



Hunting for Prions: Propagating Putative Prion States in Budding Yeast

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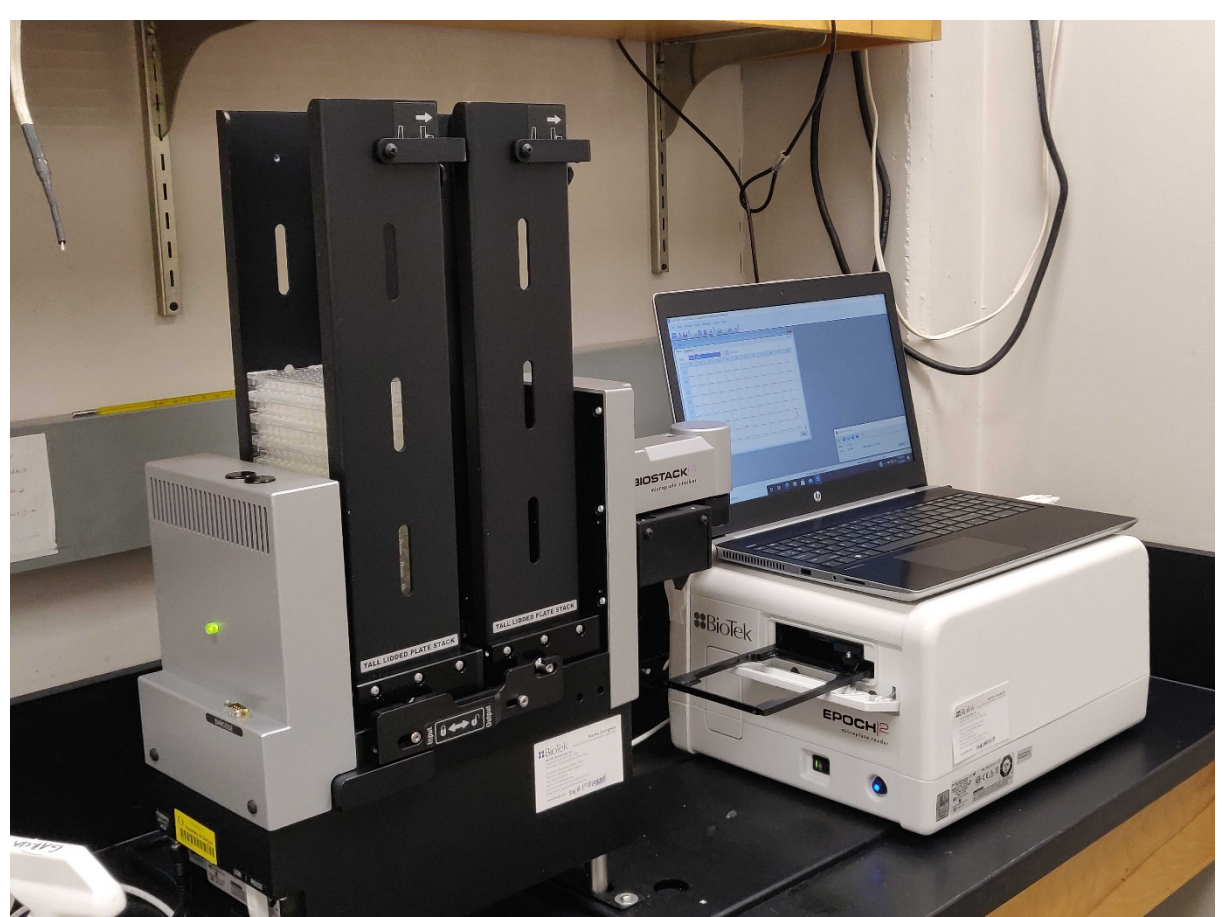
Introduction

Environmental stressors can negatively affect cell processes and transform cells into a diseased state, but cells can adapt to adverse conditions. Using the budding yeast, *Saccharomyces cerevisiae*, the Garcia Lab aims to understand the epigenetic mechanisms employed in this process. Epigenetic traits are heritable but are not caused by changes in a cell's DNA and include many different mechanisms. The lab focuses on prion proteins, which are misfolded versions of proteins that inherit into future generations of cells.¹

Research Question

Previous experiments have established yeast strains with putative prion conformations of the enzymes Abd1, Cet1, Ppm2, Pus4, Pus6, and Trm5 that are resistant to the effects of chemicals. Do these strains of yeast pass on those phenotype in patterns consistent with prion proteins?

Methods

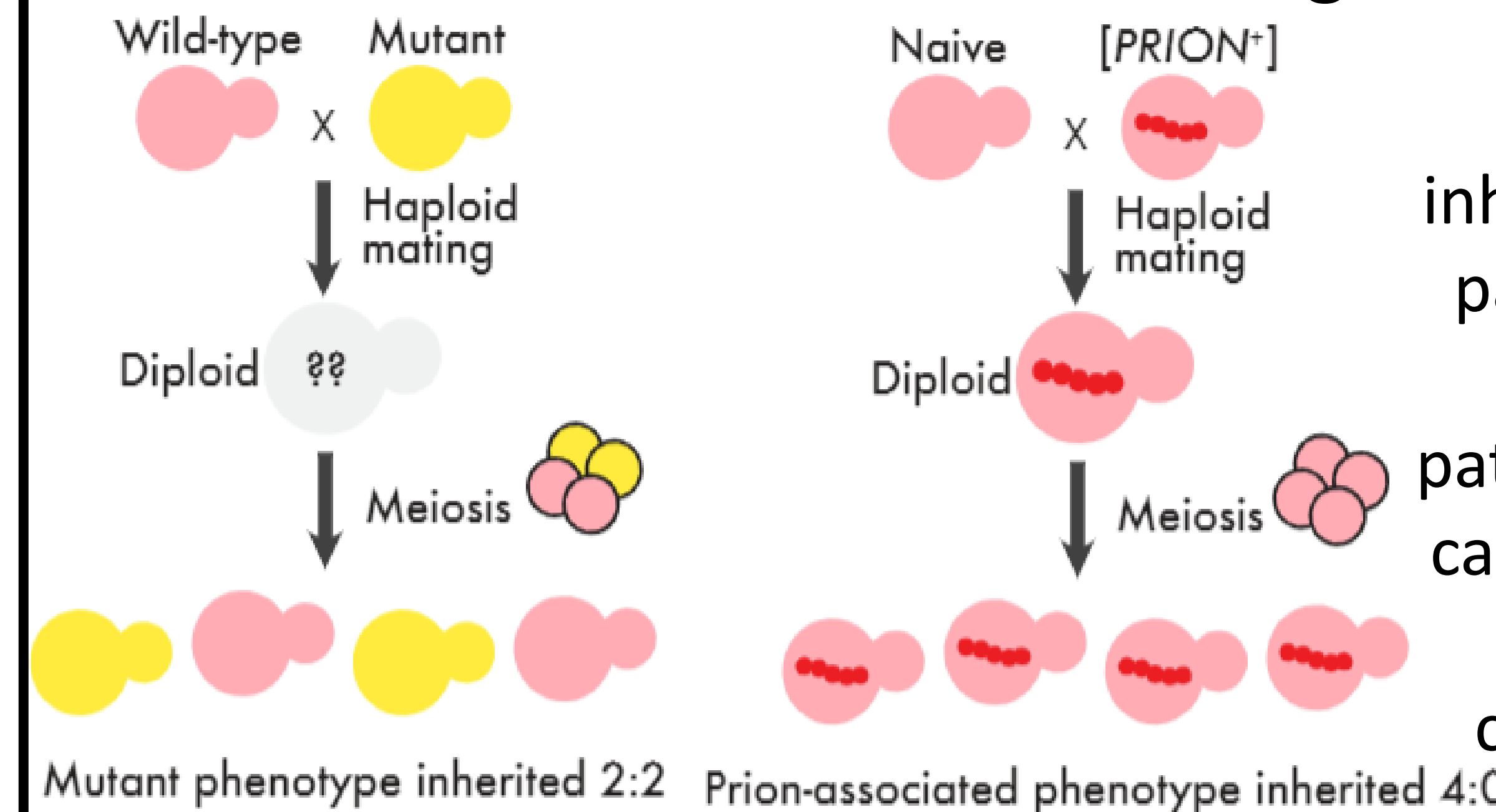


This project employed three sets of methods: creating and isolating offspring strains of yeast; performing growth assays on these strains; and analyzing the data to compare the growth dynamics of a strains with a putative prion to those of a control strains.

Pictured:

Top: dissection microscope used for tetrad dissections, a key method in this project
Bottom: plate reader used for growth assays

Method Diagram



Mutant phenotype inherited 2:2 Prion-associated phenotype inherited 4:0
Figure 1. Graphical methods explaining distinct patterns of inheritance for prion-based compared to mutation-based traits. Source: Garcia Lab presentations

Prion-based traits exhibit unique patterns of inheritance.² Determining the patterns for the strains here and comparing them to patterns established for prions can attribute these resistance phenotypes to prion conformations of proteins.

Results

Traits caused by prion proteins are always dominant in a diploid background and inherit through meiosis in non-Mendelian inheritance patterns.

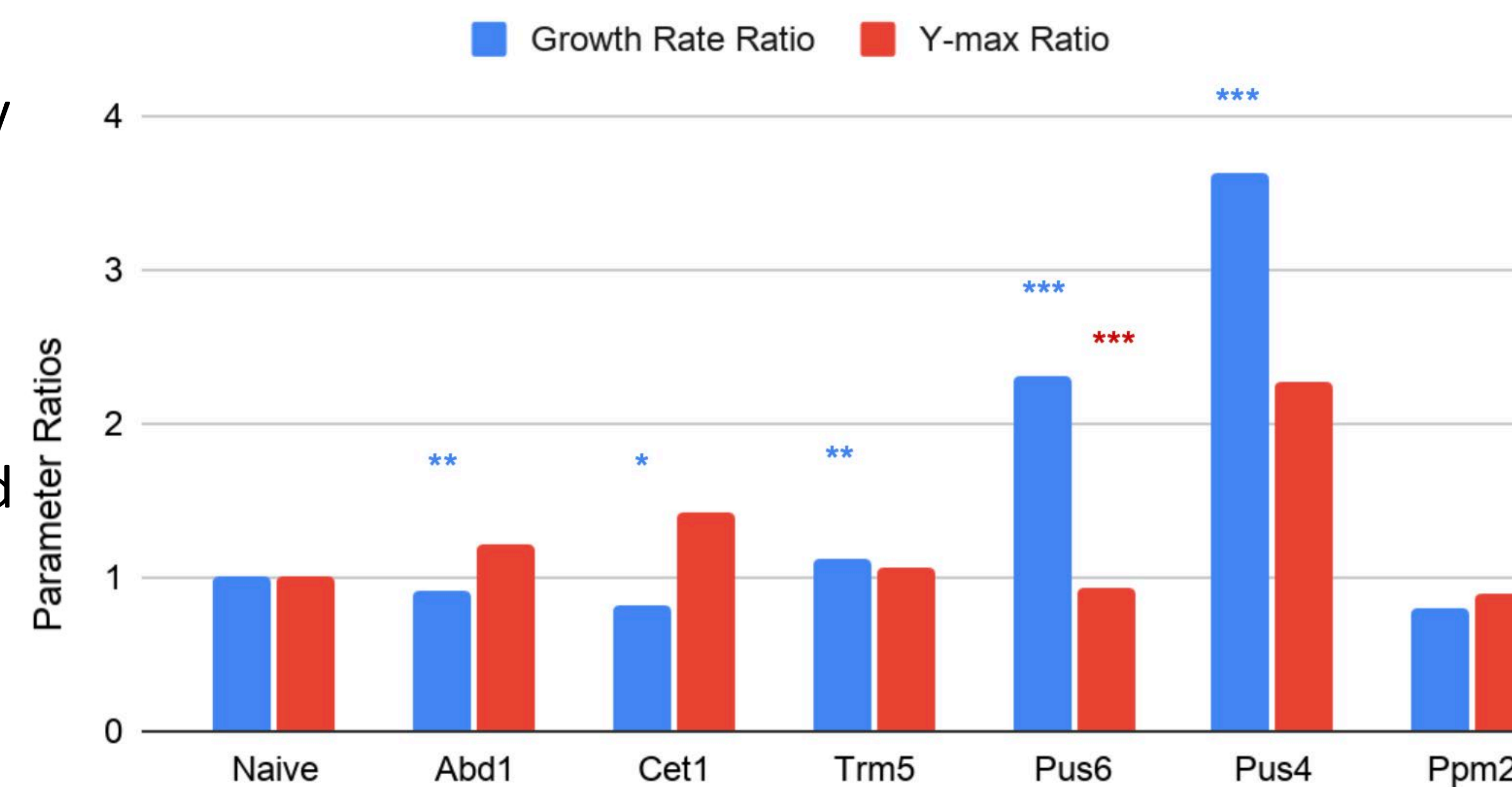


Figure 2. Bar graph showing average growth rates and y max values for six putative prion strains

	# Abd1 Tetrads	# Cet1 Tetrads	# Ppm2 Tetrads	# Pus6 Tetrads	# Trm5 Tetrads
4:0	4	1	0	0	0
3:1	0	1	0	2	1
2:2	0	0	3	0	1
1:3	0	0	1	2	0
0:4	0	0	2	0	0

Figure 3. Table showing number of tetrads demonstrating each pattern of inheritance for each candidate strain.

Results show dominance in diploids in 5 of our 6 strains, and non-Mendelian inheritance in 5 of our 6 strains (including both 3:1 and 4:0 inheritance patterns). In both experiments, the strain associated with the enzyme Ppm2 did not show inheritance patterns consistent with prion proteins.

Conclusions

Prior work has demonstrated that prion proteins, acting as an epigenetic mechanism, may benefit cells that are exposed to environmental stressors.³ Identifying novel prions in the yeast proteome will continue to build evidence of a role for prions in adapting to stress. Here, six strains that have demonstrated resistance to the effects of harmful chemical stressors were tested to determine if the inheritance patterns for the resistance phenotypes were consistent with prion proteins. Through creating and isolating target strains of yeast and performing growth assays, this project found that five of the six strains exhibited inheritance patterns consistent with prion proteins. In both experiments, the strain associated with the enzyme Ppm2 did not exhibit prionic inheritance patterns. Future experiments in the Garcia Lab will determine if these strains exhibit other hallmarks of prion proteins, including cytoplasmic inheritance and aggregation. These findings will add to our understanding of the role of prion proteins as a form of inheritance and of epigenetic mechanisms in a cell's response to stress.

References

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