FINDING THE GENETIC UNDERPINNINGS OF AN ANCIENT THERMOTOLERANCE DIVERGENCE IN YEAST

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Abstract

Saccharomyces cerevisiae and its closest relative, Saccharomyces paradoxus are two closely related species of yeast that differ with respect to thermotolerance. Weiss et al. (2018) found that S. cerevisiae alleles of eight genes confer a modest growth advantage at 39°C when they replace the native allele at the endogenous locus in an S. paradoxus background by creating an interspecific hybrid of the two species and subjecting it to transposon mutagenesis. While each S. cerevisiae allele has a modest effect on its own, the effects of the alleles in combination are unknown. This work seeks to invesigate the effects of a combination of these eight *S. cerevisiae* alleles in the *S. paradoxus* background. Relative to *S. paradoxus*, these multi-allele swaps demonstrate a significant increase in growth at 39°C with minimal epistasis. An additive model, in which effects of the alleles on thermotolerance are independent of each other, can describe the effects of these alleles. Without extensive epistasis between these loci, we can reconstruct a simple picture of the history of this evolutionary process.

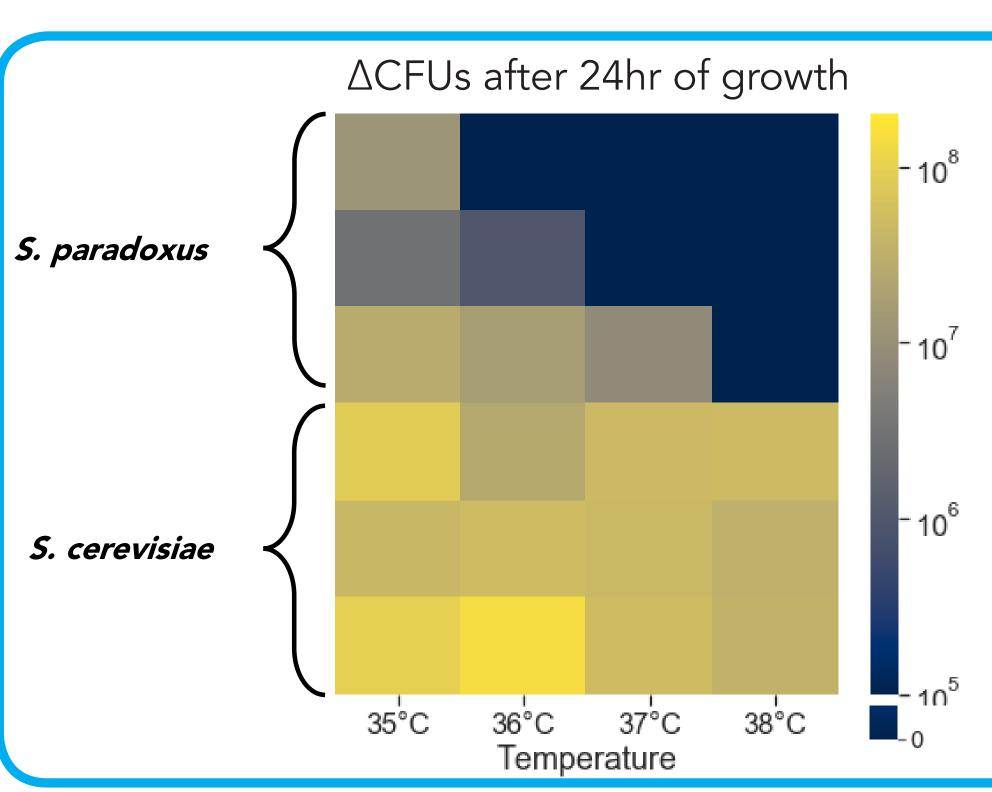


Figure 1 – Thermotolerance divergence between S. cerevisiae and S. paradoxus. Each box is an average of the difference in the number of viable colonies after 24 hours growth at a particular temperature for 4 replicates of a given strain of a species. We can use *S. para*doxus as a proxy for the ancestral state.

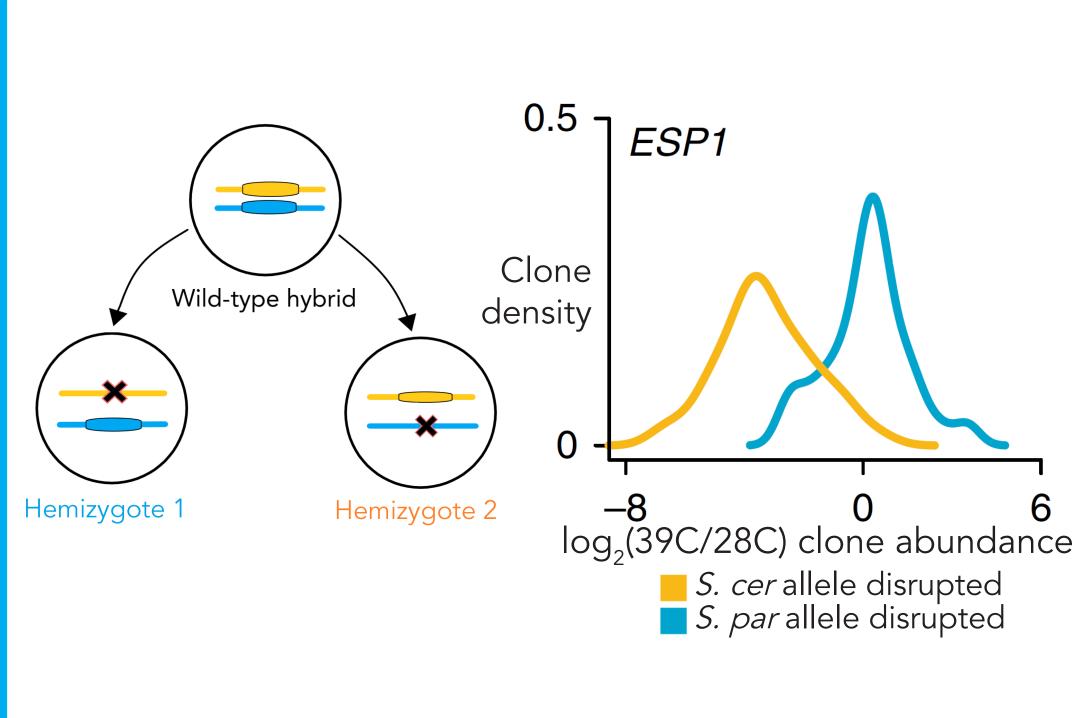


Figure 2 – Mapping thermotolerance genetics. (Left) At a given gene, in mutants of a diploid hybrid with each species allele disrupted in turn, a difference in thermotolerance can be ascribed to species divergence at the locus. (Right) ESP1, a hit from high-throughput reciprocal hemizygosity mapping. Each trace reports the distribution of growth phenotypes across transposon mutants at the indicated allele.

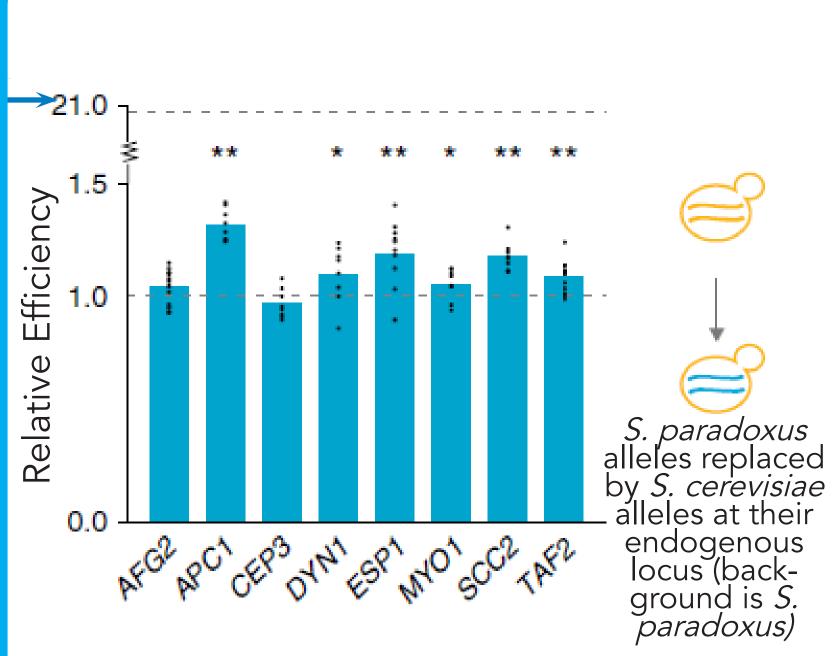


Figure 3 – The eight candidate S. cerevisiae alleles identified through RH-seq confer a modest growth advantage at 39°C. Alleles swapped into the wild-type background of *S. paradoxus* individually. (S. paradoxus \rightarrow S. paradoxus $\triangle YFG :: ScYFG$) The identified alleles are mostly at essential housekeeping genes involved in chromosome segregation and mitosis. Most of the phenotype is not recapitulated by these swaps (WT *S. cerevisiae* denoted by blue arrow). Swaps in the other direction had the opposite effect.

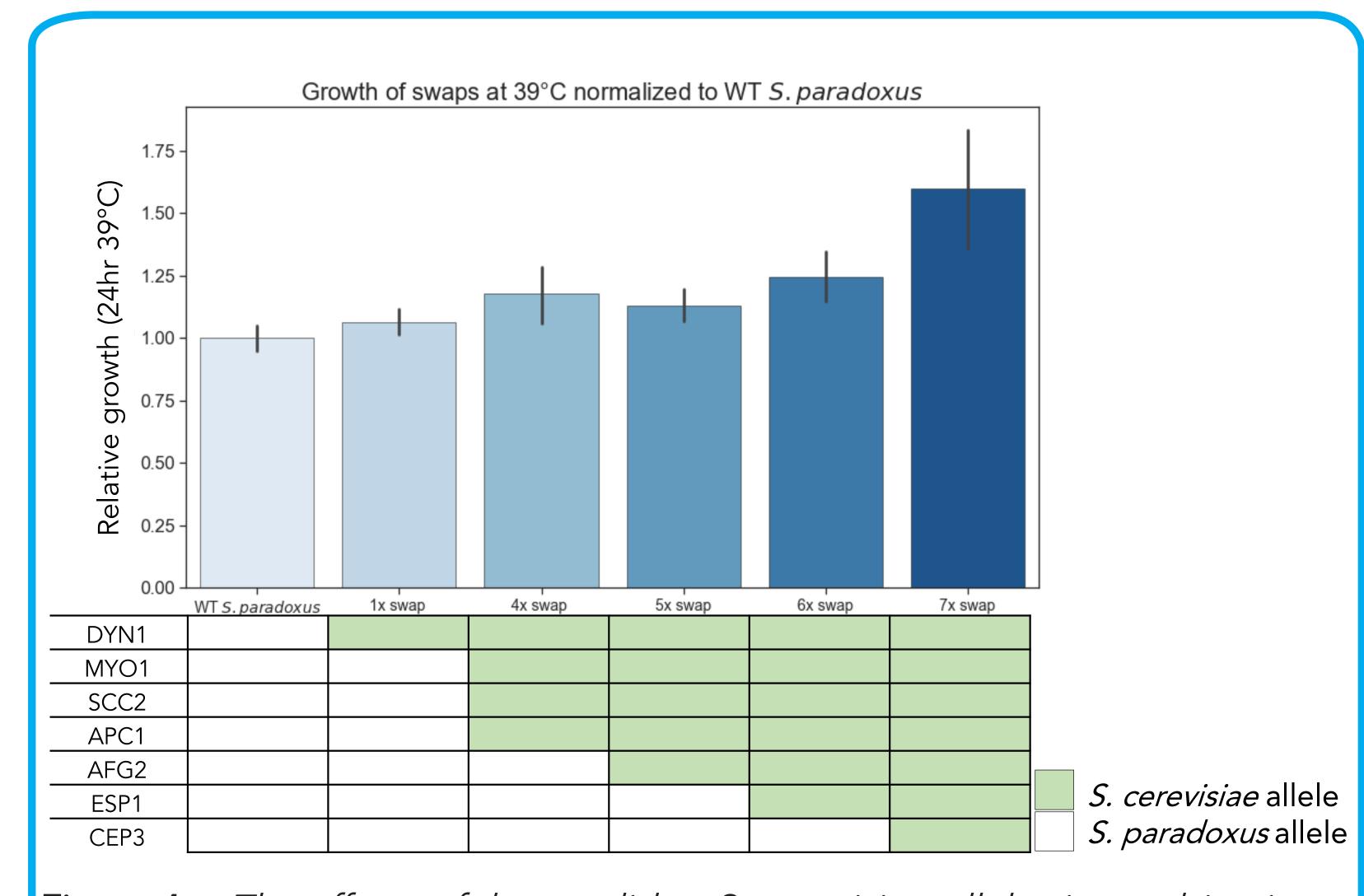


Figure 4 – The effects of the candidate S. cerevisiae alleles in combination are roughly additive. Each bar represents growth of a swap after 24hrs at 39°C, normalized to the growth of the *S. paradoxus*. Each allele confers a mostly independent increase in thermotolerance. In **combination**, the effects of the S. cerevisiae alleles are additive. These seven candidate alleles recapitulate $\sim 10\%$ of *S. cerevisiae's* phenotype.

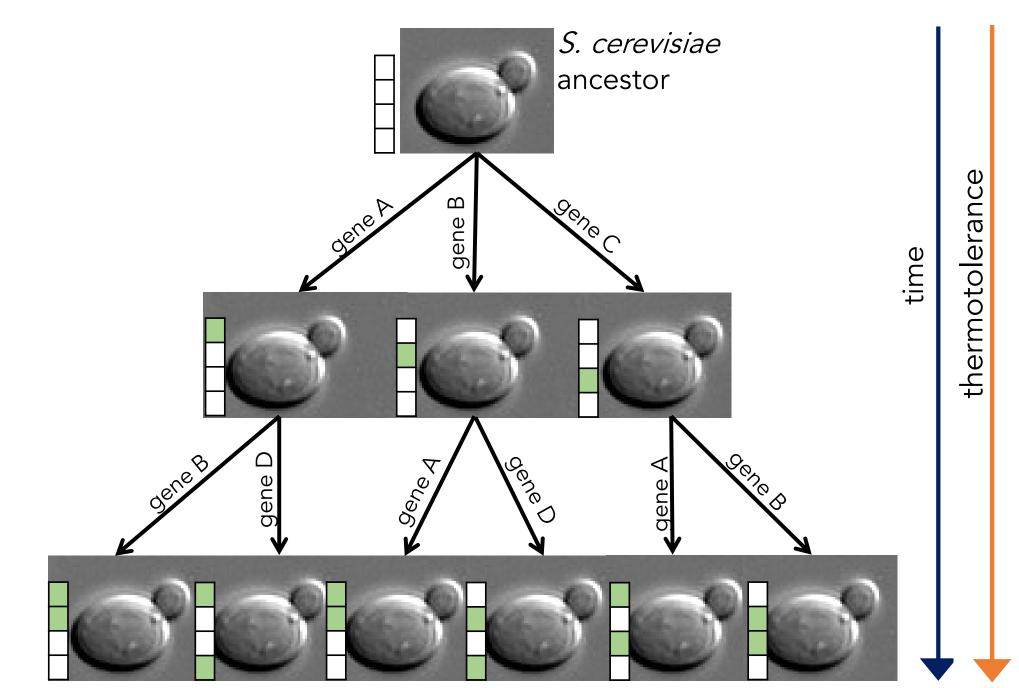


Figure 5 – Our data agree with a model in which the mutational steps to thermotolerance could have happened in almost any order.
Phenotyping results agree with a model in which the mutational steps to thermotolerance could have happened in any order. The effects of genetic changes are mostly independent of each other and the genomic background and each confers a small increase in thermotolerance. Under this model, different lineages of the *S. cere*visiae ancestor may get to thermotolerance by acquiring changes in different parts of the genome without having to wait for the perfect combination of mutations to arise. Changes that confer a slight advantage could have risen to high frequency, and later come together with other adaptive loci by recombination other, yielding an even more thermotolerant descéndant. This would make it easy for the whole population to become more fit. The S. cerevisiae ancestor could easily traverse fitness landscape, arriving at thermotolerance in many, potentially different ways.

Sources:

Weiss, C.V., Roop, J.I., Hackley, R.K., Chuong, J.N., Grigoriev, I.V., Arkin, A.P., Skerker, J.M., and Brem, R.B. (2018). Genetic dissection of interspecific differences in yeast thermotolerance. Nat. Genet. 50, 1501.

Thanks to













