

PROBING THE EFFECT OF THE GENOTYPE ON ADAPTATION AND EVOLVABILITY. D. Aggeli¹ and G. Sherlock², Stanford University Medical School, 259 Campus Drive, Stanford CA 94305, dangeli@stanford.edu, gsherloc@stanford.edu

Abstract: Epistatic interactions among beneficial mutations have repeatedly been shown to play a significant role during adaptation and can be key determinants for processes such as speciation, and niche construction and exploitation. In this project, we are exploring the relationship between genotype and adaptation and evolvability to determine the effect that the founding genotype has on the adaptation rates and evolutionary trajectories. Our lab has developed a high-resolution lineage-tracking system, based on genome-integrated molecular barcodes, which was used to monitor a wild-type laboratory *Saccharomyces cerevisiae* strain evolving under glucose limitation via serial batch transfer every 48 hours [1]. Subsequent analysis of the adaptive lineages from that experiment determined that the majority of the adaptive mutations were in the Ras/PKA and Tor pathways, while diploidization was the most frequent adaptive strategy [2]. Here, we are exploring the further adaptation of three lineages from this experiment, which have mutations in *TOR1*, *GPB2* and *CYR1*. Random barcodes were re-introduced into segregants derived from each of the adapted lineages and barcoded populations of each genotype were evolved in duplicate under the same original evolutionary environment for 160 generations. Over the course of the evolutions, the cultures were frequently inspected for contamination, the cell density was measured after each transfer cycle, and the frequency of diploids was estimated. Surprisingly, the cell density did not always increase, but it was somewhat reproducible between the replicates. Furthermore, it appears that diploidization does not confer the same fitness advantage to all genotypes. We are currently performing barcode sequencing to track the emergence of adaptive lineages, to directly compare adaptation rates between adaptive mutants and wild-type (the founder from which they emerged). We hypothesize that adaptive mutants will have lower adaptation rates compared to the wild-type, due to diminishing-returns epistasis and increased constraint. We do not exclude the interesting possibility that ecology-based forces will drive each adaptive founder to eventually give rise to phenotypically convergent lineages. By employing the lineage tracking system we will be able to probe the relationship between genotype and evolvability in an unprecedented depth.

References:

[1] Levy S. F., Blundell J. R. *et al.*, (2015) *Nature*, 519, 181-186. [2] Venkataram S., Dunn B. *et al.*, (2016) *Cell*, 167, 1585-1596