

# Proteotoxicity from Aberrant Ribosome Biogenesis Compromises Cell Fitness

## Background/objective

Ribosome assembly requires rapid, coordinated synthesis of multiple components across multiple cell compartments. These factors, combined with the abundance of ribosomes within the cell, makes the process vulnerable to perturbations which can impact cell fitness. Here, researchers used novel chemical-genetic tools to better understand cellular adaptations to perturbations in ribosome assembly.

## Approach

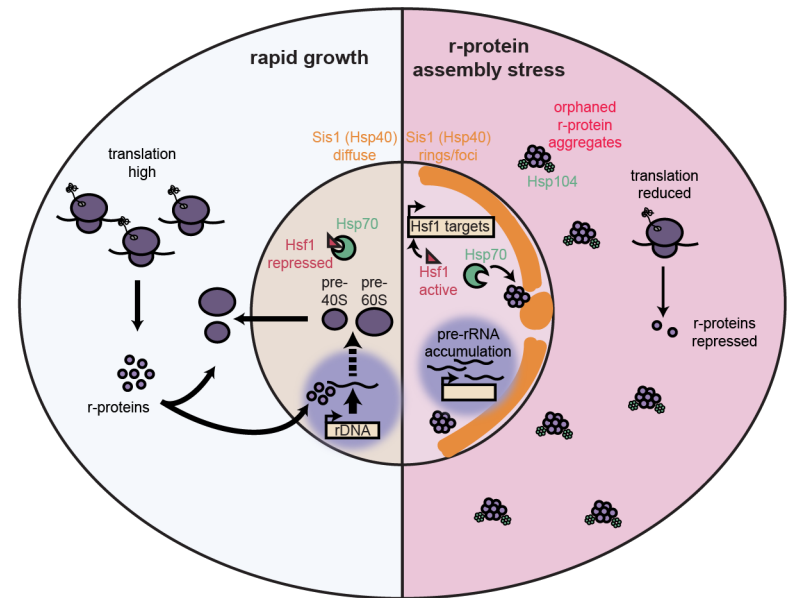
- Ribosomal protein and rRNA levels were artificially imbalanced. Effects on cellular physiology were assessed with multiple methods including imaging, sequencing, and quantitative proteomics.

## Results

- Ribosome assembly is a key vulnerability of proteostasis maintenance in proliferating cells that may be compromised by diverse factors.

## Significance

- Metabolic engineering of yeasts for bioproduct production inherently involves disruption of native metabolic processes. A better understanding of the regulation of ribosomal assembly will aid researchers in avoiding deleterious effects in engineered strains.



**Model of how disruptions to ribosome biogenesis leads to RPAS and the impacts on cellular physiology.** During proliferation, cells rapidly produce ribosomes through coordinated synthesis of r-proteins (purple circles) in the cytoplasm and rRNAs in the nucleolus. Perturbations that result in orphan r-proteins result in proteotoxic stress following r-protein aggregation.