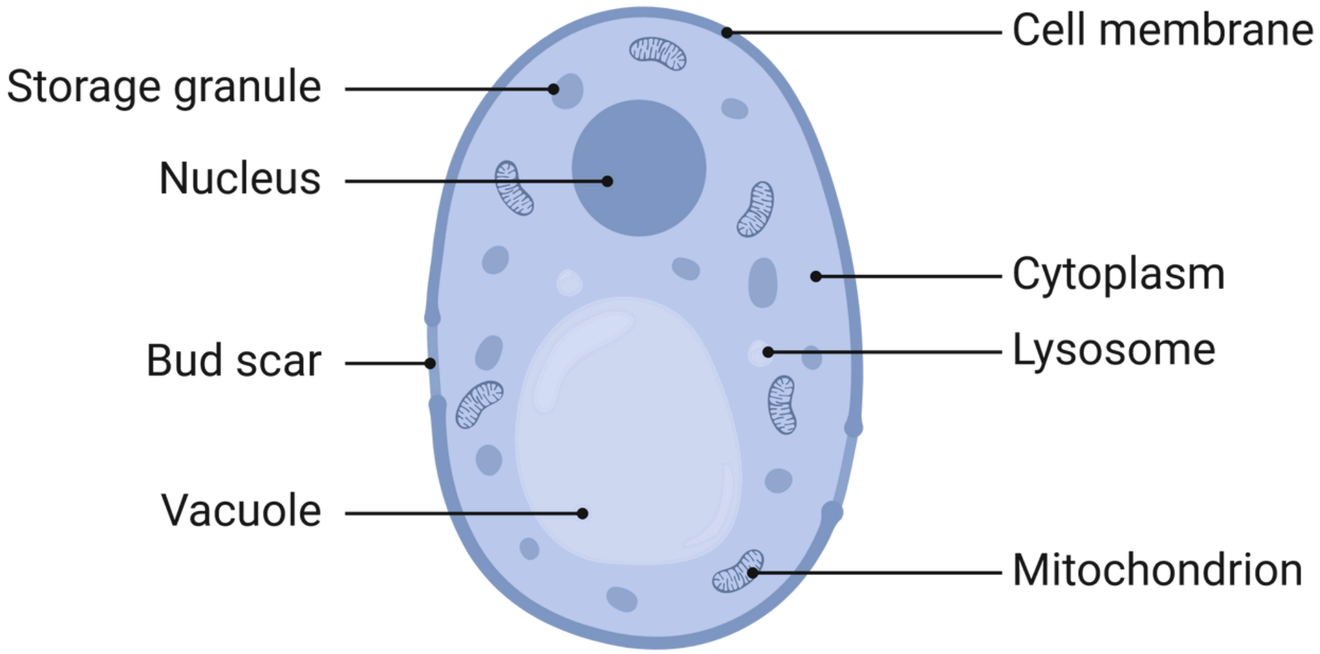
9504: Model Organism Presentation

Saccharomyces cerevisiae (Budding Yeast)

By: Balwinder & Rishika

WHAT IS SACCHAROMYCES CEREVISIAE AKA BUDDING YEAST



- Saccharomyces Cerevisiae are **1 of 1500** different forms of yeast.
  - Colloquially known as **Budding Yeast**
  - Classified phylogenetically as a **fungus** or a **mold**
- Single cellular **eukaryotic** organisms
  - Membrane bound organelles
  - 2/3rd of all genes have ortholog
- The name “cerevisiae” derives from old world terminology for **beer!**

TIMELINE OF YEAST

1676

Antonie van Leeuwenhoek describe yeast cells for the first time

1857

Louis Pasteur confirmed that fermentation results from the action of living yeast transforming glucose into ethanol

1883

Emil Christian Hansen isolated the first pure yeast culture

1935

Øjvind Winge, known as the Father of Yeast Genetics, demonstrated the alternation of haploid and diploid phases in yeast, establishing the basis for yeast genetics

1996

Yeast became the first eukaryote to have its genome fully sequenced

2001

Dr. Leland H. Hartwell used yeast to identify genes that contributed to cancer development and was awarded the Nobel Prize

2005

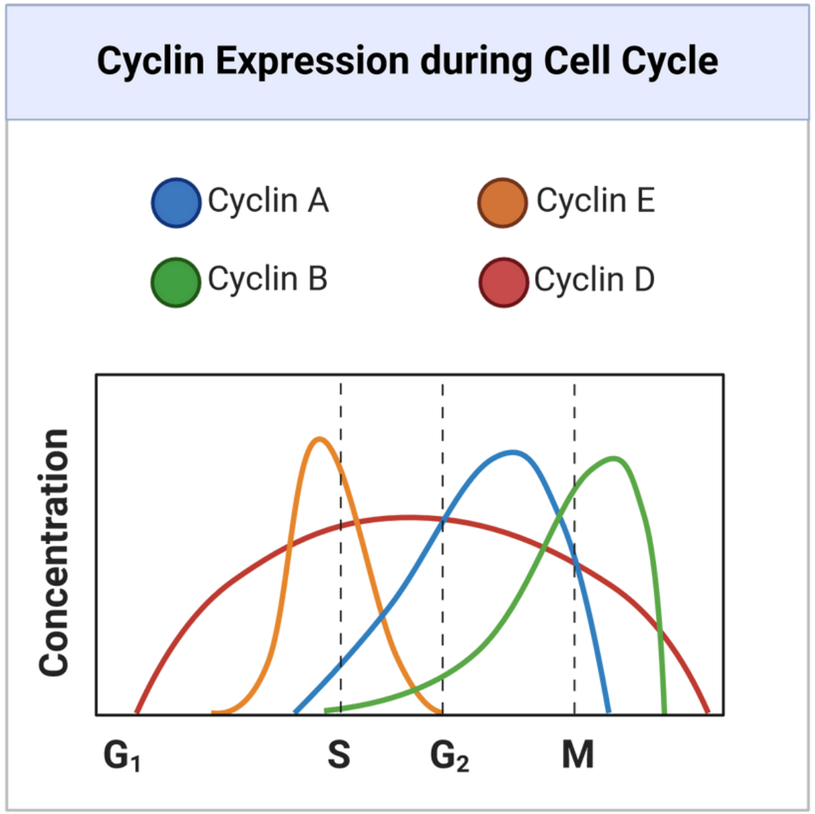
The laboratories of Brenda Andrew and Charles Bone at UofT released the Yeast ORF Collection, a set of 5000 strains over-expressing individual yeast genes

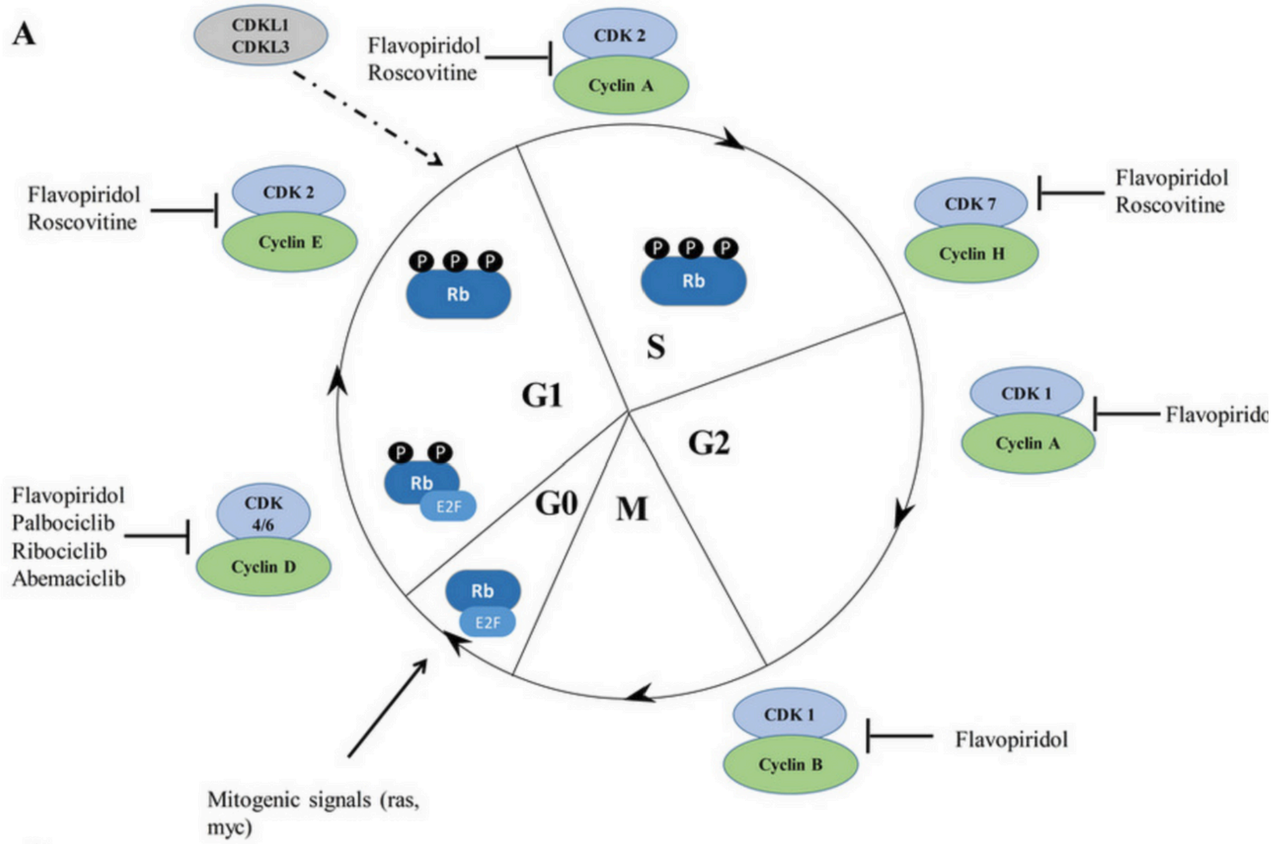
2020

A study using 30,000 yeast strains created a network of 5,000 disease-linked proteins, this network, called NeuroNet, provided new insights into how protein aggregated in neurodegenerative diseases, including Alzheimer's, are formed

Applications in Biomedial Research

With cancer, they are powerful tools in understanding oncogene/tumor suppressor gene mechanisms and they also have led to the development of numerous CDK-inhibitor based therapies





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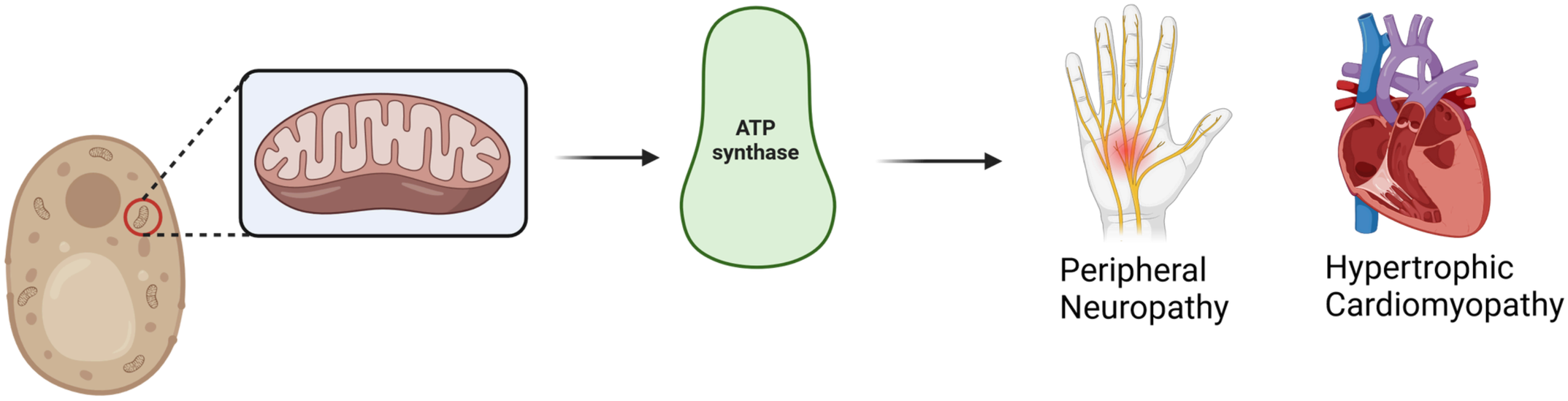
Cancer

Yeast can be used for the investigation of mitochondrial disease, ATP and energy production, and have established protocols for editing mitochondrial DNA



Cancer

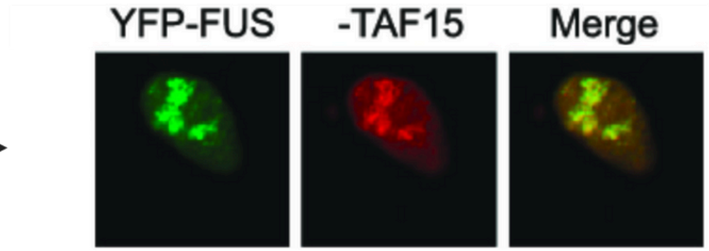
Mitochondrial Disorders

Application in neurodegenrative diseases related to protein misfolding such as Huntingtons, Alzheimers, and ALS

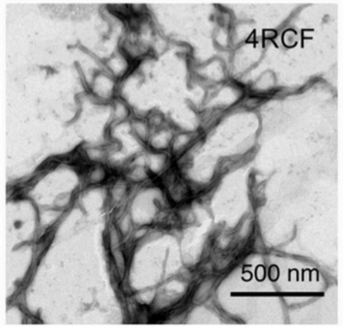
Appropriately Folded Protein

vs

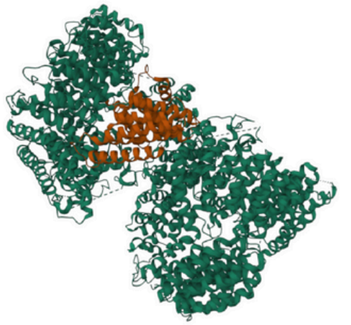
Misfolded Protein



FUS protein in ALS



Tau misfolded protein in Alzheimers



Huntingtin Protein in Huntington Disease

***Obtained from**: High resolution cryoEM structure of huntingtin in complex with HAP40. (2020). https://doi.org/10.2210/PDB6X9O/PDB*

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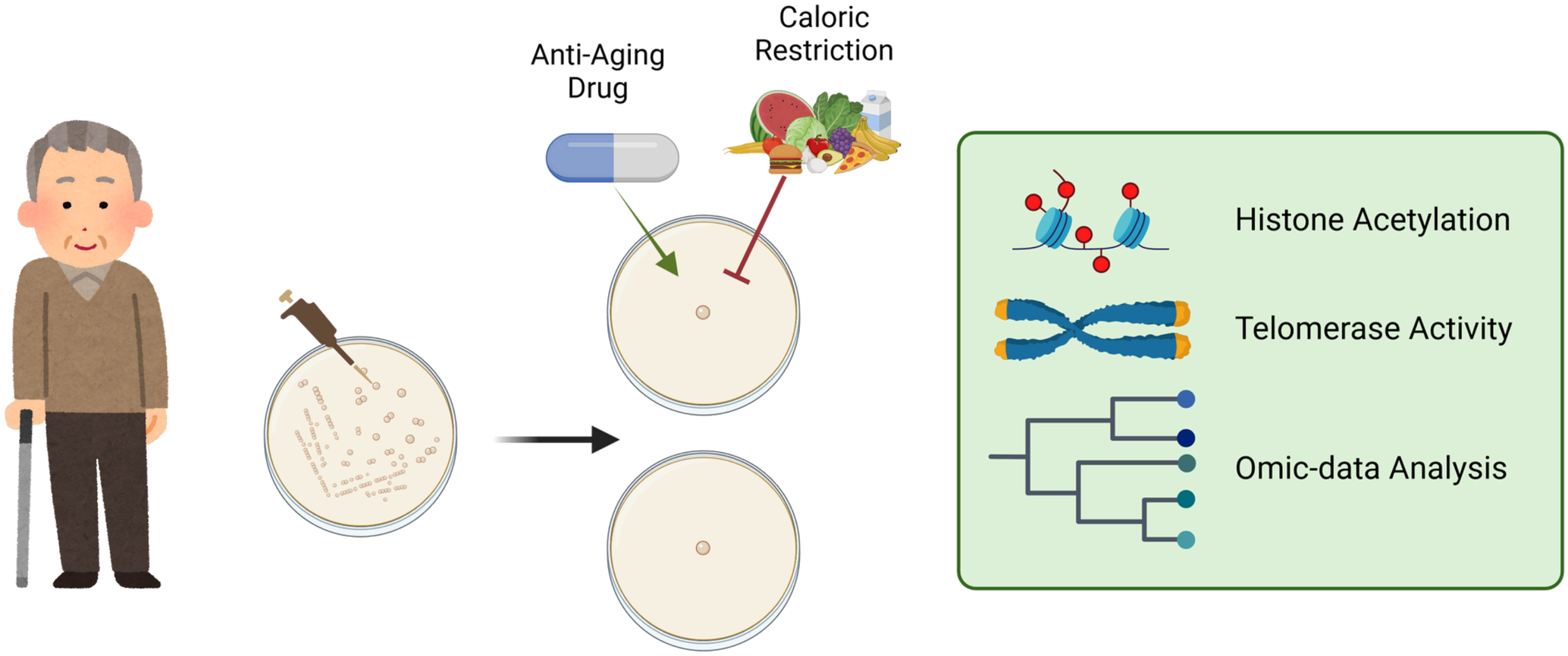
Cancer

Mitochondrial Disorders

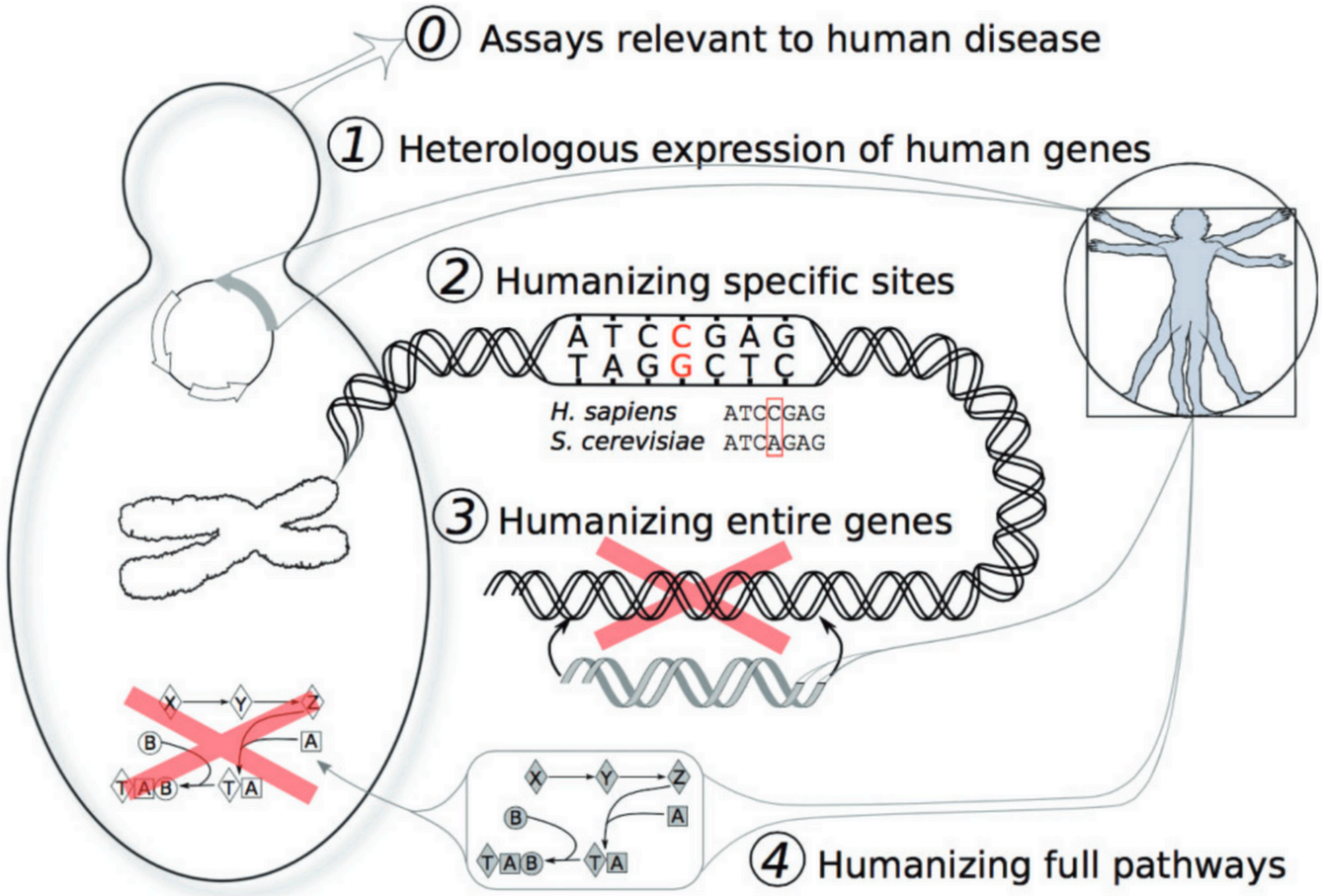
Protein Misfolding

Measuring replicative lifespan (RLS) or the chronological lifespan (CLS) and downstream analysis



Advantages Budding Yeast

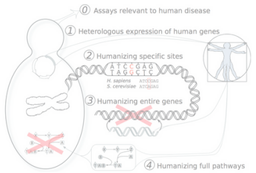
GENETIC HOMOLOGY/ORTHOLOGS AND CAPACITY TO HUMANIZE



- 2/3rds of genome conserved with **direct orthologs.**
- Allows for the study in multiple ways including
  - **Direct**
  - **Heterologous** expression
  - **Humanizing** genes/pathways
- **Post-tranlastional modifications** potential conserved
  - Allows us to measure proteiomic shifts/changes

Obtained from: Laurent, J. M., Young, J. H., Kachroo, A. H., & Marcotte, E. M. (2016). Efforts to make and apply humanized yeast. Briefings in Functional Genomics, 15(2), 155–163. https://doi.org/10.1093/bfgp/elv041

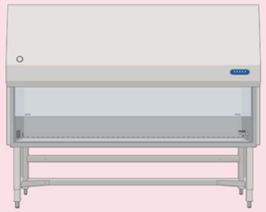
COST AND TIME EFFECTIVE PLATFORM



Genetic Homology

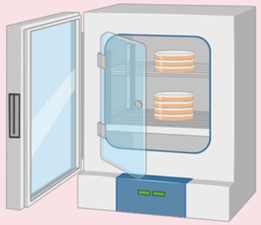
- Basic requirments for cell culture far exceed yeast-culture
  - Dedicated **space**
  - **Specialized media** for prolonged time
  - Trained and employed **personnel**
- Typical culture times
  - Cell culture **1.5-2 weeks**
  - Yeast **1-3 days**

Cell Culture Requirements



Biosafety Cabinets

Basic Culture Media



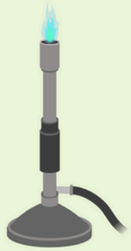
CO_2 & O_2 Regulated Incubator

HQP trained in Cell Culture

Yeast Culture Requirements

Shaking Incubators

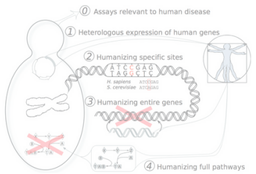
YPx Media



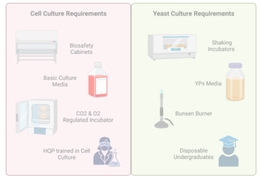
Bunsen Burner

Disposable Undergraduates

WELL-ESTABLISHED AND EASILY DISCERNABLE PHENOTYPES

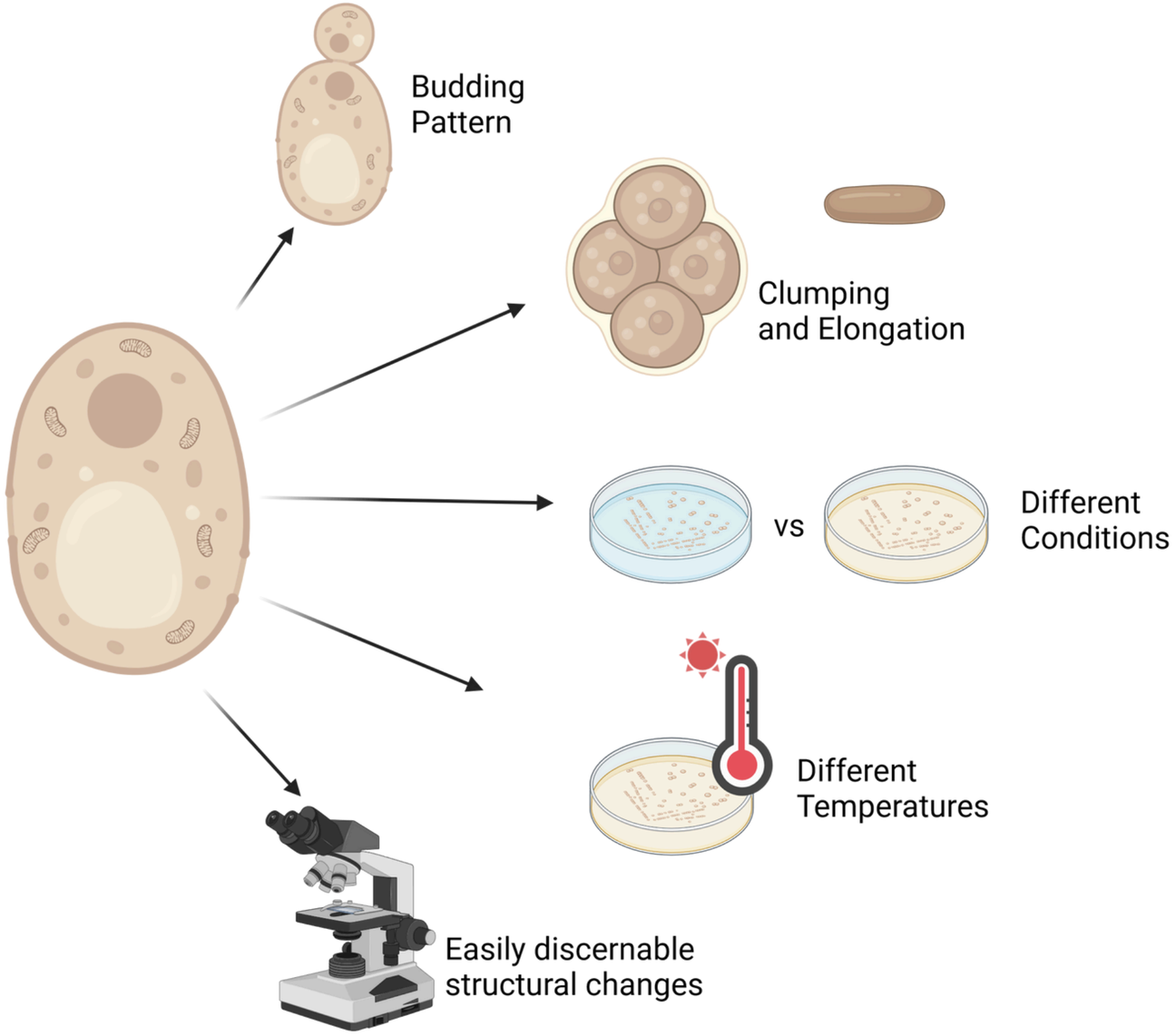


Genetic Homology



Cost & Time

- Growth characteristics are **easily measurable**
- Can have variations in:
  - Budding pattern
  - Pysical Properties
  - Metabolism/Energy Utilization
  - Discernable organelle alterations



Limitations of Budding Yeast

LACKS COMPLEX MULTICELLULAR INTERACTIONS

- Lacks tissue specific interactions seen in multicellular organisms
  - Difficulty modelling tissue-specific diseases
- In humans organs have specific intercellular communication --> unique environments
- Cannot determine what different manifestations there are of a single mutation

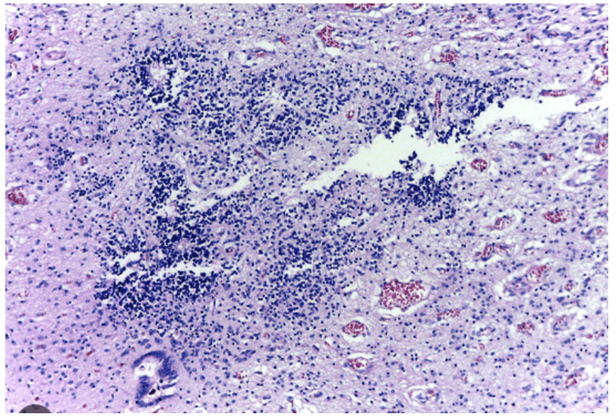


Figure 1. Microscopic brain image showing an area with immature nervous tissue with neural tube structures and gliosis

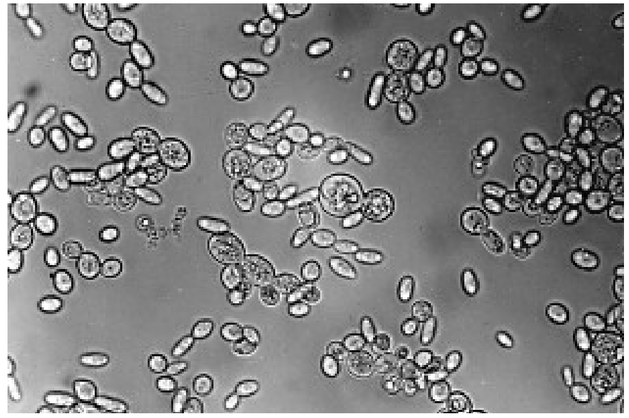
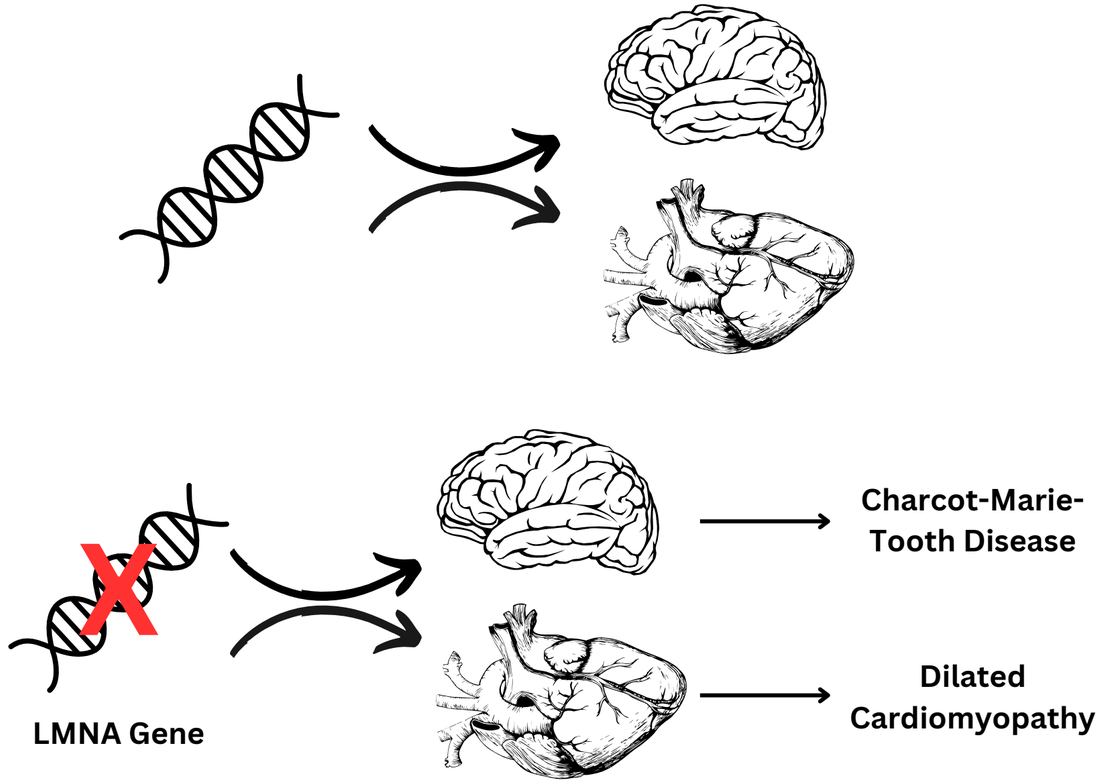


Figure 2. Budding Yeast

Figure 1 Obtained From: (PDF) Cyclopia and proboscis - the extreme end of holoprosencephaly. (n.d.). Retrieved October 26, 2024, from https://www.researchgate.net/publication/323957694_Cyclopia_and_proboscis_-_the_extreme_end_of_holoprosencephaly
Figure 2 Obtained From: Budding Yeast. (n.d.). Retrieved October 26, 2024, from https://www.biology-pages.info/Y/Yeast.html

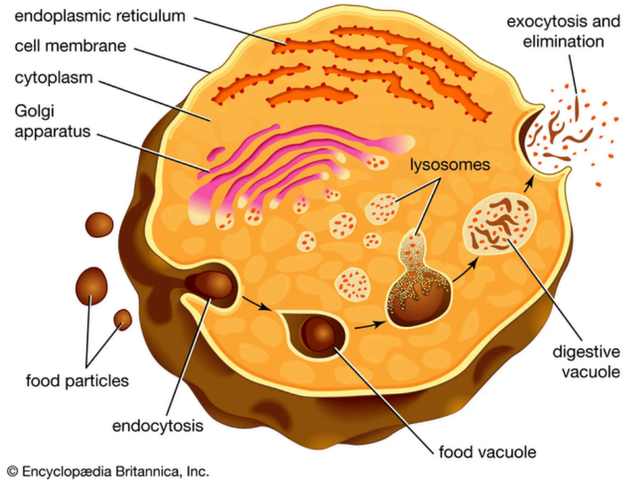
LIMITATIONS IN MODELLING HUMAN-SPECIFIC GENES

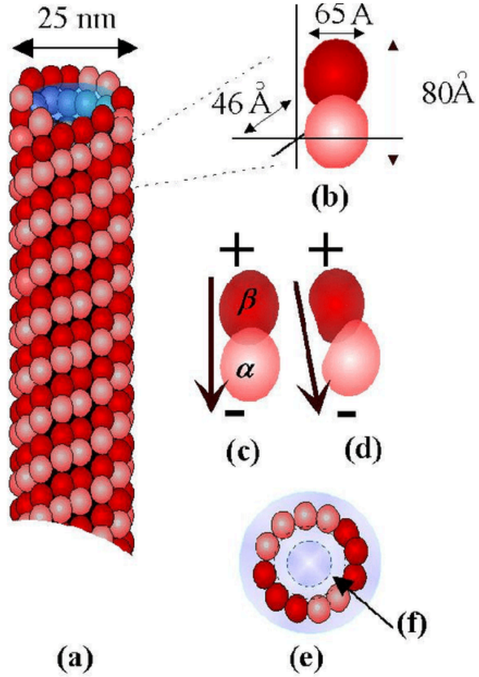
- Human genes that are highly specialized, or have tissue-specific functions, do not have yeast counterparts
- Absence = cannot model diseases rooted in these genes
  - immunity, brain function, complex organ development
- Cannot model pathways and cellular behaviour influenced by these genes

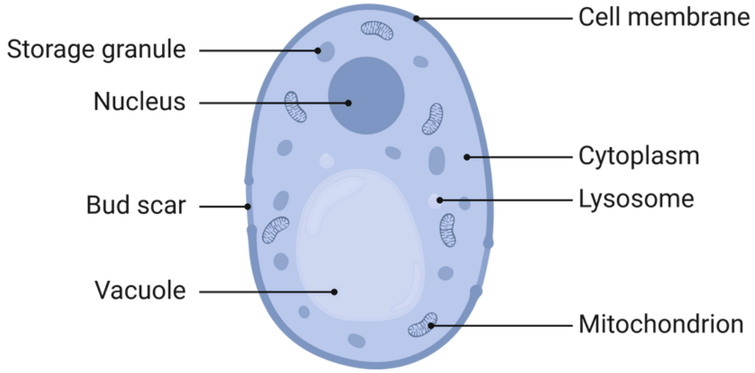


LACK MORPHOLOGICAL DIVERSITY CHARACTERISTIC OF MAMMALIAN CELLS

- Single large vacuole vs. multiple small vesicles
  - vesicular trafficking
  - compartmentalization of metabolic processes
  - cell signalling
- Differences in Microtubule Dynamics
  - yeast lack compact MT lattice
  - cannot model MT-related processes: intracellular transport





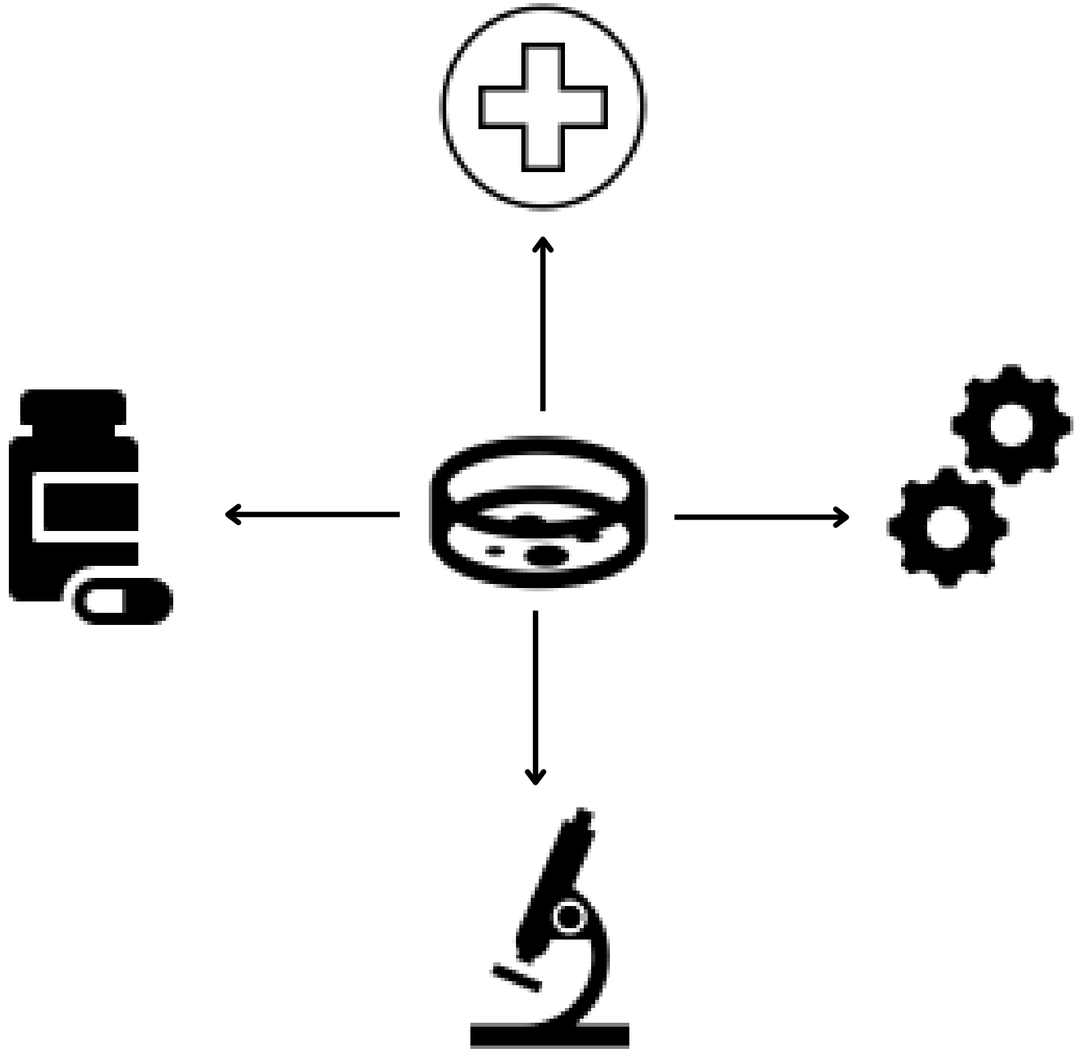


Microtubule Image Obtained From: Mershin, A., Sanabria, H., Miller, J. H., Nawarathna, D., Skoulakis, E. M. C., Mavromatos, N. E., Kolomenskii, A. A., Schuessler, H. A., Luduena, R. F., & Nanopoulos, D. V. (2006). Towards Experimental Tests of Quantum Effects in Cytoskeletal Proteins. Frontiers Collection, Part F941, 95–170. https://doi.org/10.1007/3-540-36723-3_4
Mammalian Cell Obtained From: https://www.britannica.com/science/vacuole
Yeast Cell Obtained From: BioRender

Future Implications

FUTURE IMPLICATIONS

1. **Disease Modelling and Drug Screening**
   - Simplicity and rapid growth = easy modelling
2. **Synthetic Biology and Biotechnology Applications**
   - Engineered to make valuable compounds
3. **Gene and Cellular Pathway Discovery**
   - Powerful tool for discovery of new genetic pathways



Thank You

References

Images

Made using BioRender

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