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## Genetic basis of yeast tolerance to high temperature revealed by experimental evolution

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**T**hermotolerance is a polygenic trait that contributes to cell survival and growth under unusually high temperatures. Although some genes associated with high-temperature growth (Htg+) have been identified, how cells accumulate mutations to achieve prolonged thermo tolerance is still mysterious. To understand this issue, we conducted experimental evolution of the yeast *Saccharomyces cerevisiae* with stepwise temperature increases for it to grow at 42°C. Whole genome sequencing of 14 evolved strains and the parental strain revealed a total of 153 mutations in the evolved strains, including single nucleotide variants, small INDELS, and segmental duplication/deletion events. Some mutations persisted from an intermediate temperature to 42°C, so they might be Htg+ mutations. Functional categorization of mutations revealed enrichment of exonic mutations in the SWI/SNF complex and F-type ATPase, pointing to their involvement in high-temperature tolerance. In addition, multiple mutations were found in a general stress associated signal transduction network consisting of Hog1 mediated pathway, RAS-cAMP pathway, and Rho1-Pkc1 mediated cell wall integrity pathway, implying that cells can achieve Htg+ partly through modifying existing stress regulatory mechanisms. Using pooled segregant analysis of 5 Htg+ phenotype-orientated pools, we inferred causative mutations for growth at 42°C and identified those mutations with stronger impacts on the phenotype. Finally, we experimentally validated a number of the candidate Htg+ mutations. This study increased our understanding of the genetic basis of yeast tolerance to high temperature. The experimental evolutionary process. The parental strain, strain P, was used for experimental evolution through repeated subculturing. The yeast populations were incubated under the described temperatures and hours in the right panel, and the cultures were refreshed by the described transferred cycles as indicated on the right panel. Only lineages B and F survived up to 42°C. Blue color indicates the strains whose genomes were sequenced.

### Biography

Wen-Hsiung Li's expertise is in molecular evolution and genomics. He has used yeast as a model to study the evolution of protein interaction networks, the evolution of gene regulatory networks, and the roles of cis and trans elements in the evolution of gene expression. He has also developed many methods for DNA and protein sequence analysis, genomics data analysis and transcriptomics study. His lab has also developed methods for predicting the binding sites of transcription factors and for constructing gene regulatory networks. His talk will present his recent study on the experimental evolution of yeast for thermotolerance.

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