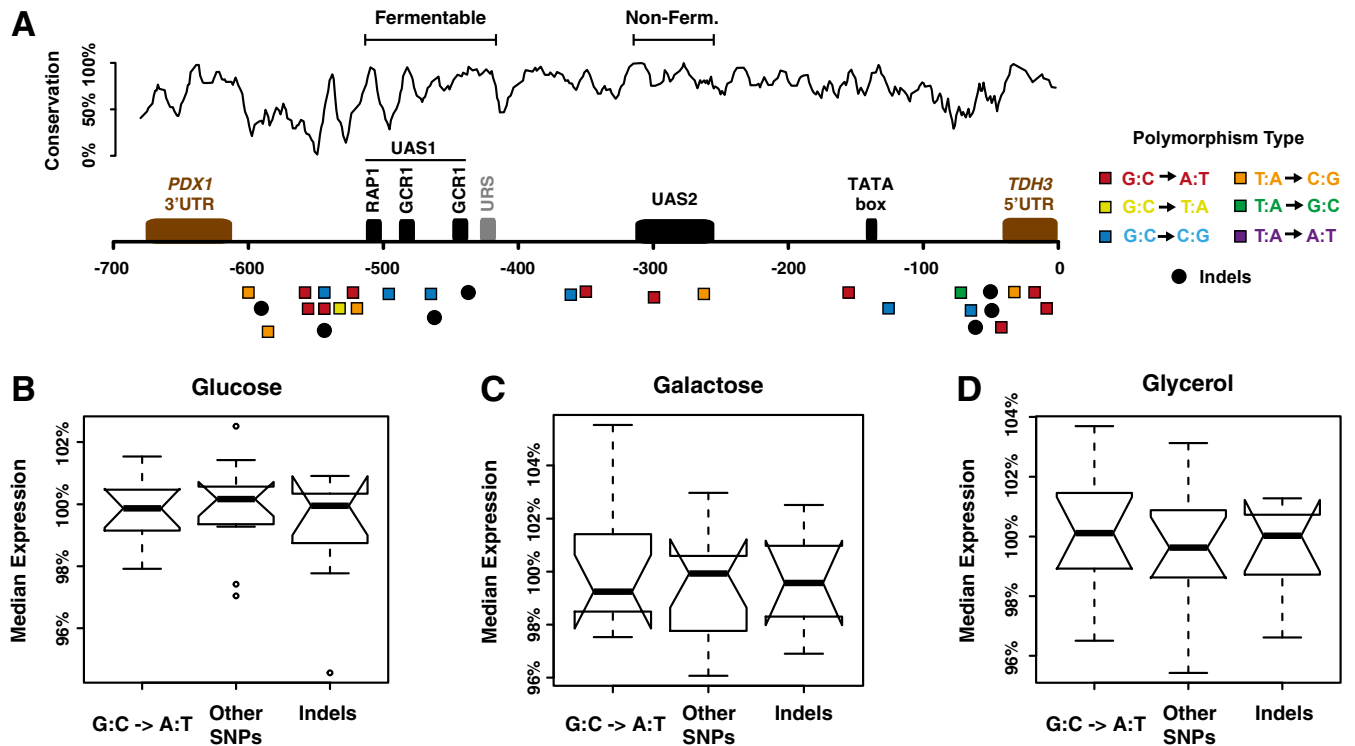
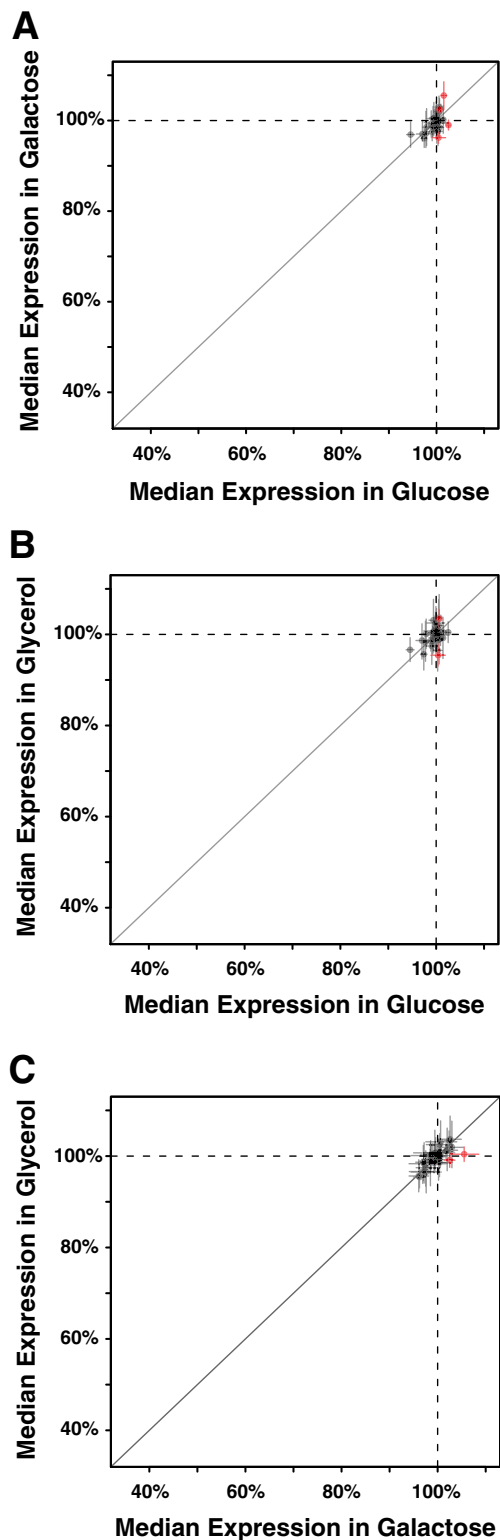


# Supporting Information

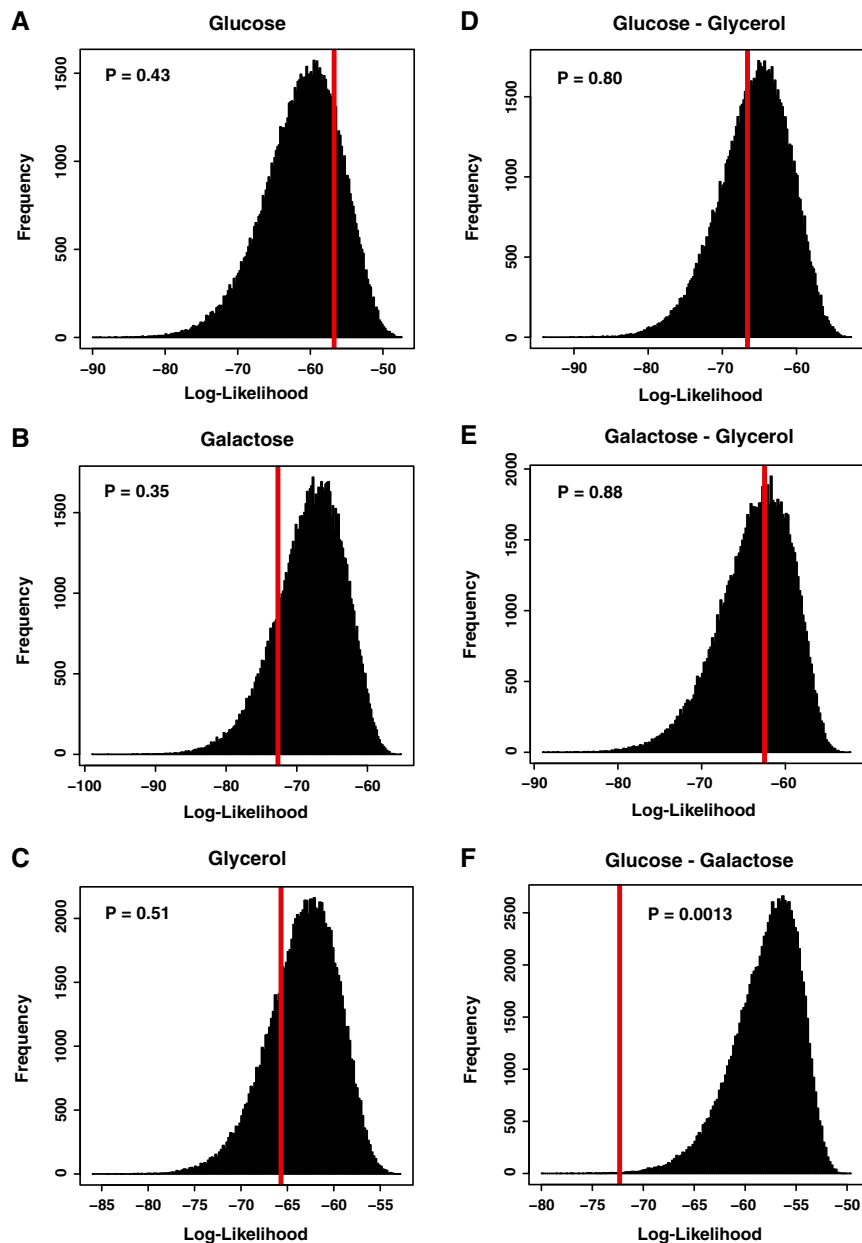
Duveau et al. 10.1073/pnas.1713960115



**Fig. S1.** Polymorphisms in  $P_{TDH3}$ . (A) Schematic showing the positions and types of the 30 unique polymorphisms examined in this study. SNPs are indicated, with squares of different colors corresponding to the type of base change, as described in the legend to the right. Small indels are indicated with black circles. Key functional elements are also shown, with UAS1, UAS2, and URS discussed in the main text. Note that none of the polymorphisms affected the RAP1 or GCR1 binding site or the TATA box. The black curve shows sequence conservation across species of the *S. sensu stricto* genus. Non-Ferm., nonfermentable. Box plots comparing the effects of different types of polymorphisms on  $P_{TDH3}$  activity upon growth in glucose (B), galactose (C), or glycerol (D) are shown. Each box includes the average effects of six replicates for the 10 G:C-to-A:T transitions, 13 other kind of SNPs, or 7 indels shown in A. Thick horizontal lines represent median effects across all polymorphisms of each type in each environment. Notches indicate the 95% confidence interval of the medians, and boxes show the interquartile range. Mann-Whitney-Wilcoxon tests were performed to compare the average effects of different types of polymorphisms and resulted in nonsignificant  $P$  values ( $P > 0.5$ ) for all pairwise comparisons.



**Fig. S2.** Pairwise comparisons of the effects of polymorphisms on  $P_{TDH3}$  activity in different environments. The median effect of each polymorphism on  $P_{TDH3}$  activity relative to the ancestral haplotype used to infer its effect is compared between glucose and galactose (A), glucose and glycerol (B), and galactose and glycerol (C). Dots indicate the effect of polymorphisms in each environment, calculated as the ratio of the mean fluorescence (across six replicates) of pairs of haplotypes that differed by a single polymorphism. Error bars show 95% confidence intervals calculated using Fieller's theorem. Red dots indicate polymorphisms with no overlap of the 95% confidence intervals between the two environments considered, which were interpreted as showing significant G×E interactions.



**Fig. S3.** Testing for evidence of selection acting on  $P_{TDH3}$  activity and plasticity among environments. Histograms show the distribution of log-likelihood for 100,000 random sets of 30 mutational effects drawn with replacement from the 235 effects of mutations measured in glucose (A), galactose (B), and glycerol (C). Two-sided  $P$  values represent twice the proportion of random sets of 30 mutation effects with a log-likelihood more extreme than the log-likelihood value calculated from the effects of the 30 polymorphisms in each environment (red lines). A low  $P$  value indicates that the distribution of effects of polymorphism is different from random sampling of mutational effects. Histograms show the distribution of log-likelihood for 100,000 random sets of 30 GxE effects randomly drawn with replacement from the 235 GxE effects measured between glucose and glycerol (D), galactose and glycerol (E), and glucose and galactose (F). The red lines indicate the log-likelihood value calculated from the GxE effects measured for the 30 polymorphisms between each pair of environments. Two-sided  $P$  values were calculated as twice the proportion of random GxE effects with a more extreme log-likelihood than the log-likelihood calculated from the GxE effects of polymorphisms. Low  $P$  values indicate that the plasticity of expression caused by polymorphisms differs from the plasticity sampled from random mutations.

#### Dataset S1. Output data files produced by analysis

[Dataset S1](#)

**Dataset S2. Summary of naturally occurring  $P_{TDH3}$  haplotypes and polymorphisms**

[Dataset S2](#)

**Dataset S3. Input data files used for analysis**

[Dataset S3](#)

**Dataset S4. R script used to analyze flow cytometry data testing for plasticity of the wild-type  $P_{TDH3}$  allele**

[Dataset S4](#)

**Dataset S5. R script used to analyze flow cytometry data estimating and comparing the effects of mutations and polymorphisms on  $P_{TDH3}$  activity**

[Dataset S5](#)