The Functional Basis of Adaptation to Resource-limited Environments
Jungeui Hong¹ and David Gresham¹
¹Center for Genomics and Systems Biology, Department of Biology, 12 Waverly Place
New York University, New York, NY 10003 USA

ABSTRACT How biological networks respond to selective pressure and the features of the genome that enable adaptation to new environments is poorly understood. We subjected haploid prototrophic Saccharomyces cerevisiae (budding yeast) strains to long-term selection under continuous nitrogen limitation in steady-state chemostat cultures. A variety of individual nitrogen containing compounds (and some combinations) were provided at growth-limiting concentrations. Following several hundred generations, we obtained populations with dramatically increased fitness. Phenotypic analysis of clonal isolates revealed significant heterogeneity within populations suggesting a diversity of pathways to increased fitness.

We analyzed the genomes of representative individuals within each population using next generation sequencing. We identified extensive structural variation in the genomes of clones with increased fitness. Included among these alleles are amplifications of genes encoding the transporters PUT4, DAL4, DUR3 and GAP1 – in proline, allantoin, urea and glutamate selections respectively – highlighting the role of gene amplification in adaptation to selective pressure. Surprisingly, we also identified clones in which GAP1 was deleted. We inferred from sequence that this deletion event occurs due to LTR-mediated intrachromosomal recombination. We found that the reciprocal product of this event is selectively retained in some lines as an autonomously replicating circular DNA element. We propose that this genomic architecture facilitates evolvability of S. cerevisiae populations exposed to variation in levels and sources of environmental nitrogen. We also identified all point mutations associated with adaptation to nitrogen-poor environments. Several mutated loci encode components of the vacuolar and the TORC1 signaling pathway providing insight into the functional basis of adaptation to nitrogen-limited environments.

What are the targets of selection underlying adaptation in resource-limited environments?

Method: Selection in Chemostats
1. Enables constant nutrient limitation
2. No bottleneck or drift effects (N>10⁷ cells)
3. Haploid yeast cells reproduce asexually for 250 generations in 7 different nitrogen-limited chemostats

Repeated mutational targets in different nutrient-limited environments

The chemostat efficiently selects for mutants with increased fitness

Copy number variation is frequently associated with increased fitness

Evolving populations contain multiple competing alleles

Conclusions
1. The majority of clones and populations exhibit significantly increased fitness following long-term selection.
2. CNVs are frequently found in mutants; many of them contain genes encoding transporters that import the limiting nitrogen-containing compound.
3. Mutational targets selected in different nutrient-limited environments suggest that remodeling of the TORC1 and Ras/PKA pathways may contribute to adaptive evolution in resource-limited environments.

References and Acknowledgements

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