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The Genetics of Adaptation and Evolvability in Yeast

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Abstract

Evolution is the hereditary change in life forms that has shaped the divergence of all organisms that inhabit planet Earth. I used the yeast *Saccharomyces cerevisiae* to study how adaptive evolution increases the fitness and changes the properties of experimental and natural yeast populations. In **Paper I**, I screened for evolvability genes that control how fast *S. cerevisiae* adapts using experimental evolution and high-throughput growth phenotyping. I investigated the rate of adaptation of nearly all viable single gene deletion strains. I found that the dynamics of adaptation was decided by diminishing returns epistasis, i.e. the decreasing effect size of beneficial mutations in fitter backgrounds, with almost no impact of specific evolvability genes. In **Paper II**, my co-workers and I found that *S. cerevisiae* adaptation to high mitochondrial superoxide production paraquat was extraordinarily swift. We revealed a novel regulatory mechanism whereby this adaptation was achieved: a genetically controlled reduction in the copy numbers of mitochondrial ETC genes through induction of mitochondrial DNA deletions. Intact mitochondrial genomes were rapidly restored after release from short-term stress, while the mitochondrial genome deletions become irreversible during long-term exposure to high mitochondrial superoxide production. In **Paper III**, my co-workers and I evolved *S. cerevisiae* populations with different levels of pre-existing genetic variation under exposure to anticancer drugs. We found that a higher amount of pre-existing variation speeded up adaptation and that selection on pre-existing and new variation acted on the same proteins, albeit on different aspects of the functions of these proteins. In **Paper IV**, my co-workers and I studied how DNA introgressions from the wild yeast *Saccharomyces paradoxus* have appeared in its sister species *S. cerevisiae*, despite the reproductive isolation of these two species. We show that this can be explained by the hybrid going through a genome destabilization event that leads to scattered islands of homozygosity. These in turn provide sufficient base-pairing for meiosis to proceed, and thereby allow two reproductively isolated species to generate offspring, and in the process, also serve as origins of the *S. paradoxus* introgressions into *S. cerevisiae*. Finally, in **Paper V**, my co-workers and I studied how the domestication of *S. cerevisiae* affected its phenotypes, particularly its life cycle. We compared key properties of the life cycle across nearly 1000 wild and domesticated yeast isolates. We found that domestication recently had profoundly altered the life cycle of *S. cerevisiae*, raising questions on how suitable domesticated yeast isolates are as models. Together, these works shed light on the molecular mechanisms whereby one of our key model organism adapts, and have adapted, to changes in the environment and what the consequences of this adaptation are.