Exploring gene regulatory interactions between histones H1 and H2A.Z in budding yeast

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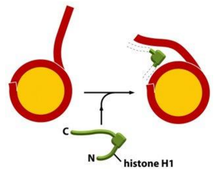
Introduction

- Nucleosomes are critical to the organization of DNA into chromosomes. DNA wraps around nucleosome, allowing the nucleosome to regulating gene expression.
- Nucleosomes contain eight core histone proteins: two of each H2A, H2B, H3, and H4. There is a fifth histone, H1, that sits at the DNA entry/exit site on the nucleosome.

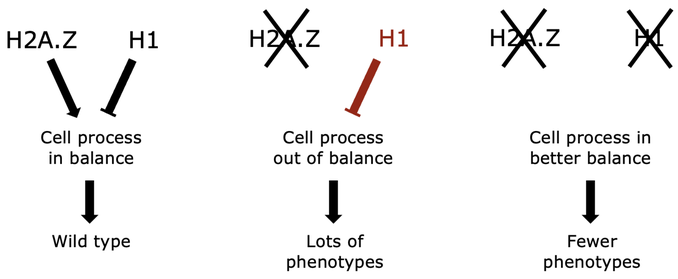


- H2A.Z is a variant of core histone H2A distributed widely across the *S. cerevisiae* genome.

Research Questions

- How does loss of H1 affect gene expression across the *S. cerevisiae* genome?
- Do H1 and H2A.Z interact in a gene-regulatory context?

Background



- We have demonstrated that phenotypes caused by the lack of H2A.Z are returned to a wild type phenotype in the absence of H1 in various contexts:
  - Condensation defects caused by lack of H2A.Z (1)
  - SIR-dependent silencing at the *HMR* (2)
- Thus, we hypothesize that we might see a similar phenotype from gene expression data, especially from two proteins involved in chromatin dynamics.

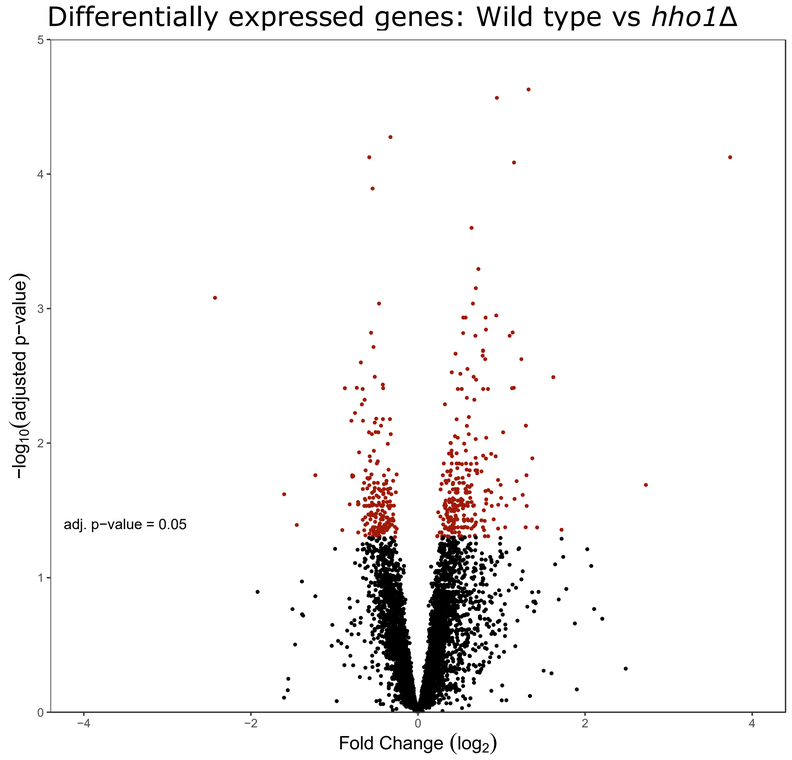
Sources

1. Rogers AM, Neri NR, Chigweshe L, Holmes SG. Histone variant H2A.Z and linker histone H1 influence chromosome condensation in *Saccharomyces cerevisiae*. *GENETICS*. 2024;226(4). doi:https://doi.org/10.1093/genetics/iyae022

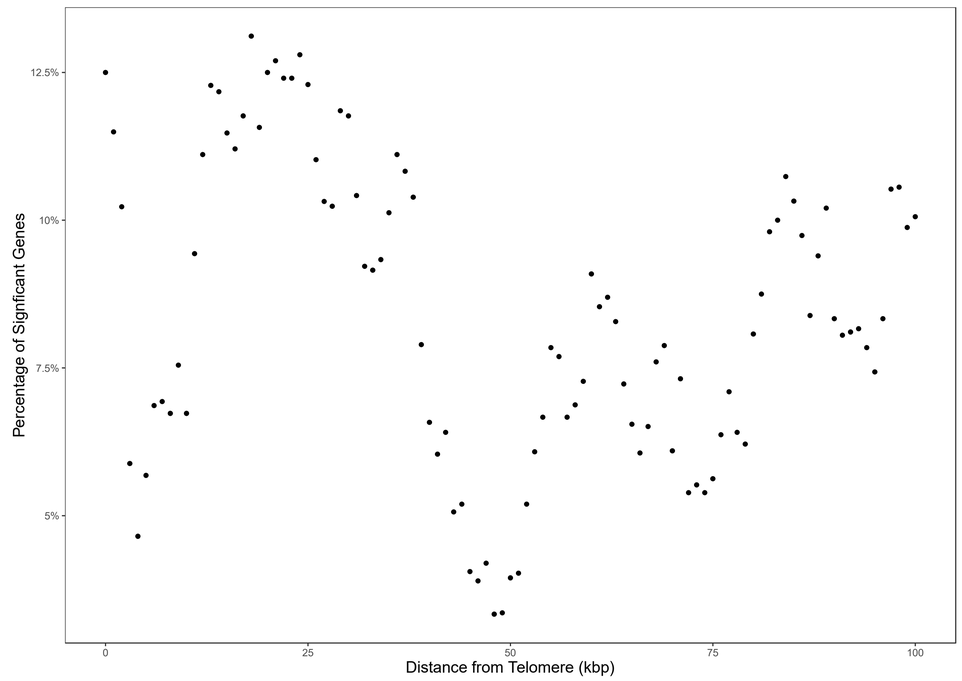
2. Chen PY. Genetic Analysis of Linker Histone H1 in Saccharomyces cerevisiae. *Wesleyan University Digital Collections (Wesleyan University)*. Published online January 1, 2008. doi:https://doi.org/10.14418/wes01.1.276

Expression Profile of *hho1Δ*

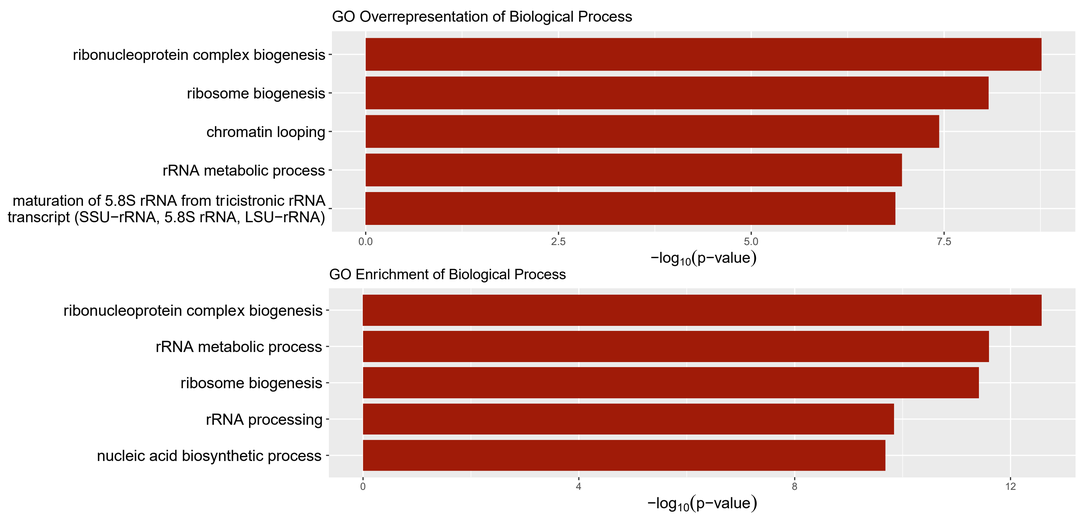
Differentially expressed genes: Wild type vs *hho1Δ*



Telomere position effect: Wild type vs *hho1Δ*

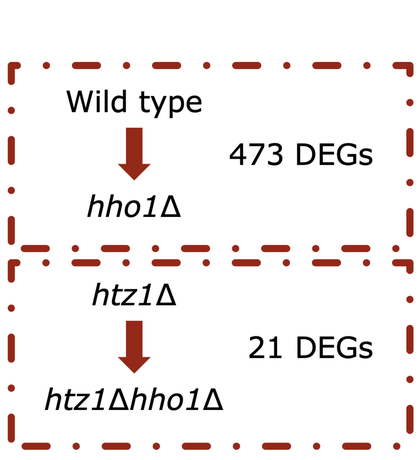


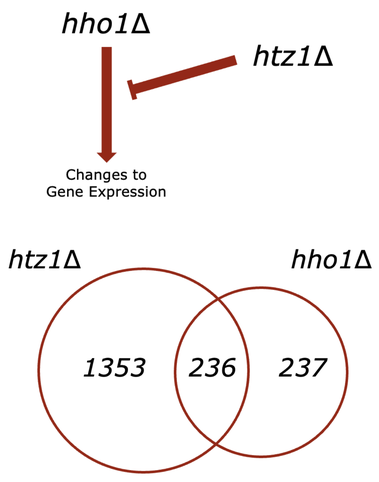
Gene Ontology: Overrepresentation and Enrichment of Biological Process



hho1Δ and *htz1Δ*

Strain	DEGs	Up-regulated	Down-regulated
Wild type vs *hho1Δ*	473	267	206
Wild type vs *htz1Δ*	1589	881	708
Wild type vs *hho1Δhtz1Δ*	1802	940	862
htz1Δ vs hho1Δhtz1Δ	21	11	10





Conclusions and Future Steps

- H1 regulates gene expression across the *S. cerevisiae* genome.
- H1 non-randomly affects genes involved in various biological pathways including ribosome biogenesis and chromatin looping, and by proximity to the telomeres.
- Lack of H2A.Z covers up the gene-regulatory influence of the loss of H1.

Next Steps:

- Build an interaction model to better represent overlapping conditions.
- Analyze co-expression to explore the regulatory network involving H1 and H2A.Z.

Acknowledgements

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