

Characterization of mutational robustness genes in yeast

INTRODUCTION

Some genes involved in unfolded protein binding and chromatin binding help to hide (“buffer”) or release the phenotypic effect of genetic variation.

We employed the toolbox of the model eukaryote *Saccharomyces cerevisiae* to perform a genome-wide screen aimed at identifying genes that influence the phenotypic outcome of random mutations.

Silent mutations



Mutations have phenotypic consequences



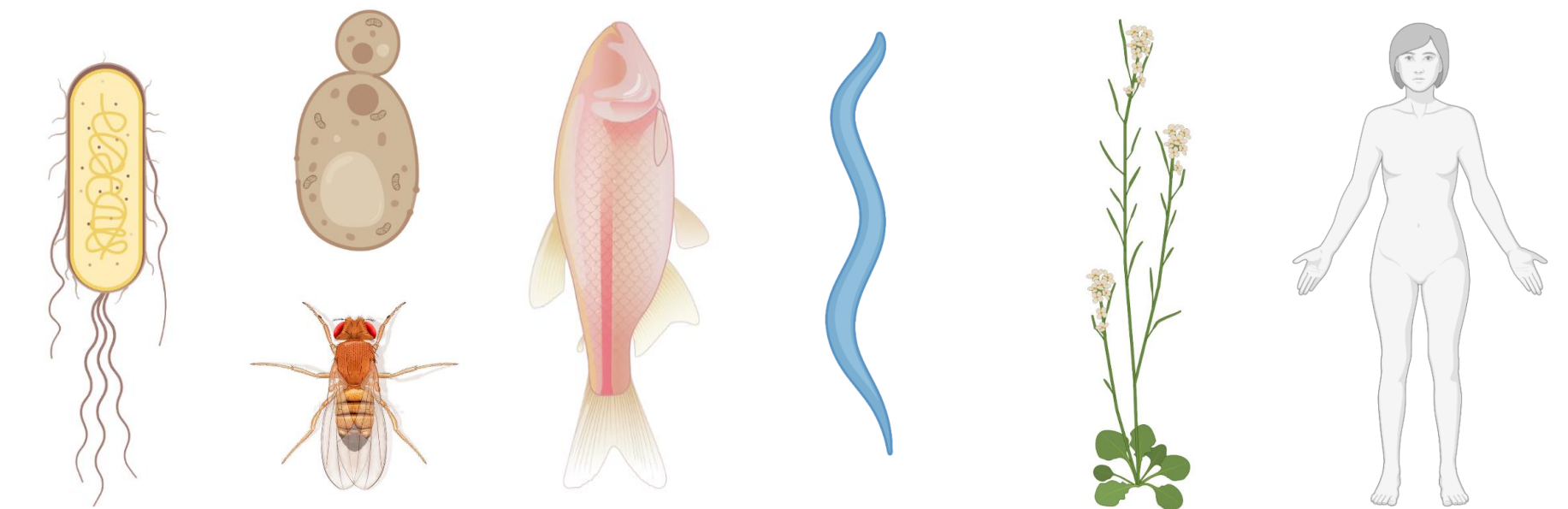
Inhibition of 1 gene



RESEARCH QUESTIONS

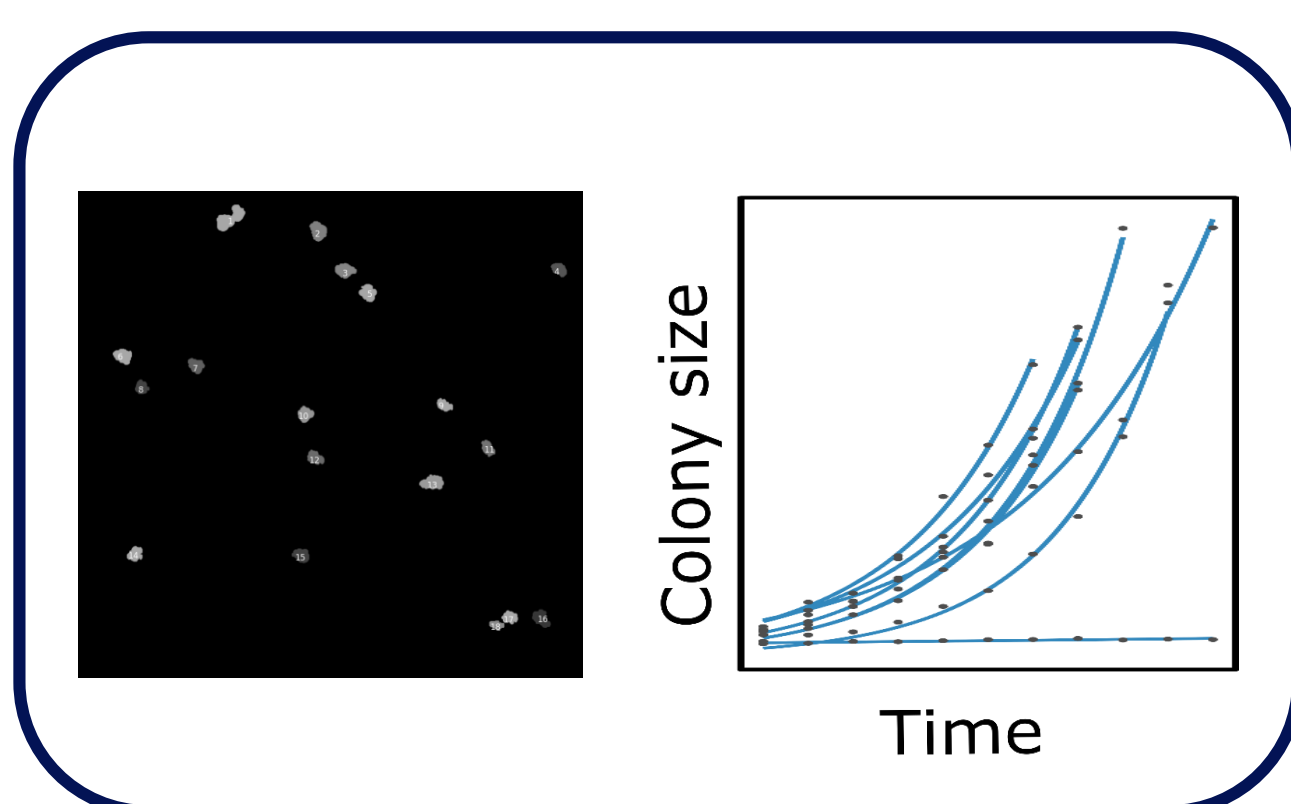
- 1 How many “mutational buffer” genes are there?
- 2 Do candidate buffering genes have buffering potential in various environments?
- 3 Does the presence or absence of a buffering gene influence the evolutionary potential?

HSP90 is the best studied example of a “mutational buffer”

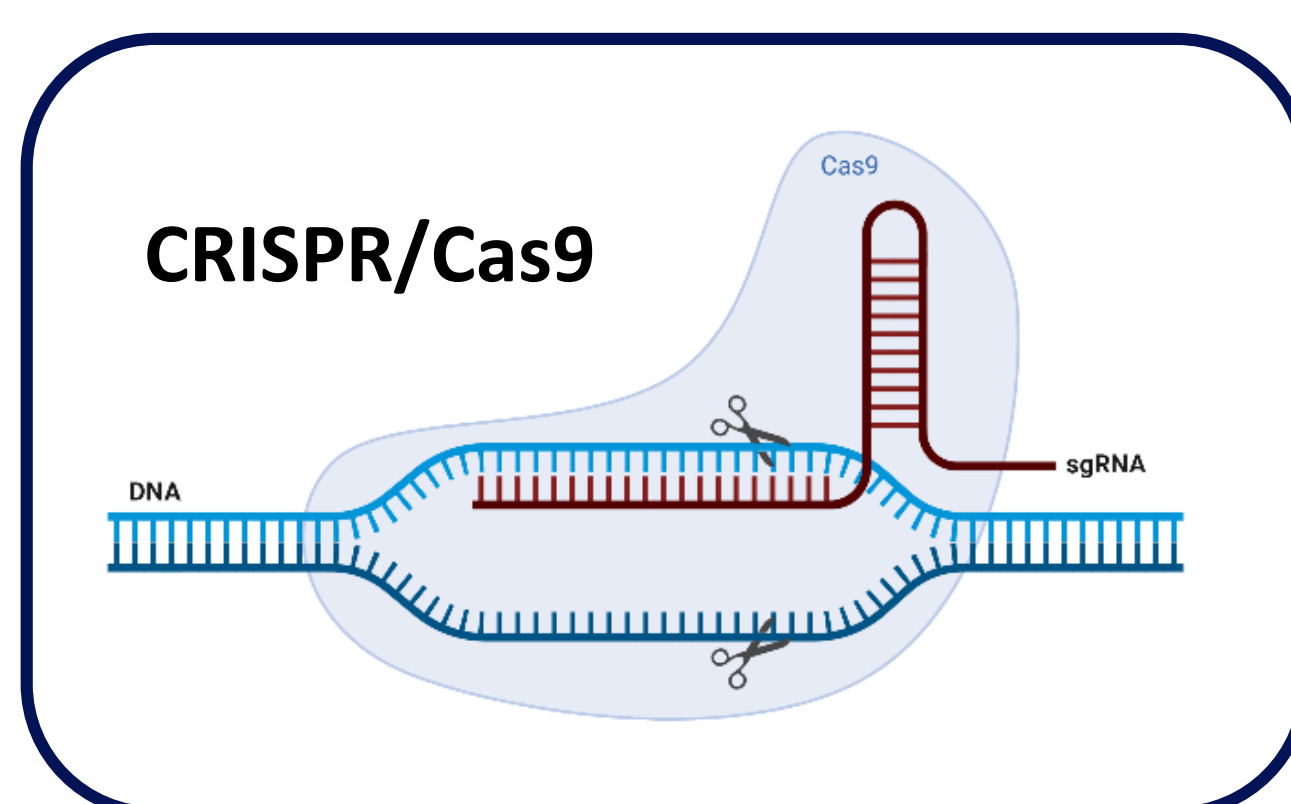


MATERIALS AND METHODS

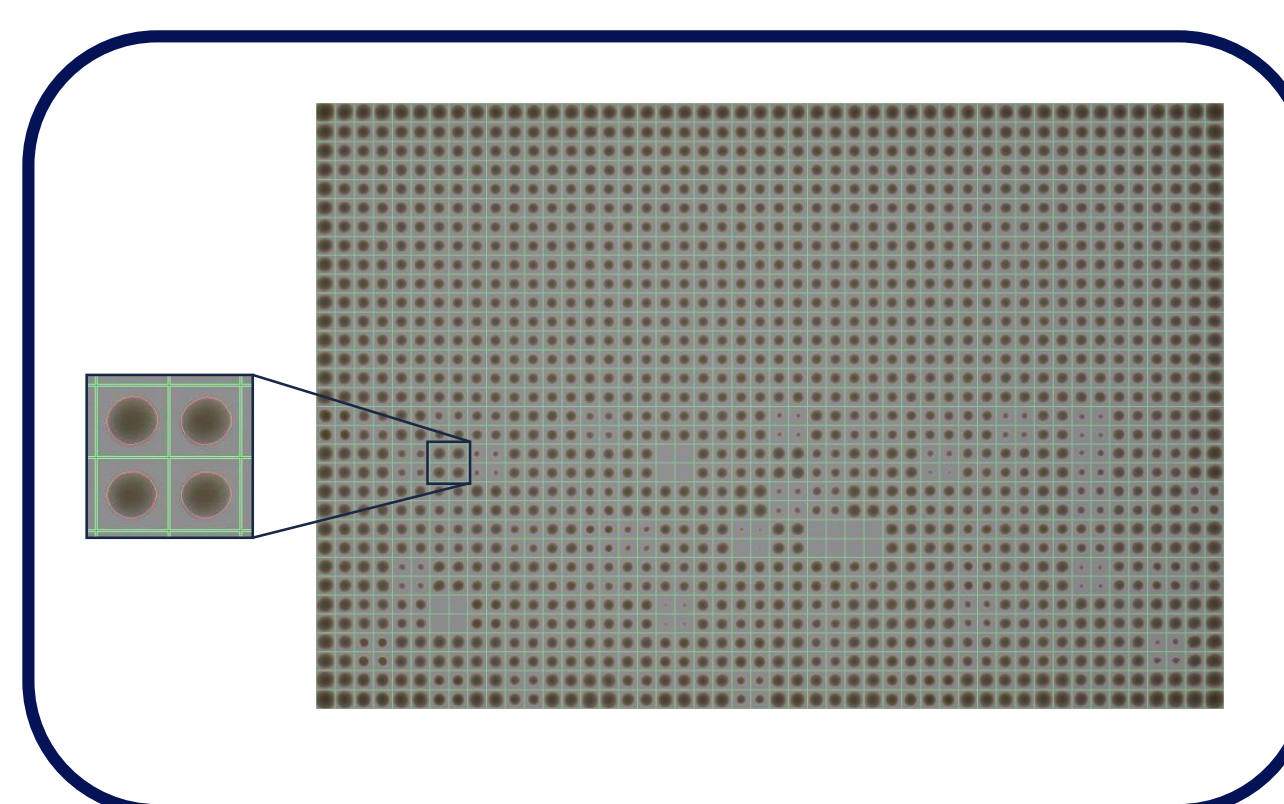
Automated microscopy



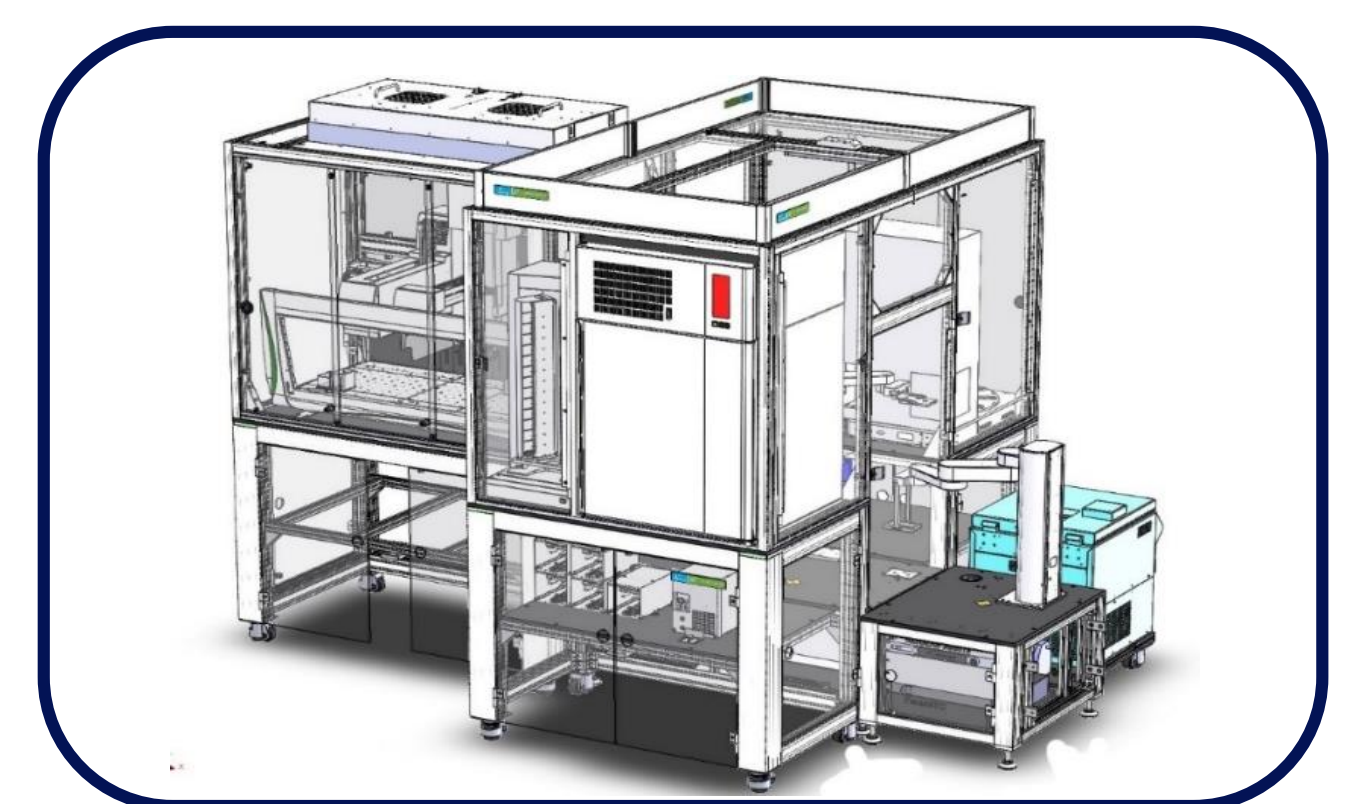
Molecular techniques



High throughput phenotyping



Robotic system for microbial evolution



RESULTS

- 1 Identification of functional groups and genes with high buffering potential.
- 2 Buffering genes have mostly negative and some positive interactions with randomly mutated strains.
- 3 The presence or absence of a buffering gene might lead to different evolutionary outcomes.

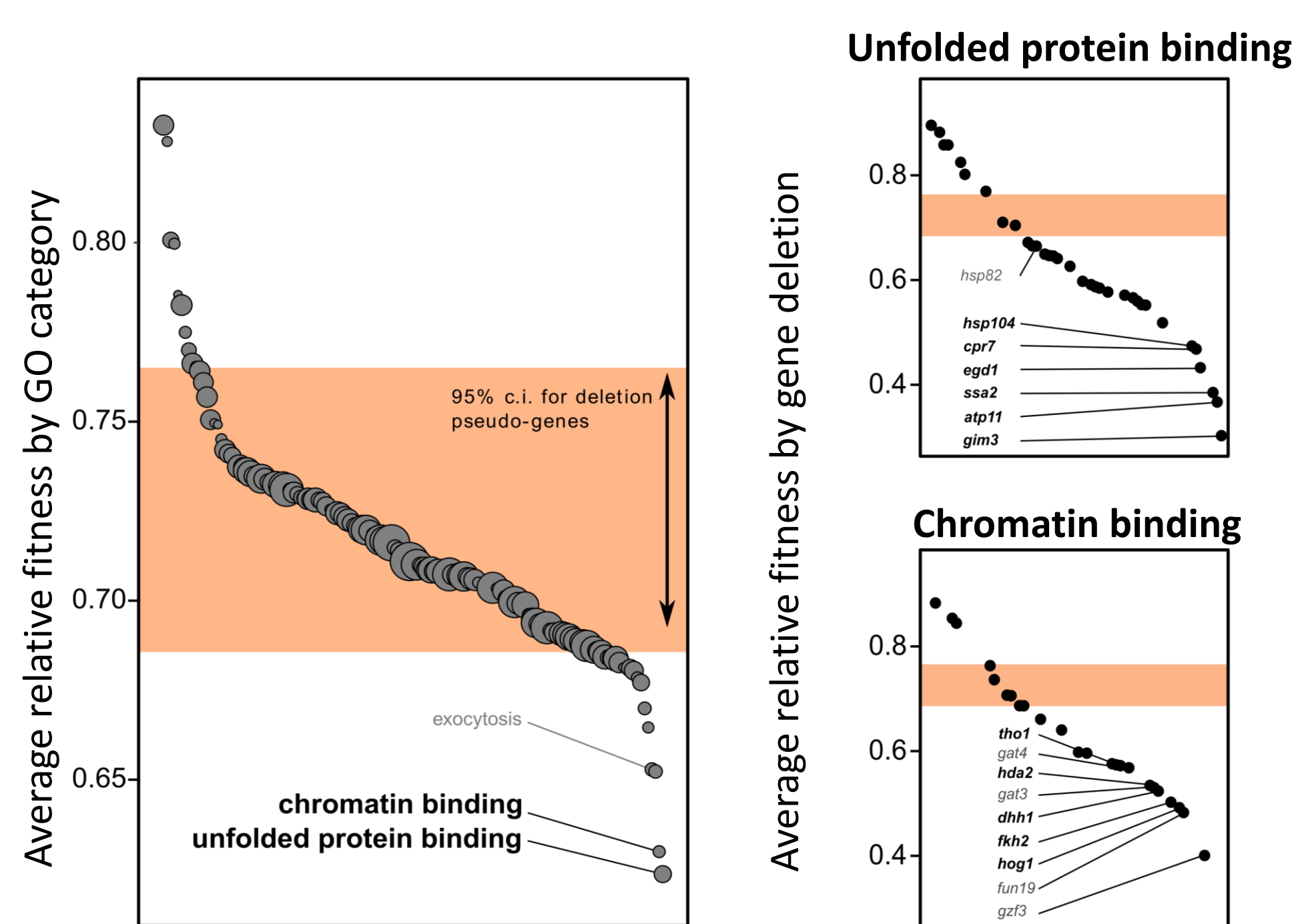


Figure 1: Relative fitness (control vs. mutant culture) of yeast deletion collection strains grouped by GO annotation. The orange zone is the effect of mutations when a pseudo gene was deleted (this serves as a baseline because the deletion of a pseudo gene is unlikely to contribute to buffering).

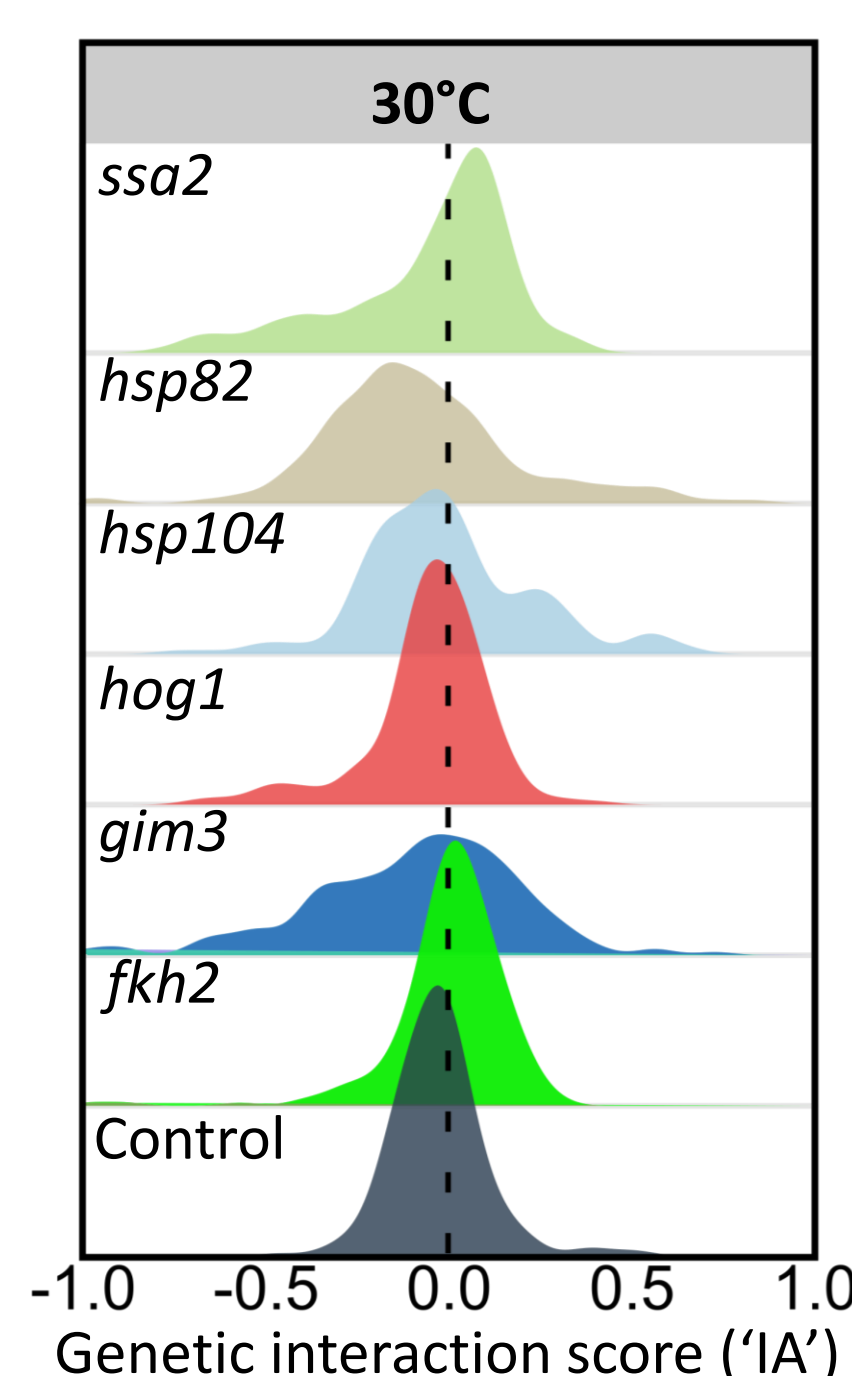
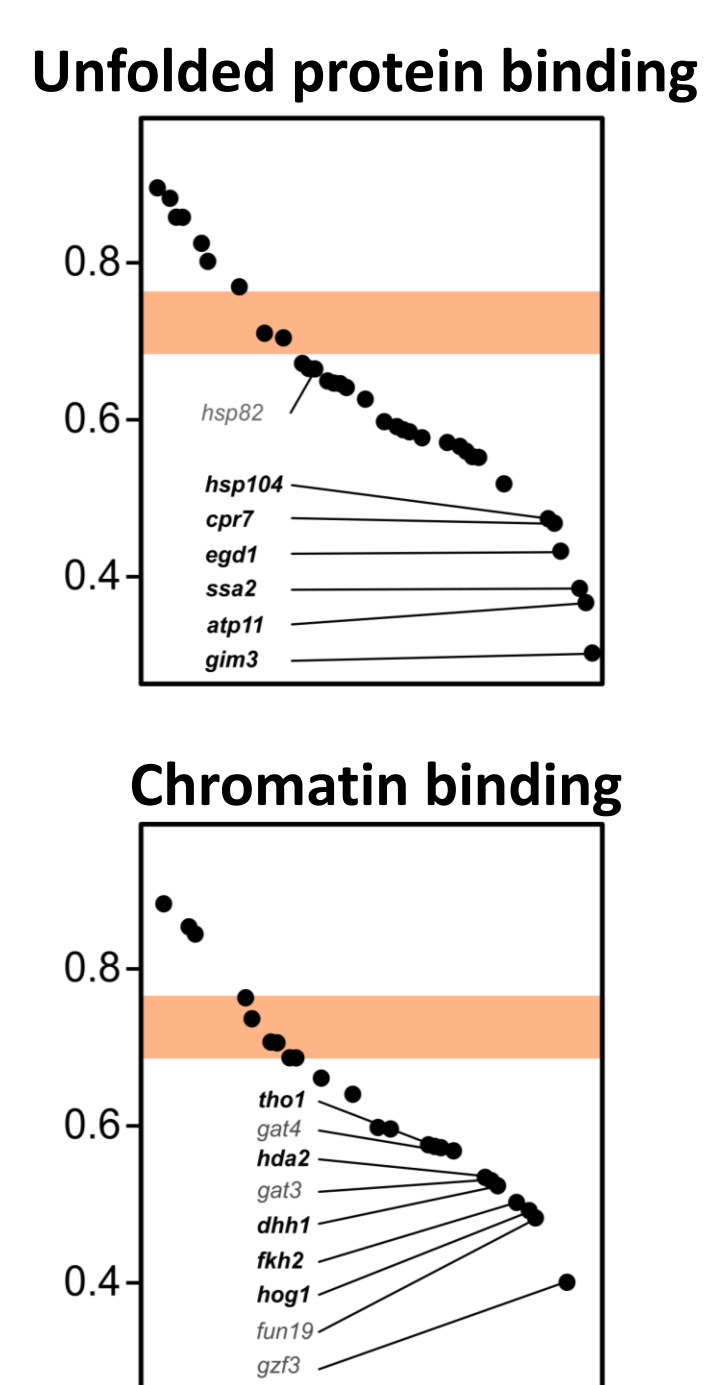


Figure 2: Left: Buffering genes have mostly negative interactions with random mutations. A genetic interaction score (‘IA’) for each mutant strain was calculated, P-value <0,0001. **Right: Deleting *hog1* in the mutated colonies mostly leads to lower fitness under selection.** However, some mutants have higher fitness when *hog1* is deleted (potentiating?).

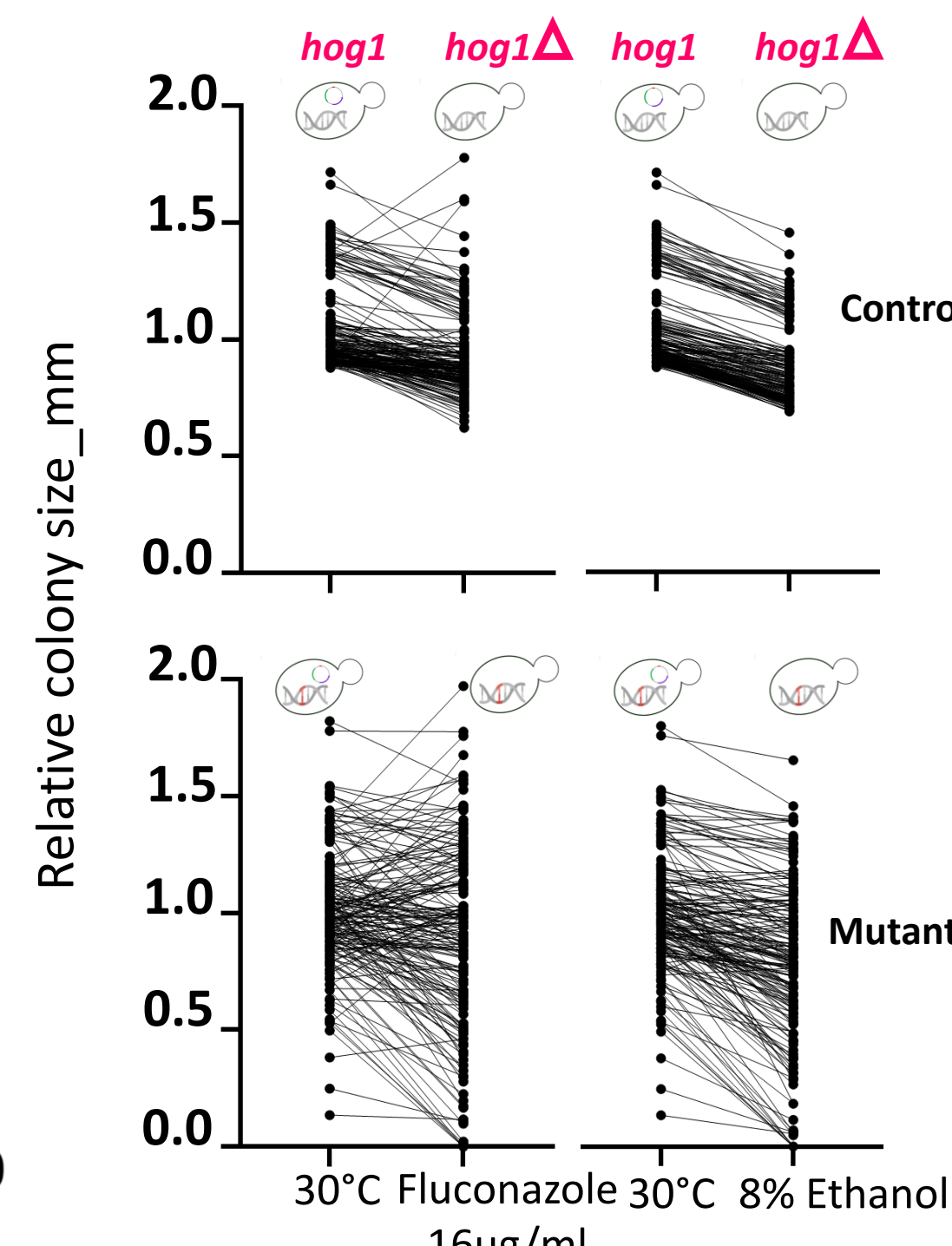
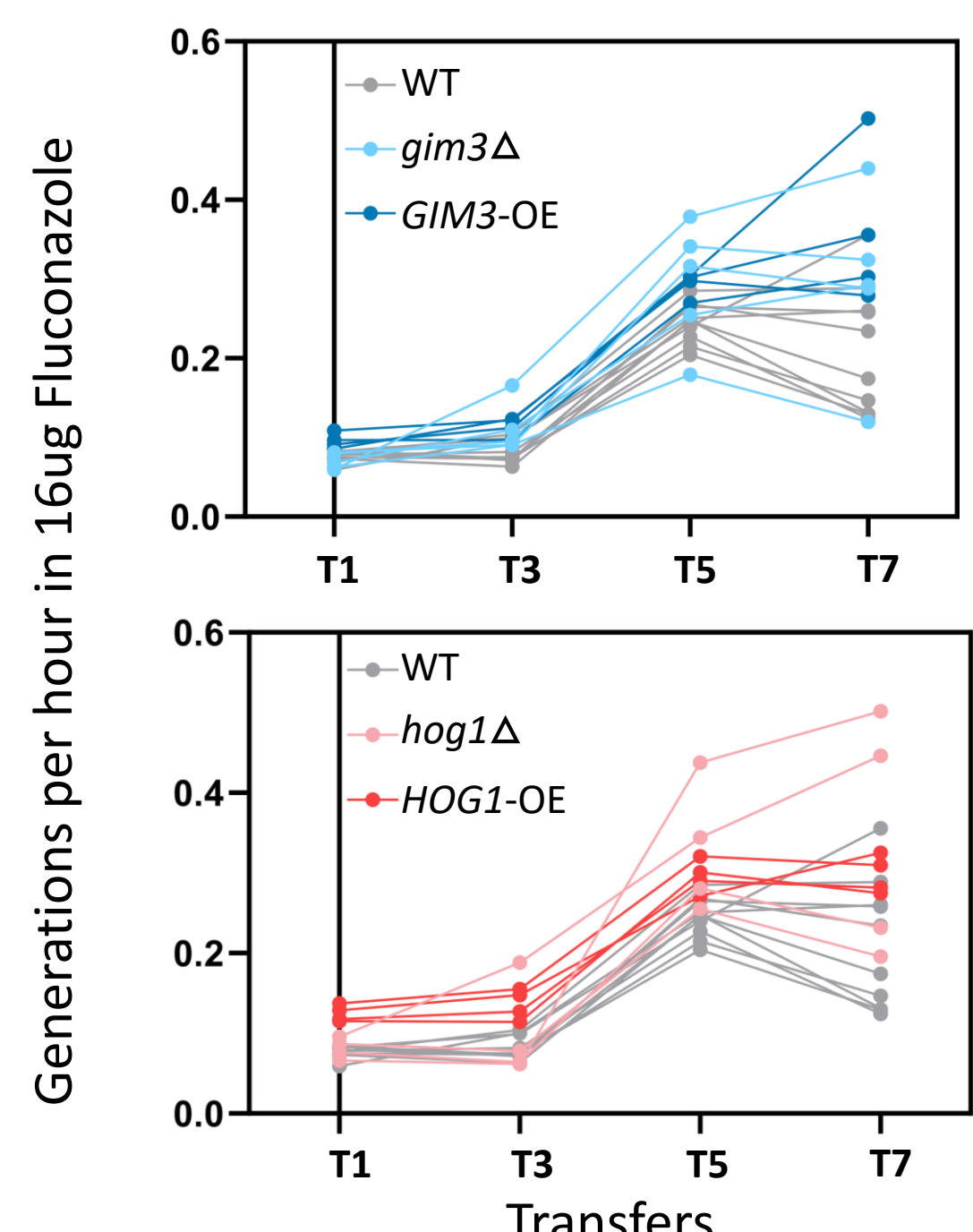


Figure 3: Deleting a buffer gene might allow for higher variation in the evolutionary trajectories which could lead to faster adaptation for some of the evolved strains.



DISCUSSION

- 1 We used the model eukaryote *Saccharomyces cerevisiae* to identify genes that act as genetic buffers, i.e. genes that influence the fitness effect of a relatively large fraction of mutations. Two GO categories, ‘unfolded protein binding’ and ‘chromatin binding’ showed enrichment for genes with a strong buffering potential (Figure 1).
- 2 These buffering genes show mostly negative interactions with random mutations, but also some positive interactions (Figure 2).
- 3 Preliminary results suggest that some of the top candidate buffering genes might influence evolutionary potential (Figure 3).

