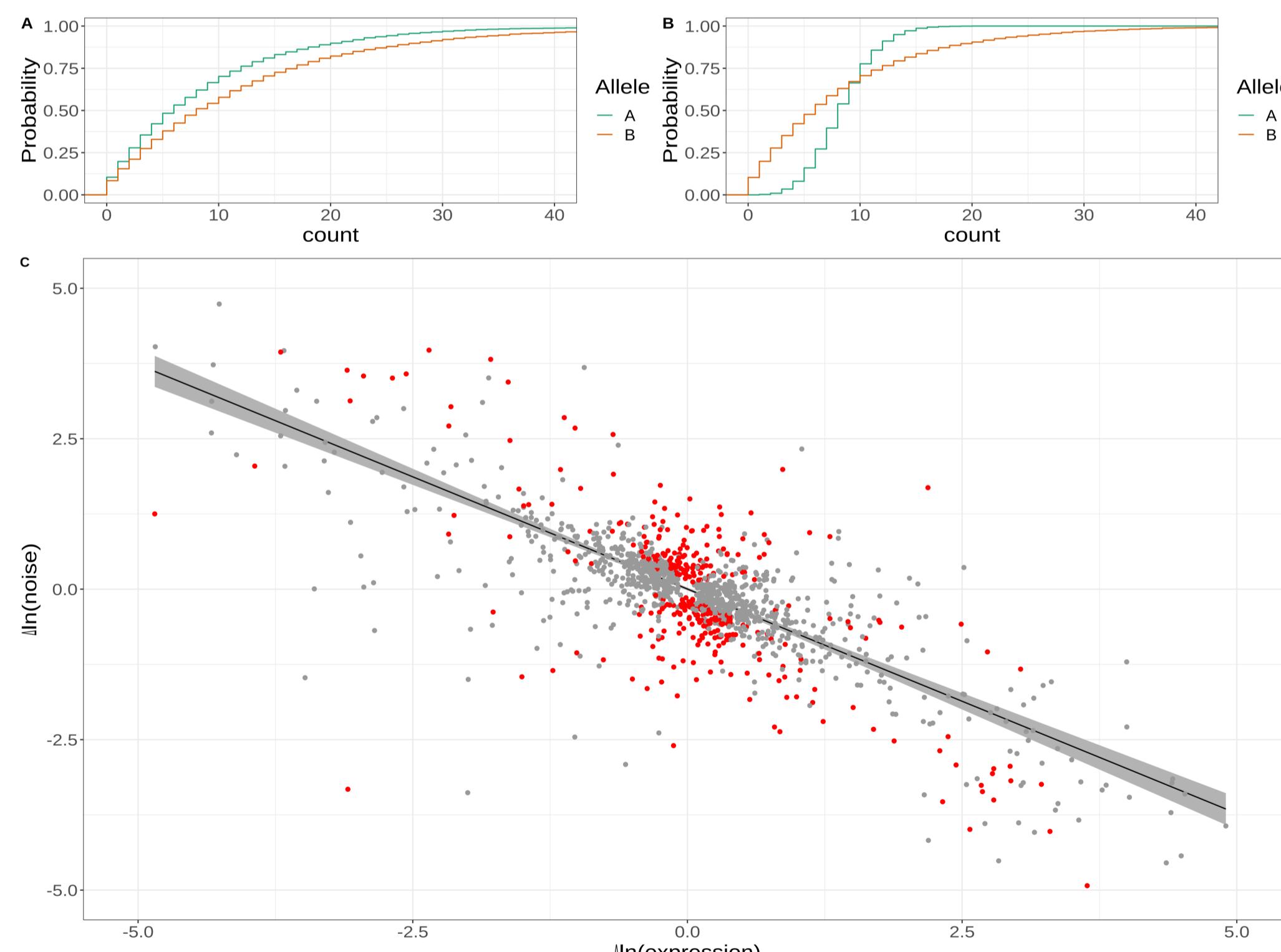
Single-cell eQTL map recapitulates bulk trans-eQTL hotspots from the BY and RM cross and identifies new hotspots.



## Single-cell eQTL maps in two new crosses

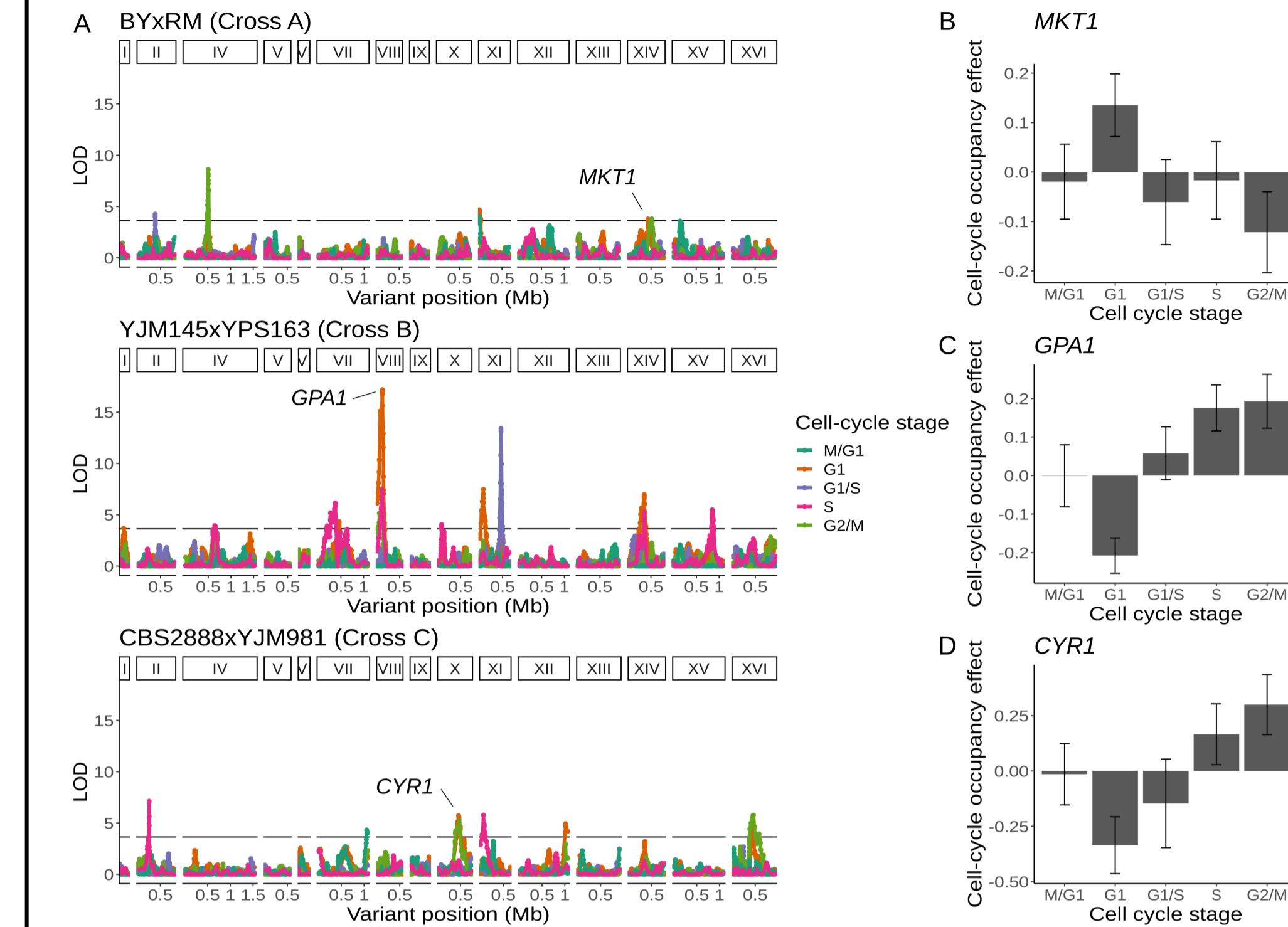


## Genetic effects on expression noise

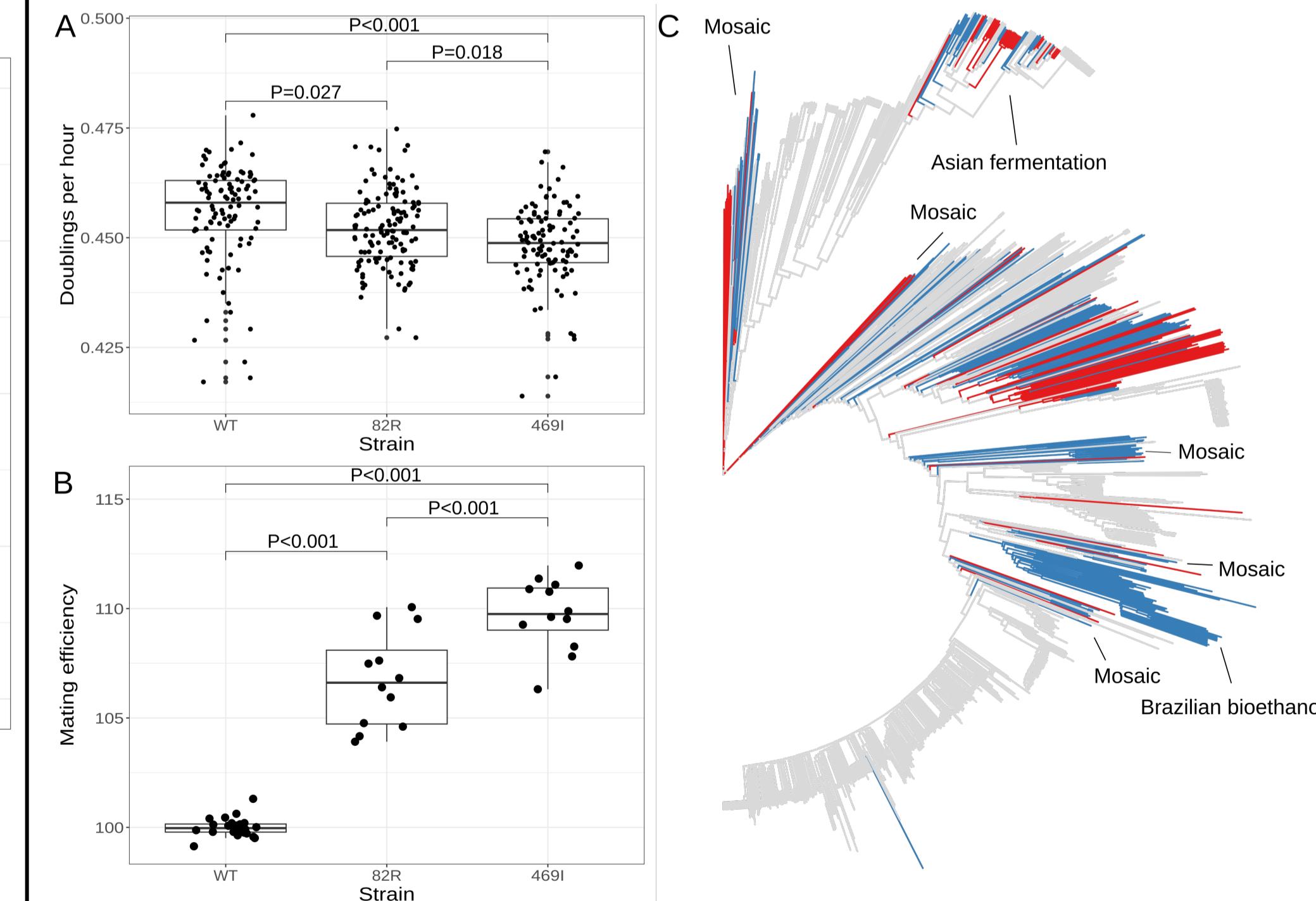


A) Cumulative distribution of simulated allele-specific counts for two alleles with different average expression but the same expression noise. B) Cumulative distribution of simulated allele-specific counts for two alleles with different expression noise but the same average expression. These simulated distributions are shown to illustrate allele-specific effects on average expression and on expression noise, respectively. C) Log-log scatter plot of change in expression noise between alleles (x-axis) against change in average expression between alleles (y-axis); points correspond to all 1,487 genes with significant allele-specific effects on expression noise and/or average expression. Black line shows the predicted change in noise given a change in expression, with the 95% confidence interval for the trend shown in gray. The 377 genes with allele-specific effects on expression noise that cannot be accounted for by the overall trend are shown in red. The x and y axes have been truncated at -5 and 5 for ease of visualization purposes, which left out 30 of 1,487 data points.

## Natural genetic variants affect cell-cycle occupancy



The 82R allele of *GPA1* increases mating efficiency at the cost of growth rate and is associated with increased outbreeding in natural populations



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