Office hours
3-4pm Wednesday, Dec. 10
304A Stanley Hall

Review session
5pm Thursday, Dec. 11
GPB100

Final exam
12:30pm Saturday, Dec. 13
277 Cory Hall (NE campus)

Marker is linked to polymorphism in
expression regulation cascade

Locally acting regulatory variant

Locally acting polymorphisms
~25% of varying mRNAs are caused by locally
acting polymorphism

Nonlocal polymorphisms

Association in multiple populations
Association of human transcripts

A new brand of genetic variation

Translation

PSI+ yeast read through STOPs
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Weird genetics of read-through

Cytoplasmic aggregates of Sup35

How would this explain the results?

Hard to make aggregate, easy to join
Protein inheritance

\[ \text{PSI}^+ \text{ begets more } \text{PSI}^+ \]

Not due to dominant genetics in the usual way.

Original from \( \text{PSI}^+ \) nucleates in all progeny

Nucleating prions in mad cow disease

Is \( \text{PSI}^+ \) the yeast analog of mad cow or Alzheimer’s?

If bad, would be lost
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**PSI+ phenotypes**

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A yeast prion provides a mechanism for genetic variation and phenotypic diversity
**Why would aggregates result in so many novel abilities and traits?**

Apparently does not happen in Alzheimer’s…

**What do you conclude?**

A. Sup35 does not cause resistance to paraquat.
B. Prions do not cause resistance to paraquat.
C. Aggregation is not necessary to cause resistance to paraquat.
D. Aggregation is not sufficient to cause resistance to paraquat.

Aggregates per se don’t cause resistance.
The clincher

Aggregates per se don’t cause resistance. Losing function of sup35 does.

Aggregation = more read-through

PSI+ allows epigenetic change in protein sequence.

Genetic effects?

Phenotypes varied between genetically diverse PSI+ strains.

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Phenotypes varied between genetically diverse PSI+ strains.

How can the cause be genetic and non-genetic (protein aggregates) at the same time?
Aggregation = more read-through

UTR mutations usually occur and have no effect, so organism doesn’t die and allele is maintained.

Sequence differences in read-through region cause phenotypic differences between PSI+ strains.

Cryptic variation: DNA sequence differences between individuals that are usually not expressed.