Propagating Putative Prion States in Budding Yeast

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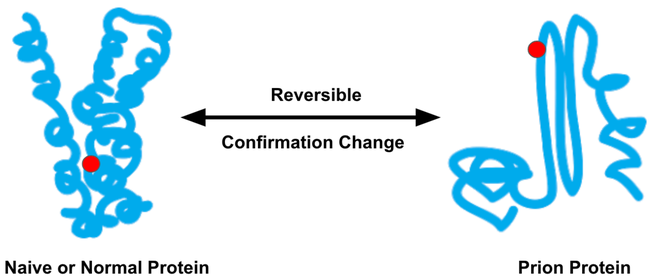
Prion proteins

- Prions are misfolded proteins that can cause other proteins of the same type to also misfold

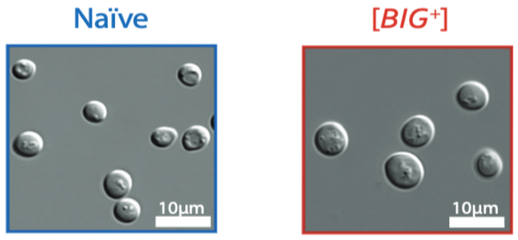


- Previously believed to be only disease causing agents, such as Bovine Spongiform Encephalopathy (Mad Cow Disease)

Challenging the convention

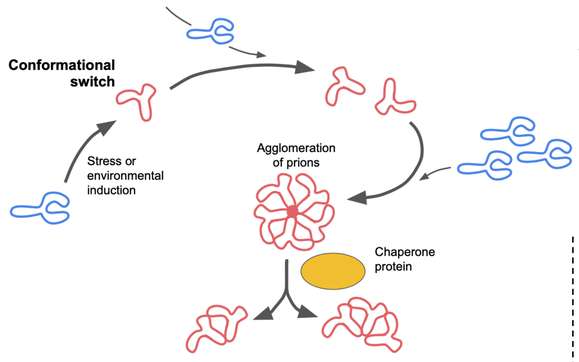
- Recent evidence suggests that prions provide an additional class of epigenetic mechanisms that work at a rapid pace

- The Garcia Lab and others recently discovered prions states, such as [BIG$^+$] that allow cells to grow faster and larger



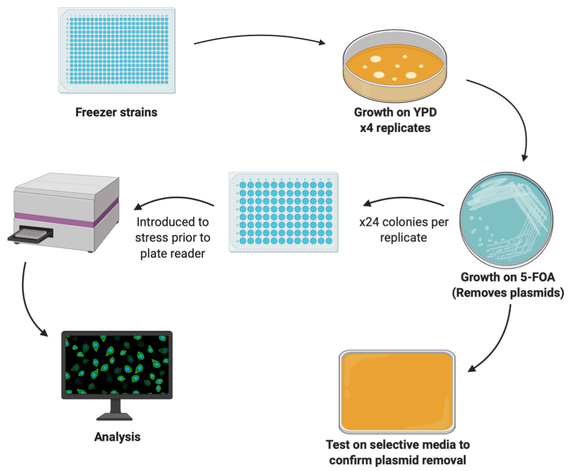
Molecular propagation of prion proteins

- Prions formations occur much more frequently than genetic mutation
- Stress from the environment and protein overexpression can induce prion formation
- Chaperone proteins help ‘seed’ prions to the next generation of cells



Screen for new prion-like proteins

- The goal of my project is to identify new RNA modifying enzyme (RME) prions

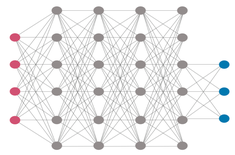


~23%
of disease associated genes have close ortholog in yeast

~50%
of mutations in RMEs are linked to diseases in humans

>5mil
data points collected measuring growth rate and carrying capacity

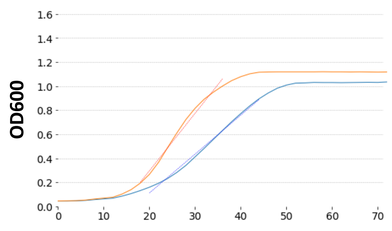
- Cell strains had previous overexpression of RMEs and were exposed to various stress conditions (heat, chemicals, nutrient deficiency, etc.)
- Data analytics and machine-learning toolsets are used to sort and classify the extreme amounts of raw data produced



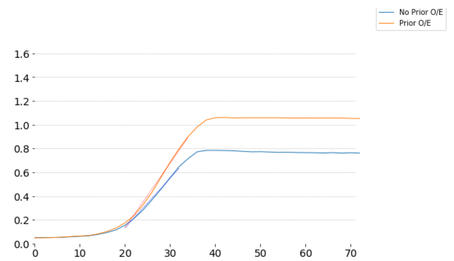
Results

- **Prion states appear to be a common form of inheritance in yeast**
- Nine different strains showed showed significant resistance to stress after having previous overexpression of an RME

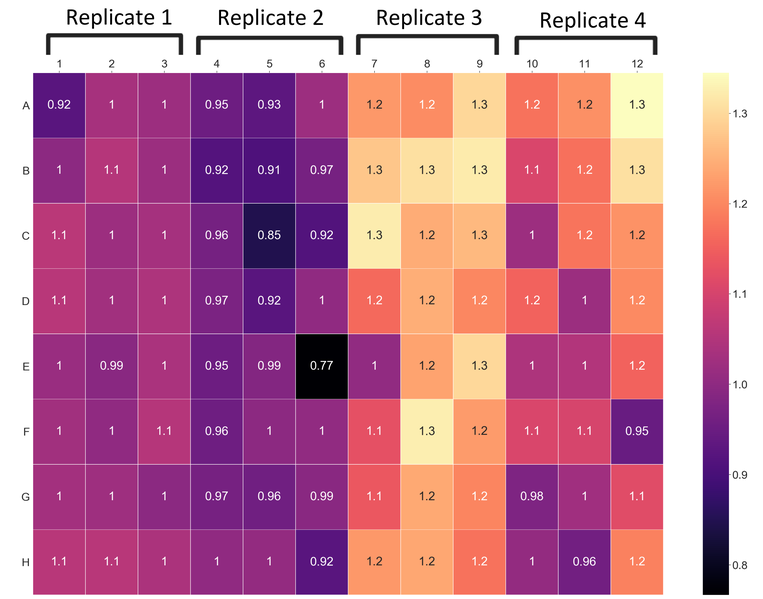
Abd1 overexpression (OE) vs no OE in cycloheximide



Pus6 OE vs no OE in amino acid dropout media



Trm5 overexpression vs. no overexpression in cycloheximide



Better growth in replicants 3 & 4

Future Experiments

- Use fluorescence microscopy to see if these proteins are agglomerating
- Test human homologs in similar assays in yeast
- Try other machine-learning models on predicting prion phenotypes

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