Identifying genes required for *Saccharomyces cerevisiae* growth in mucin

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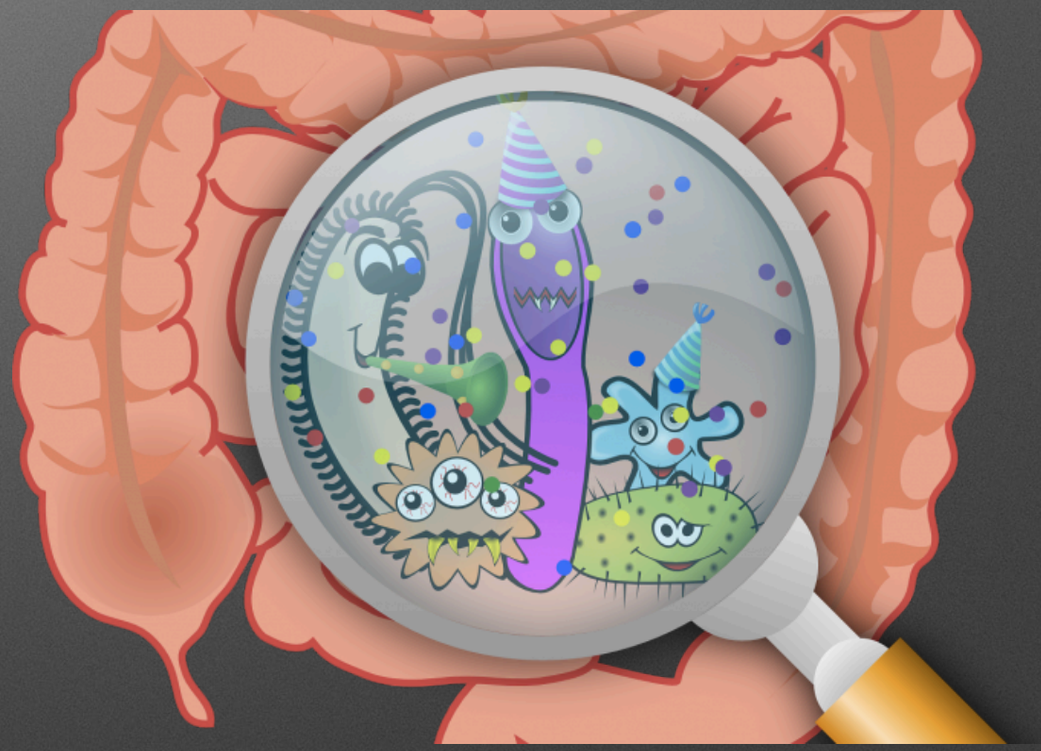
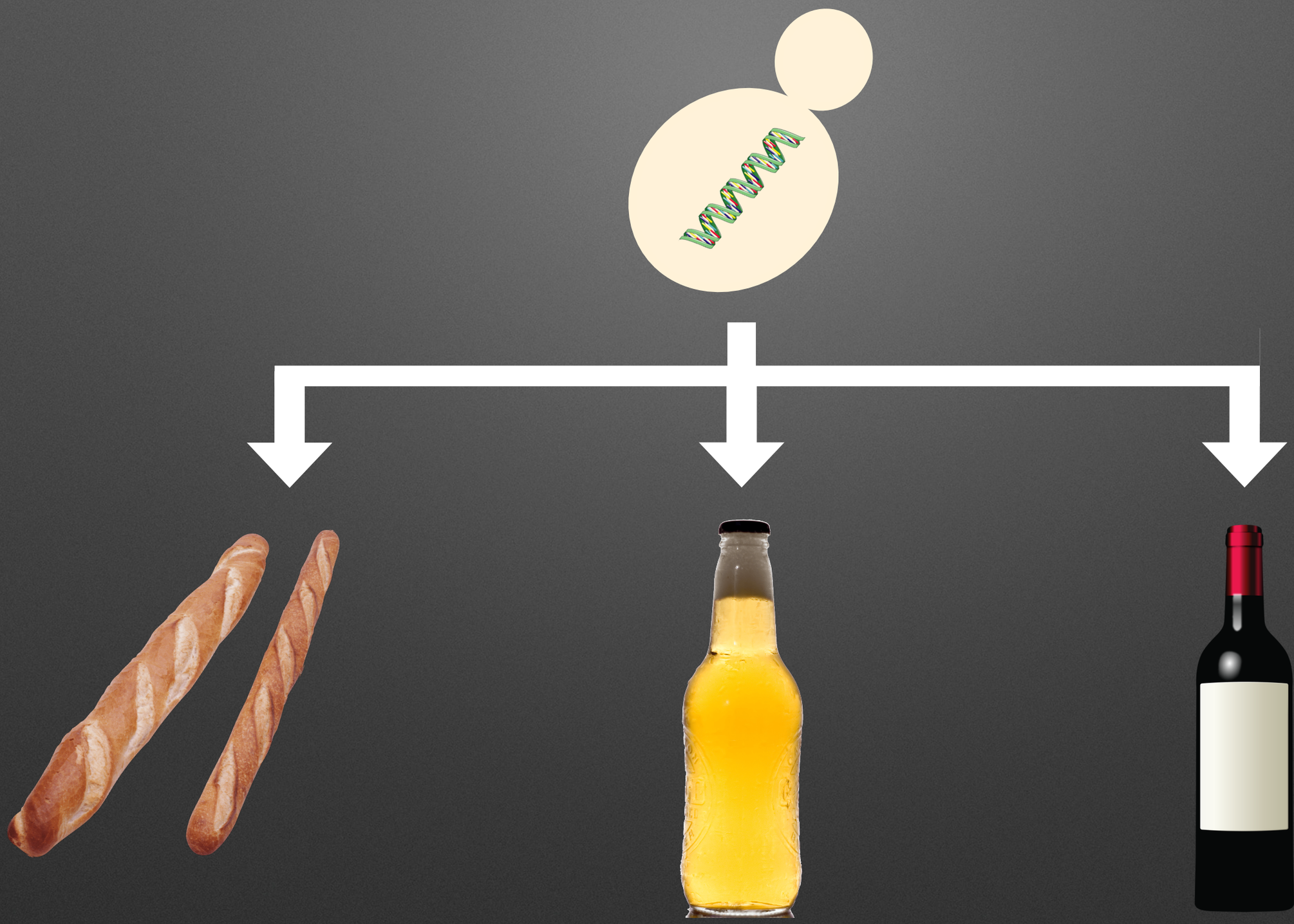
Microbiome and gut health

- Gut Physiology
- Metabolism & Nutrition
- Immune Function
- Pathogenesis (ex. IBD)



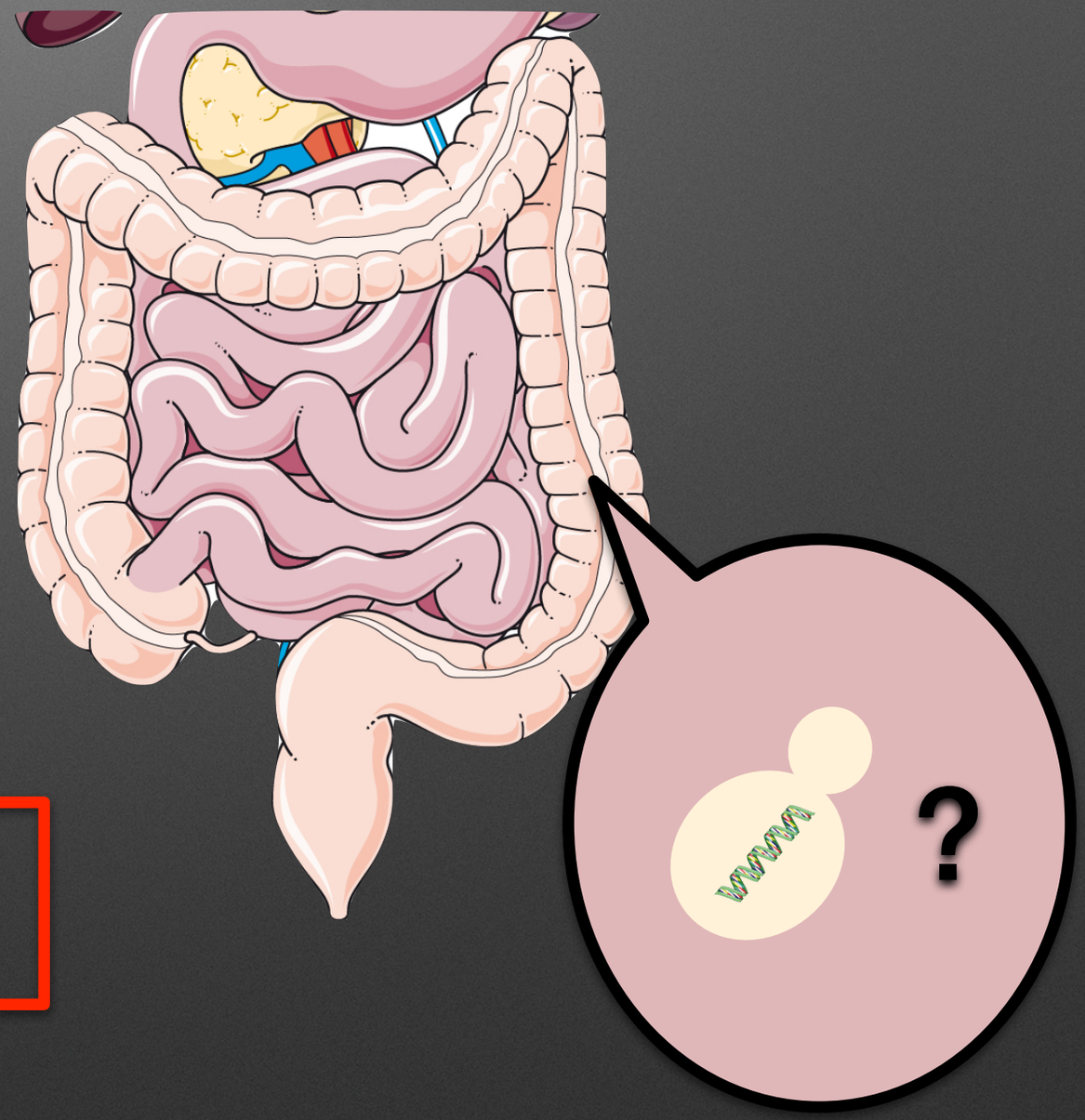
Metagenomics → NEW Gut Mycobiota

Dietary Yeast: *Saccharomyces cerevisiae*



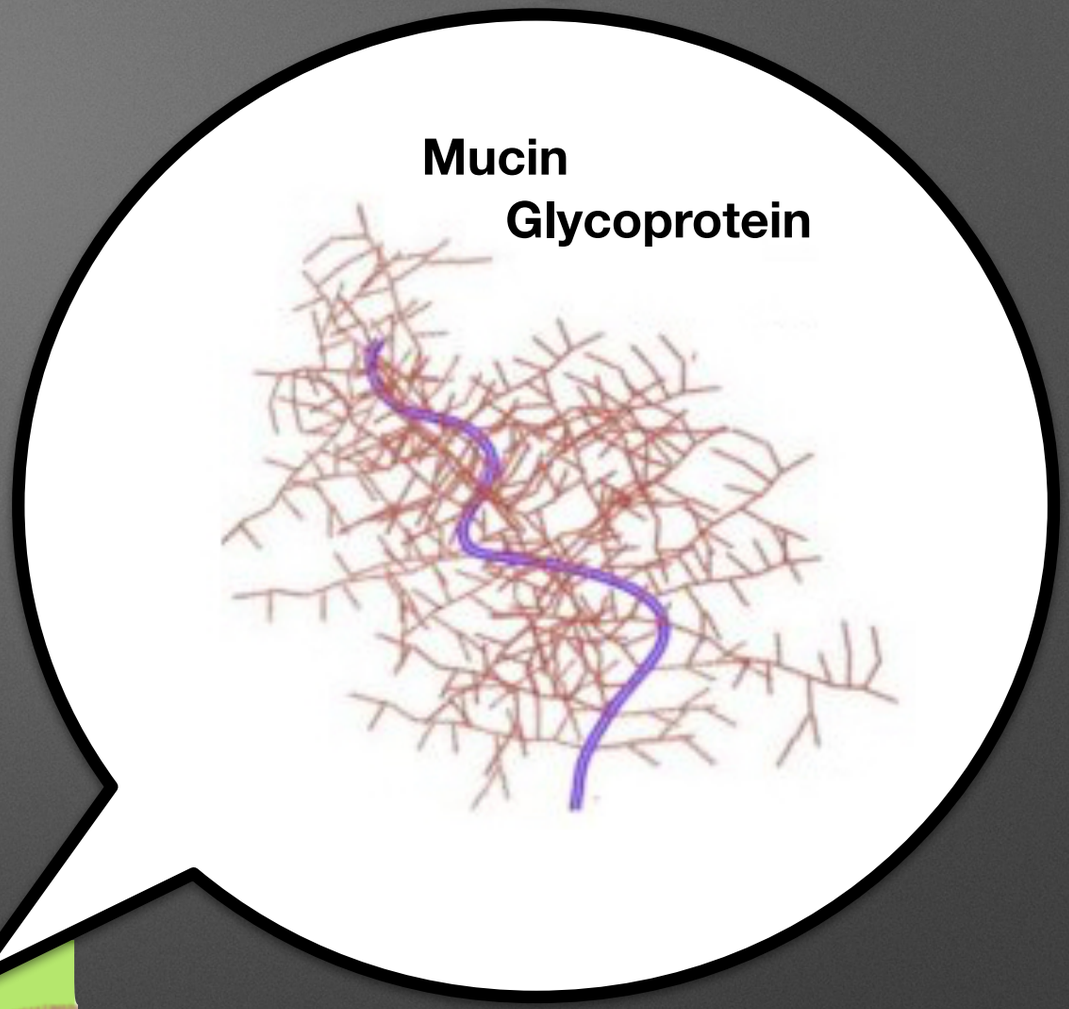
S. cerevisiae and the gut environment

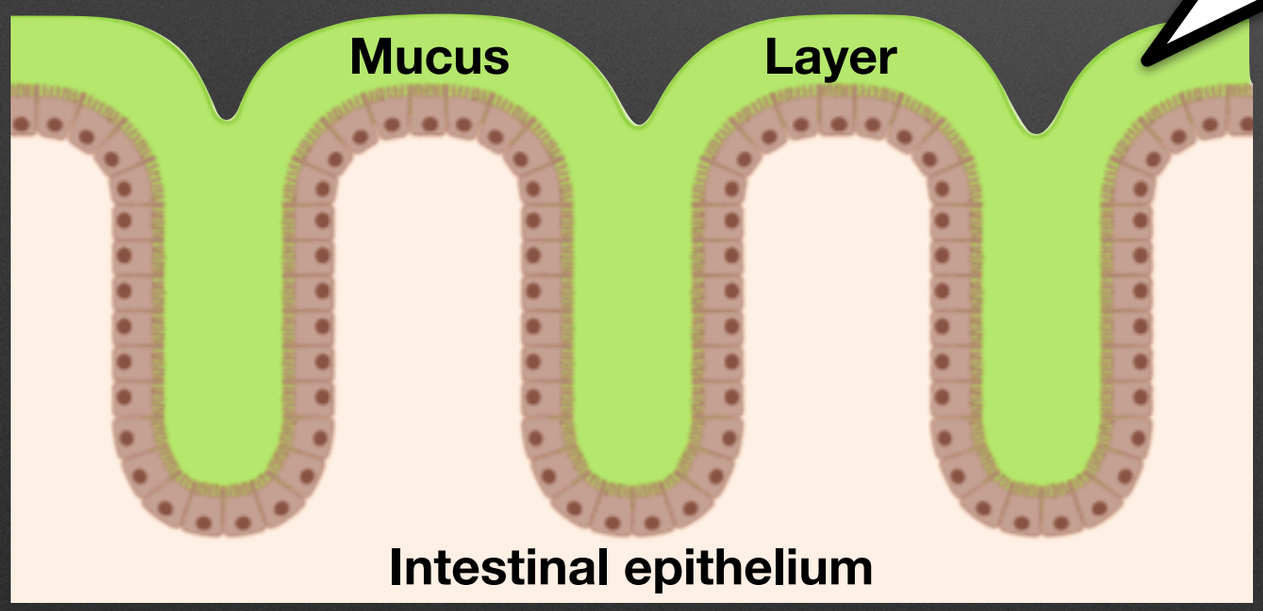
- Representative Colon Conditions:
  - O_2 limiting ✓
  - Slightly acidic ✓
  - 37°C ✓
- Mucin-rich mucus layer



Mucin in the GI mucus layer

- Protector of the intestinal membrane
- 200-200,000 kDa in size
- O-linked glycosylation





Project Questions

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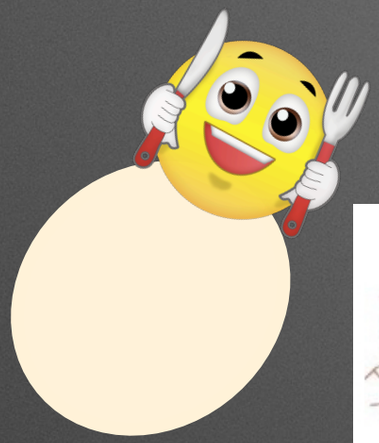
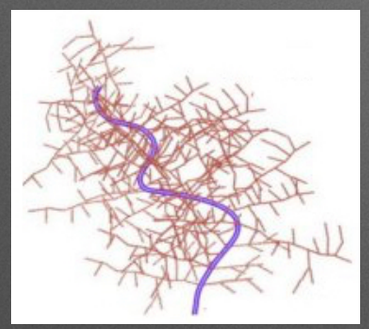
Project Questions





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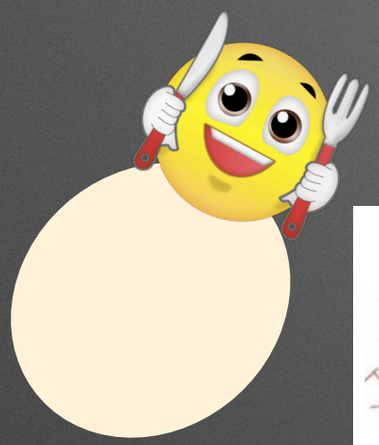
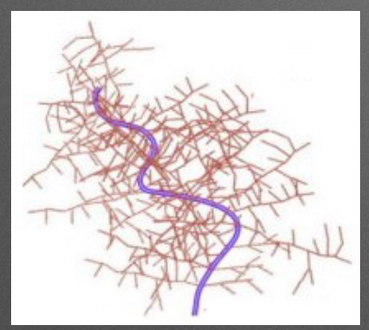
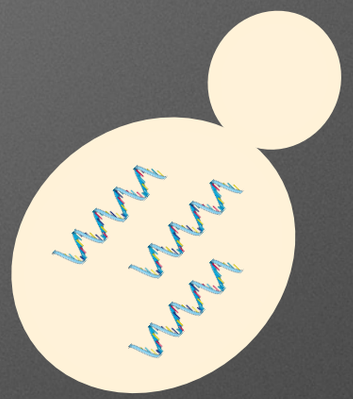
Project Questions

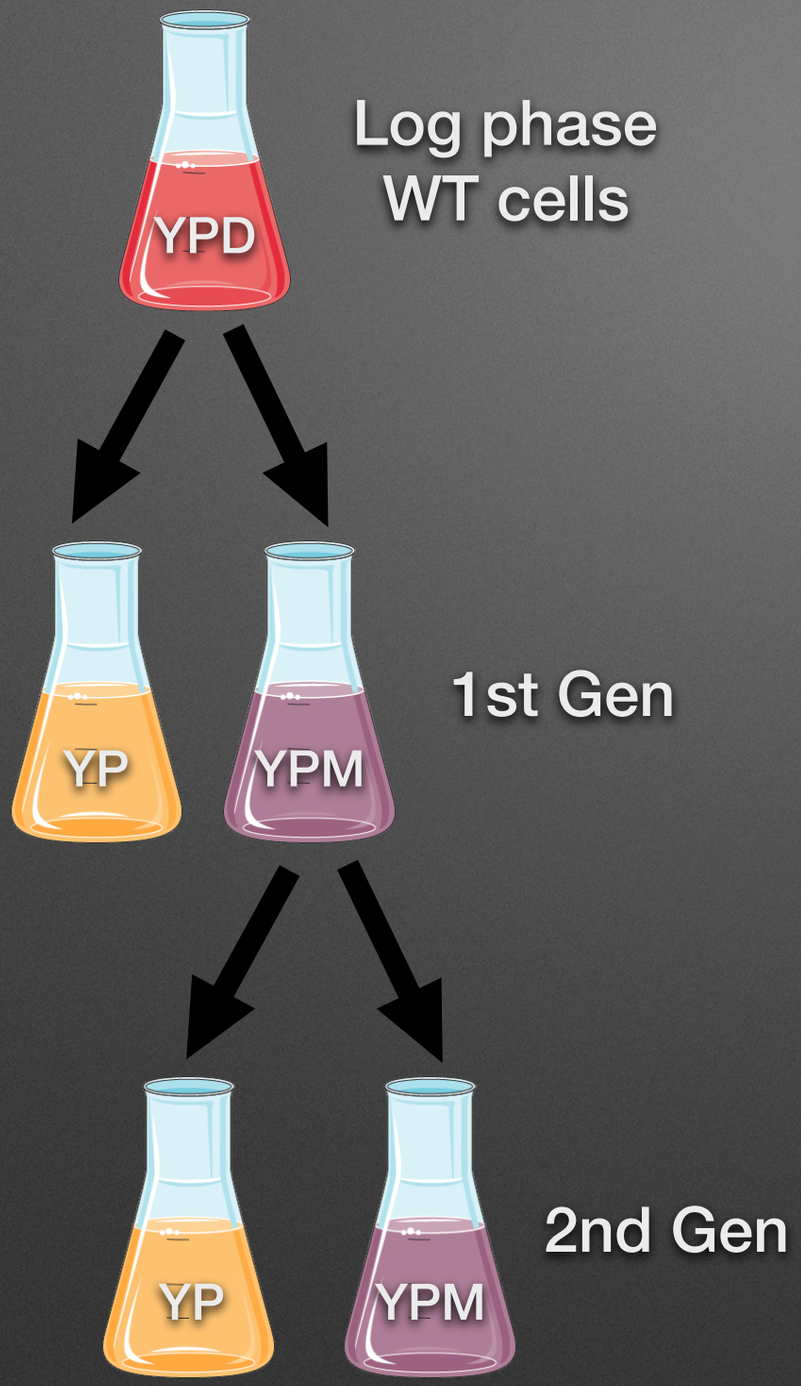


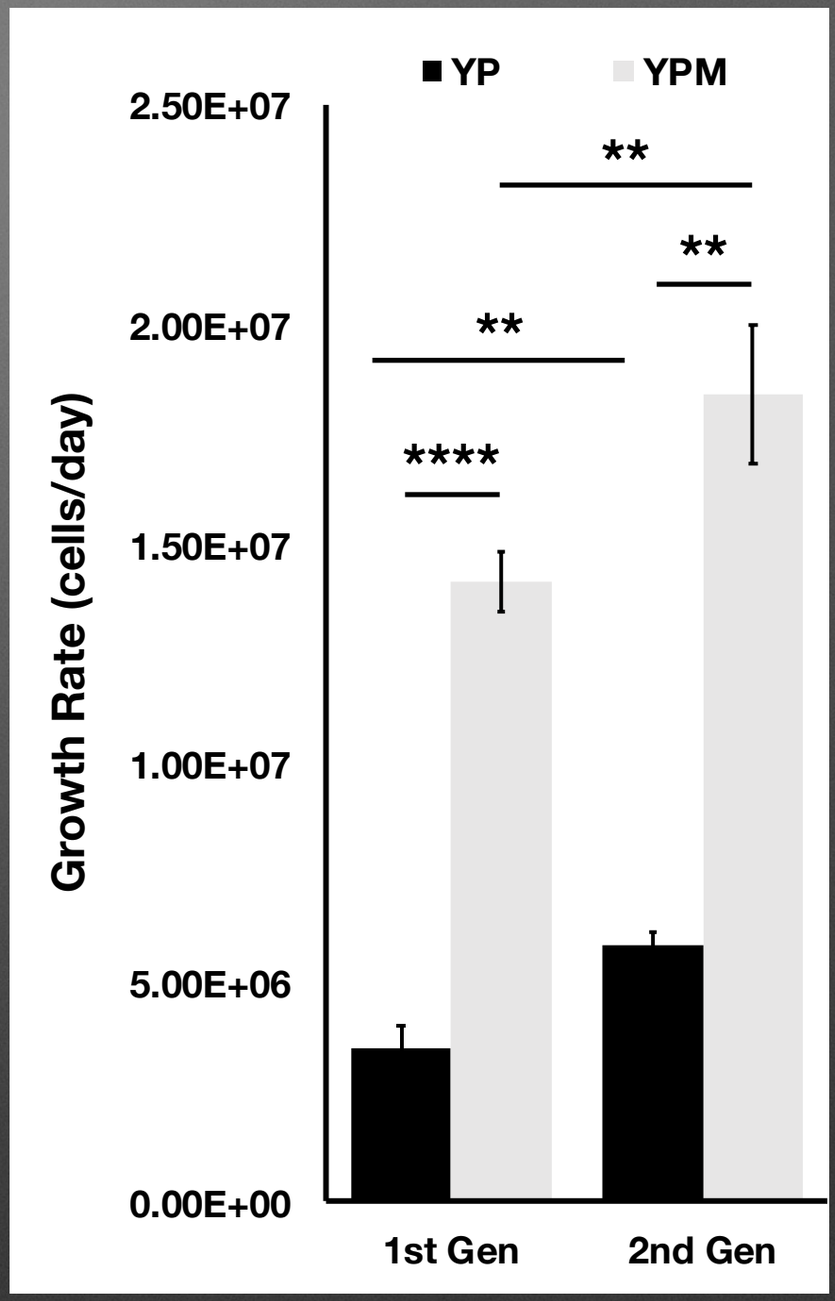




Can *S. cerevisiae* use mucin as an energy source?

S. cerevisiae can grow and adapt to growth in mucin

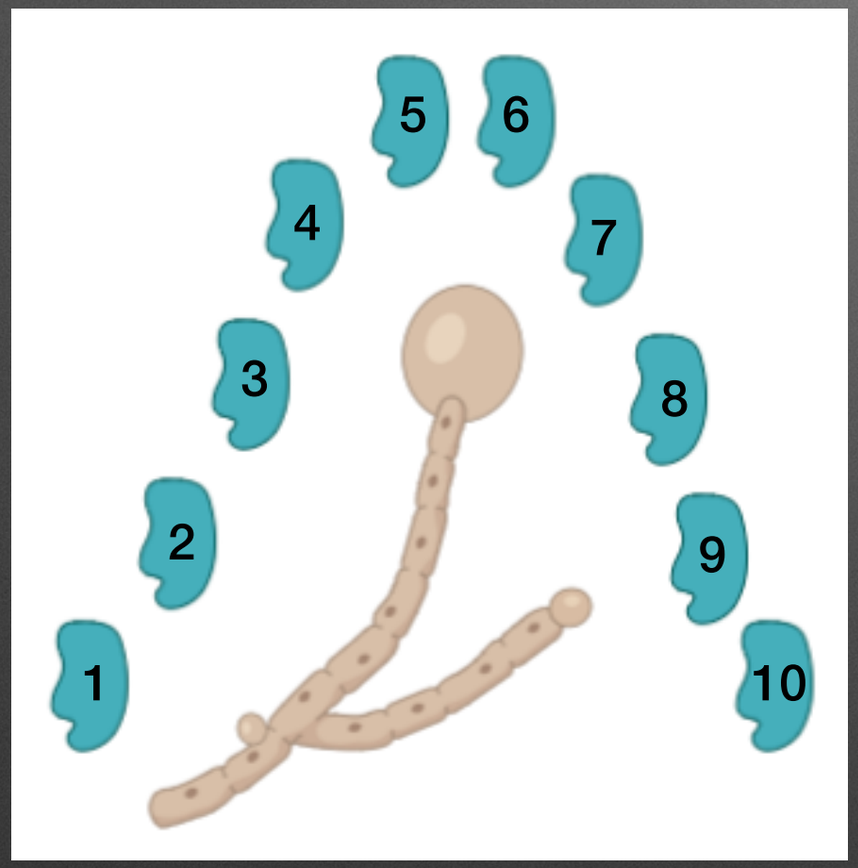




How does *S. cerevisiae* grow in mucin?

Candida albicans and SAPs

C. albicans



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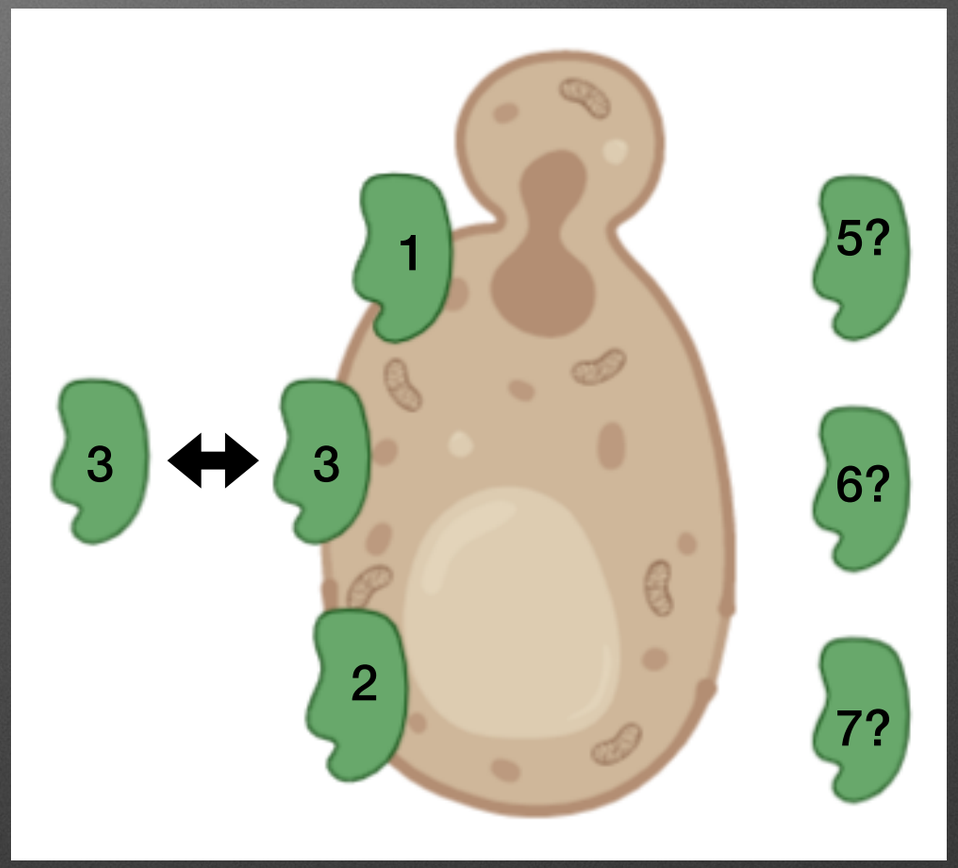
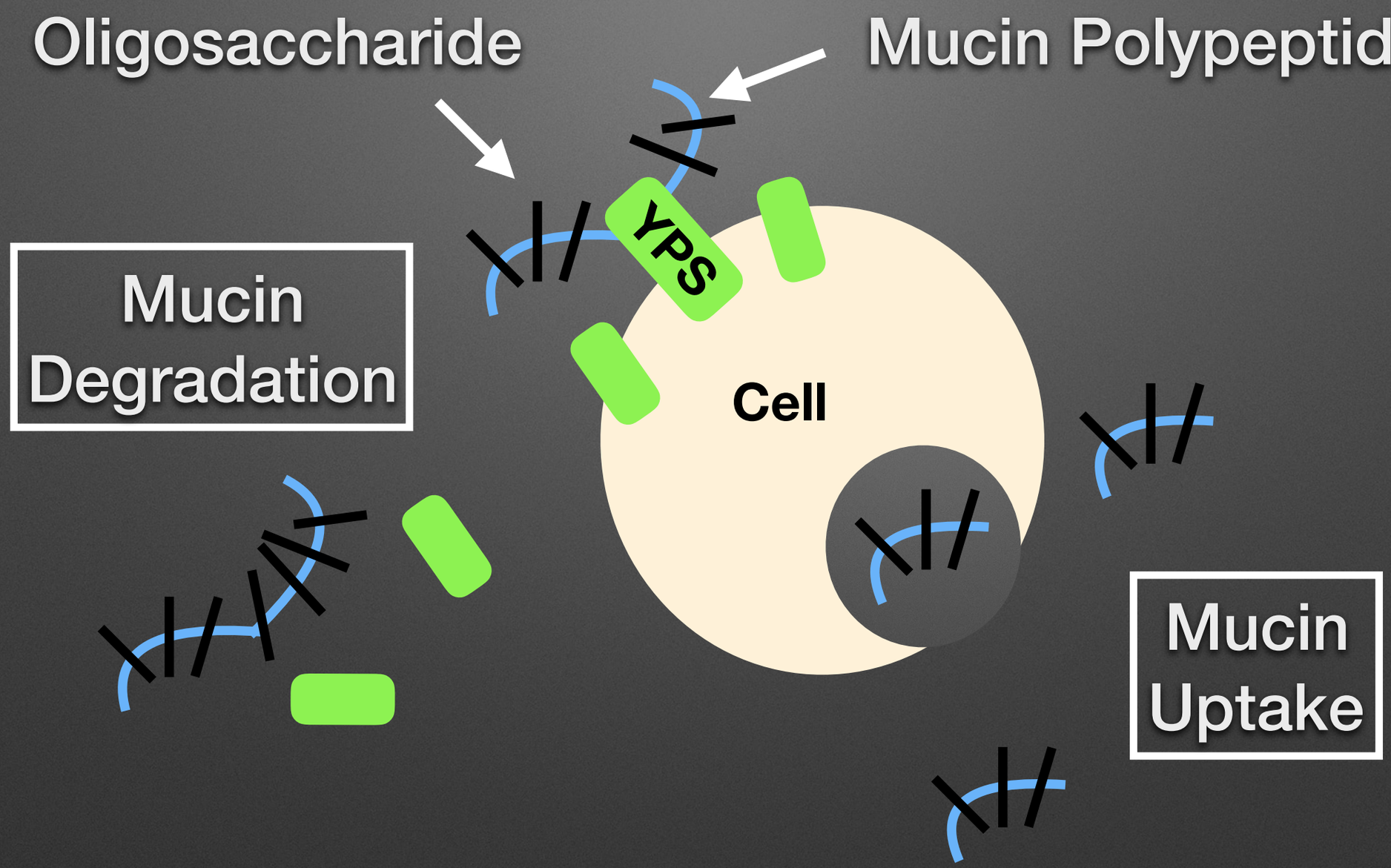
S. cerevisiae



Secreted Aspartyl Proteases (SAP)

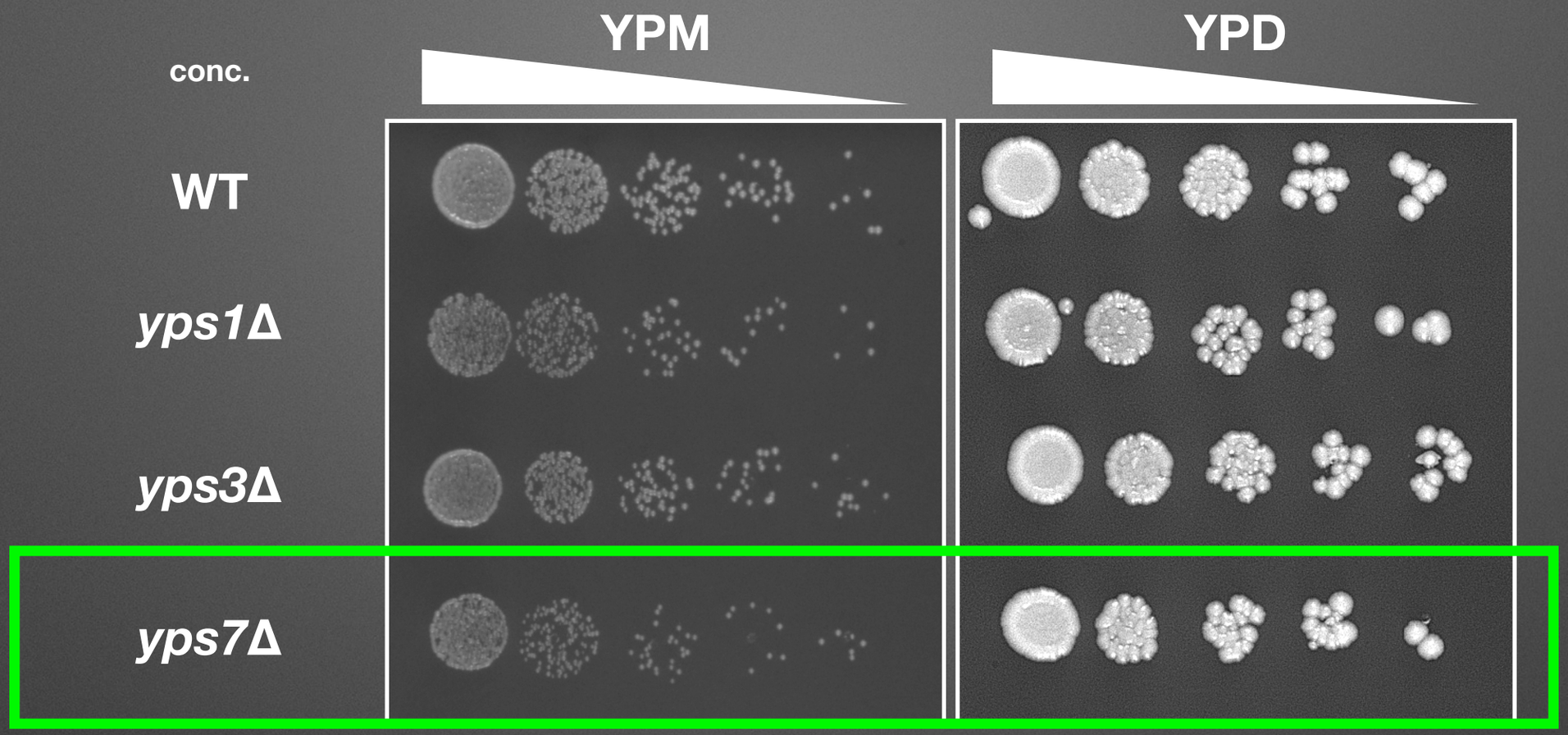
Yapsin Proteins (YPS)

Yapsin proteins



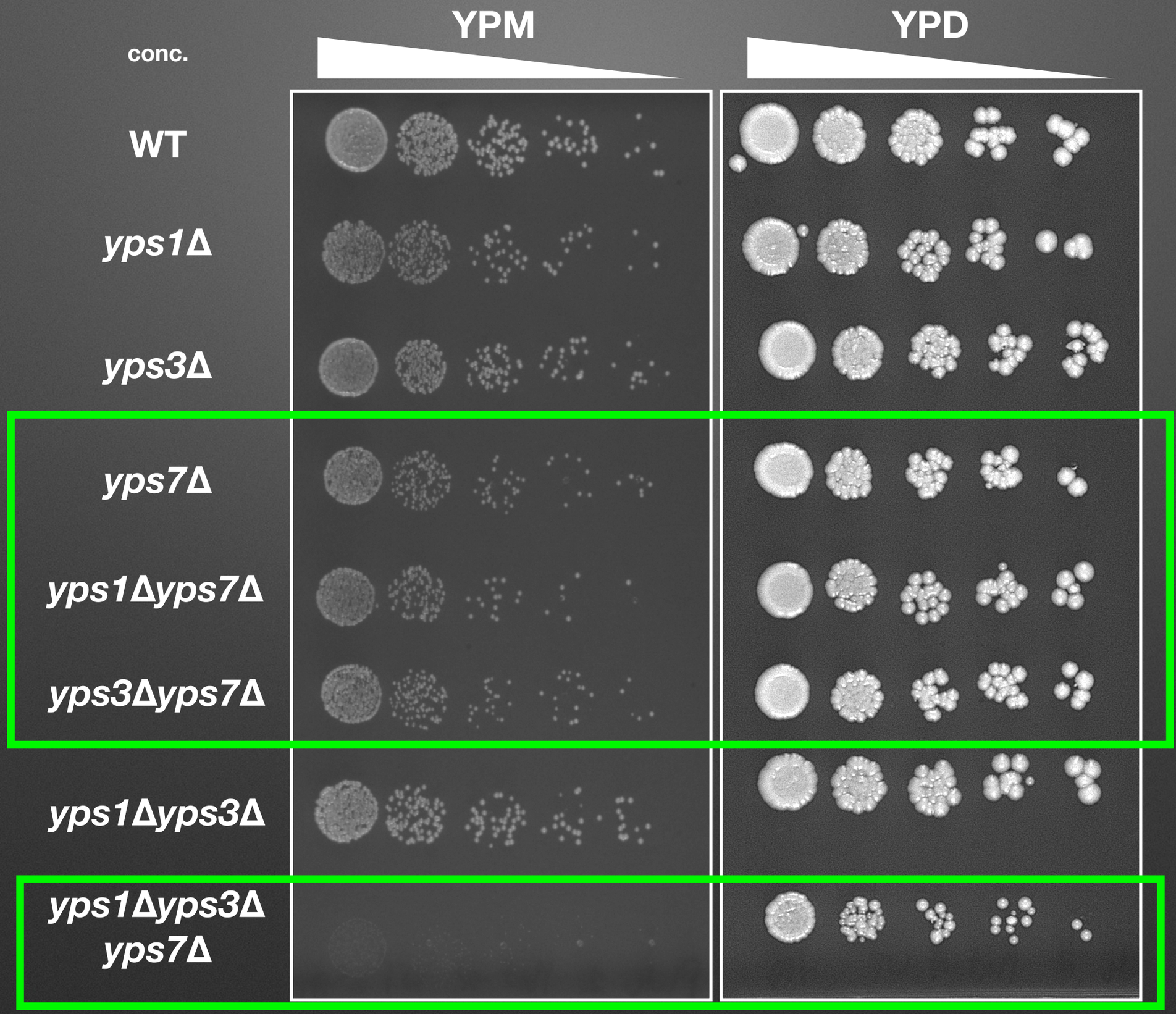
- Focus on Yps1, Yps3, Yps7

Mutants with a *yps7Δ* have a growth defect on YPM

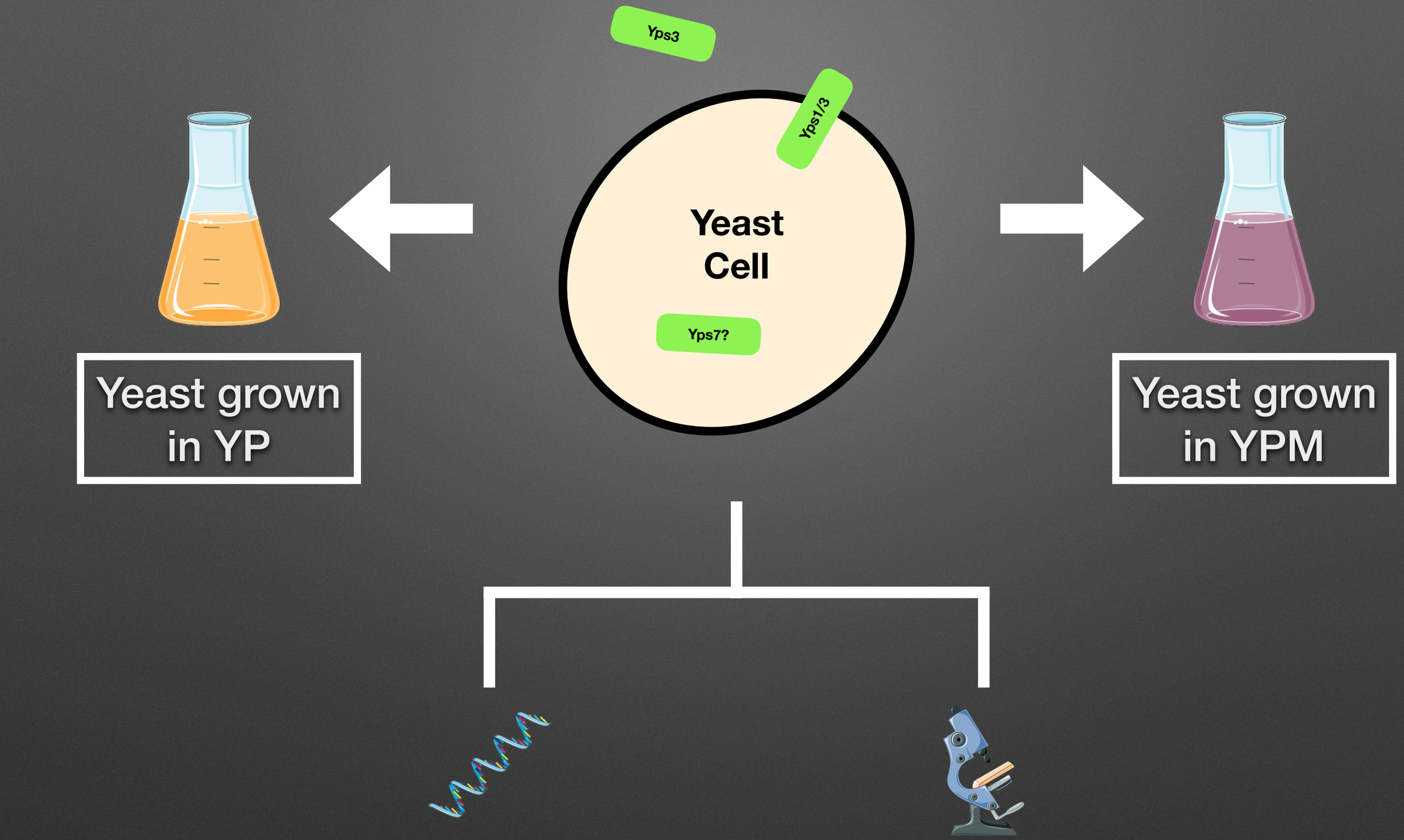


*conditions: 30C for 3 days

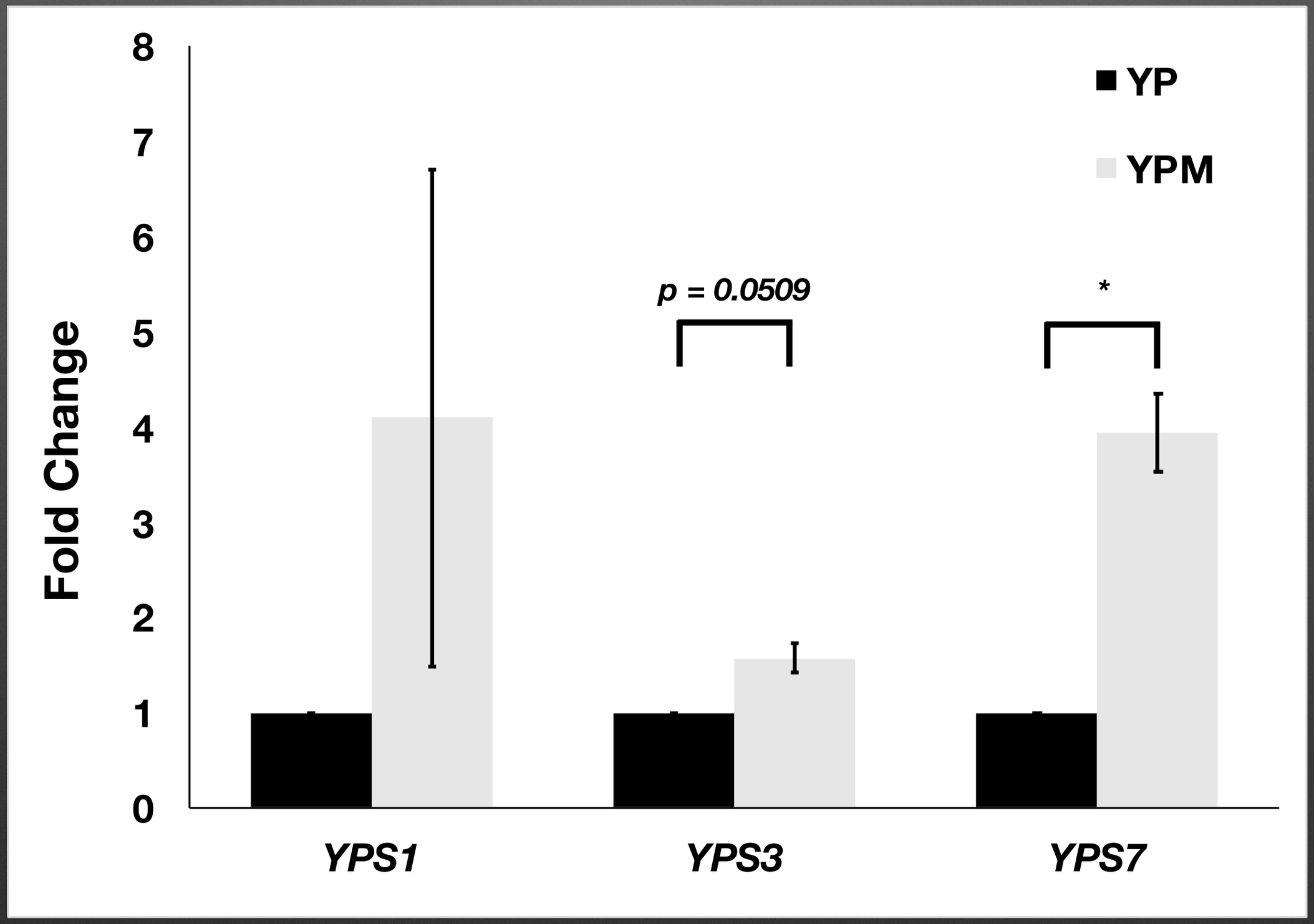
Mutants with a *yps7Δ* have a growth defect on YPM



*conditions: 30C for 3 days

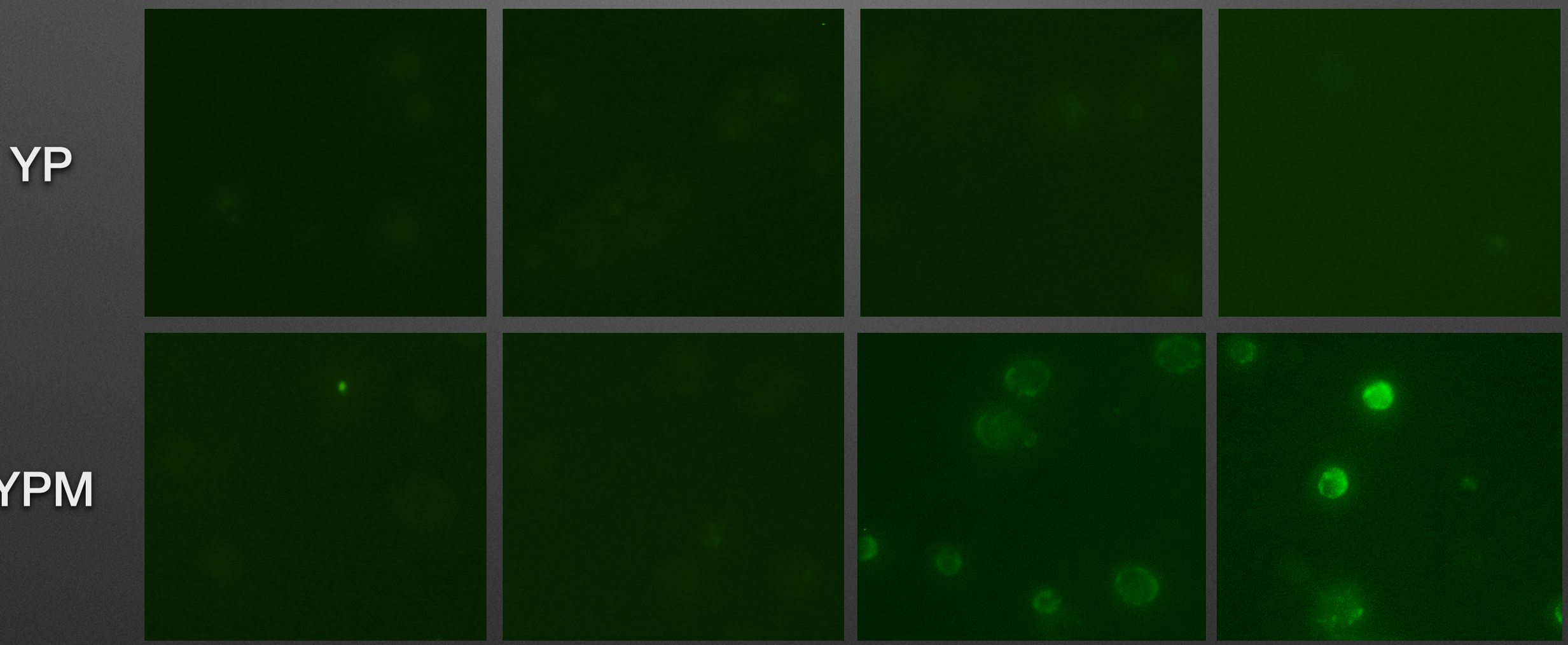

Yps3
Yps1/3
Yeast
Cell
Yps7?
Yeast grown
in YP
Yeast grown
in YPM
mRNA expression
(qPCR)
protein localization
(fluorescence microscopy)

YPS genes are upregulated in mucin media



n = 3, * = p<0.05

Mucin induces fluorescence for Yps3-GFP and Yps7-GFP



What are some other molecular networks *S. cerevisiae* uses to grow in mucin?

Mucin screen methodology

YPD

Haploid DMA

YP

YPM

Comparative Analysis (SGATools)

Mucin Suppressor

YP ● < ⬤ YPM

MRS2	*LPD1*	*MZM1*
SOK1	*SNF1*	*YPS7*
DEF1	*RAI1*	*GSH1*
VPS27	*GRR1*	*RPL43A*
VPS3	*LOA1*	*YIM2*

Mucin Sensitive

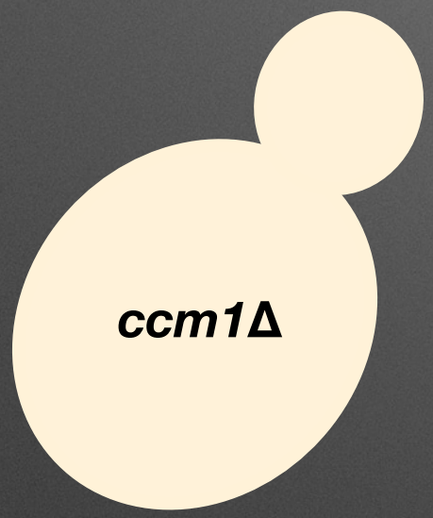
YP ⬤ > ● YPM

CCM1

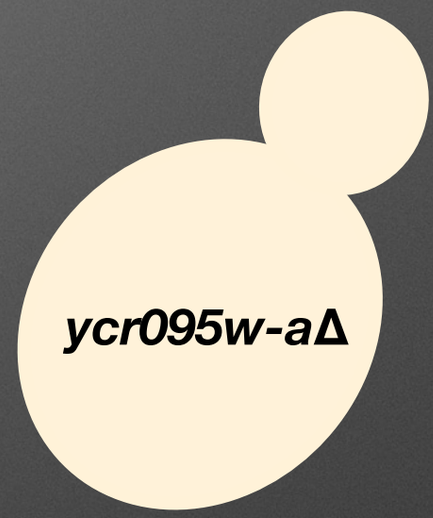
YCR095W-A

- Mucin Suppressor
- Mucin Sensitive
- Cell Wall Maintenance
- Ion/Proton Transport
- Lipid Homeostasis
- Mitochondrial Function
- Protein Degradation
- Signalling
- Stress Response
- Transcription/ RNA Processing
- Translation
- Unknown

Mucin metabolic and mitochondrial impact



- helps assemble components of the ETC



- low localization signal to the mitochondria

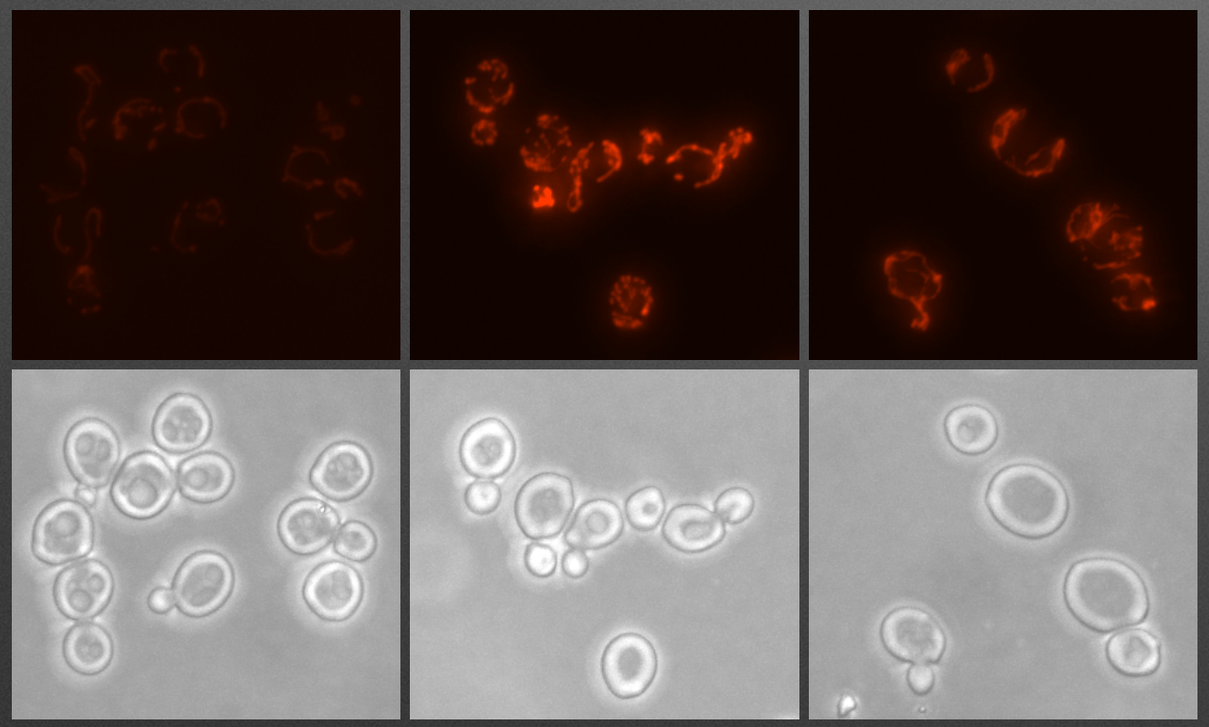
Mucin increases mitochondrial volume

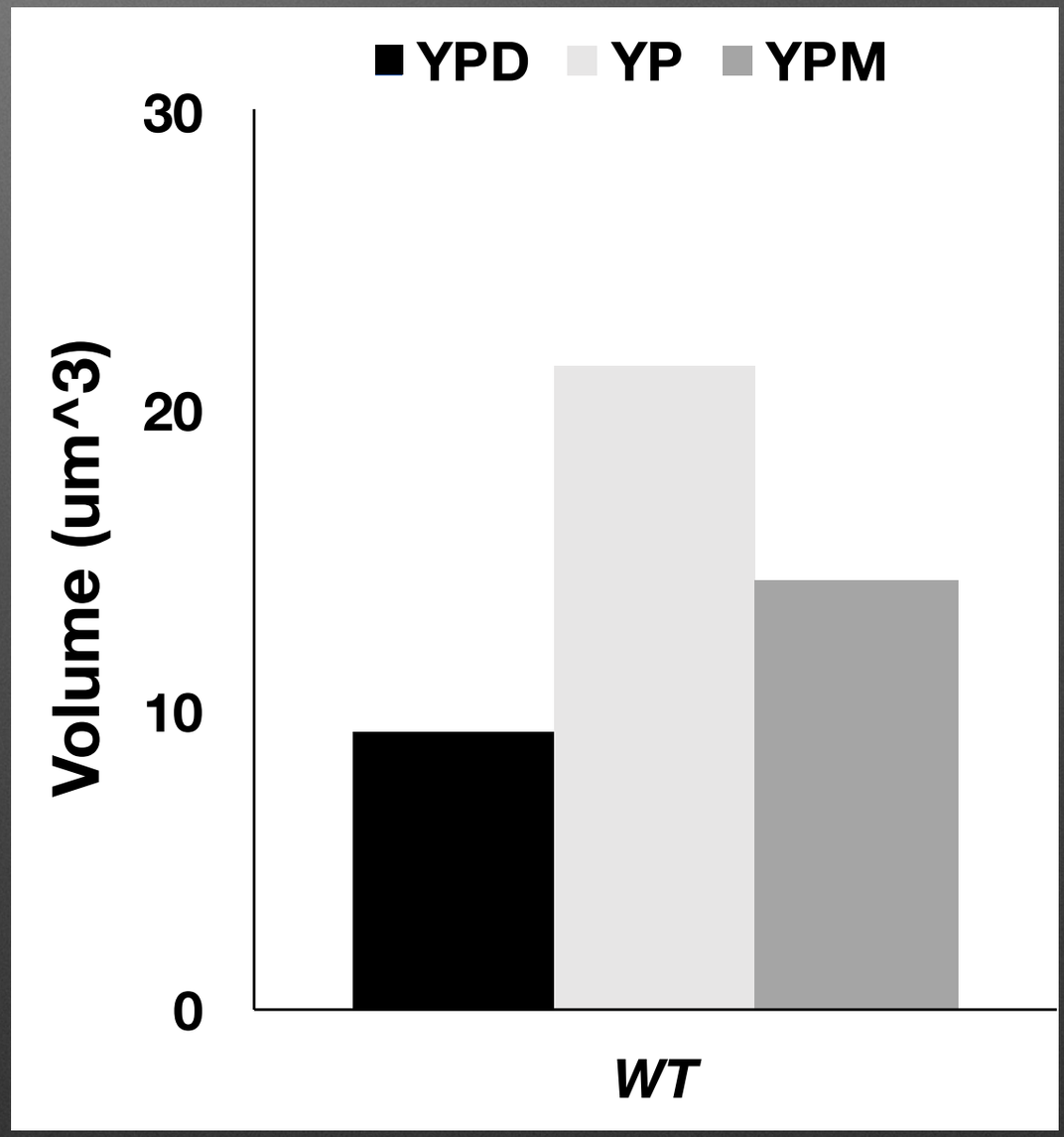
WT

YPD YP YPM

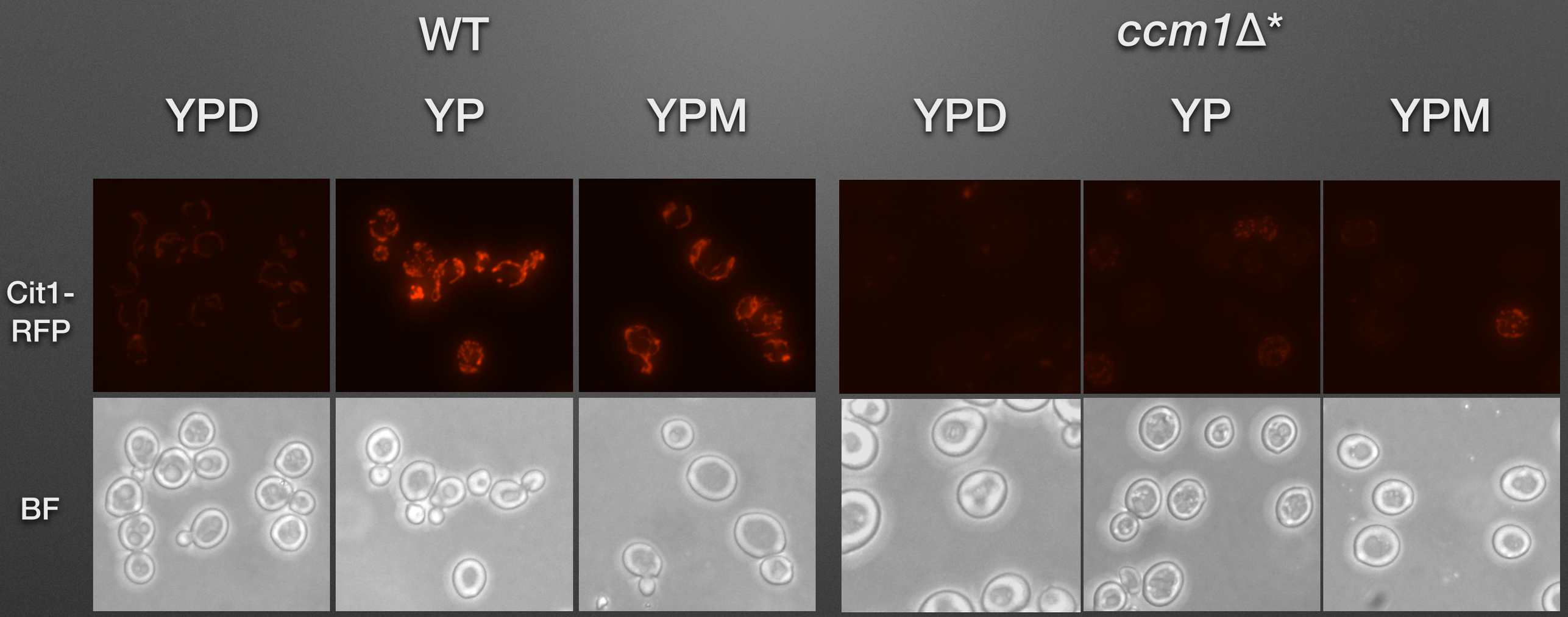
Cit1-RFP

BF



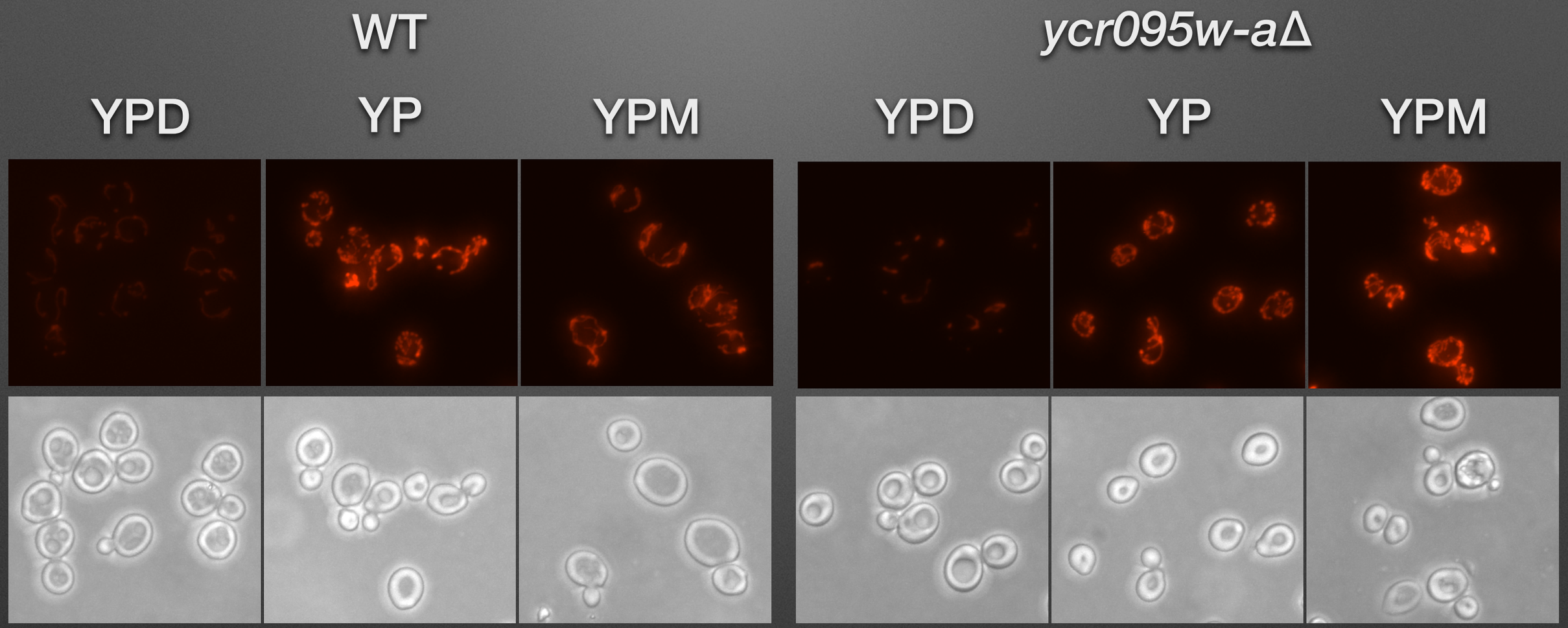


*ccm1*Δ reduces Cit1 synthesis compared to WT

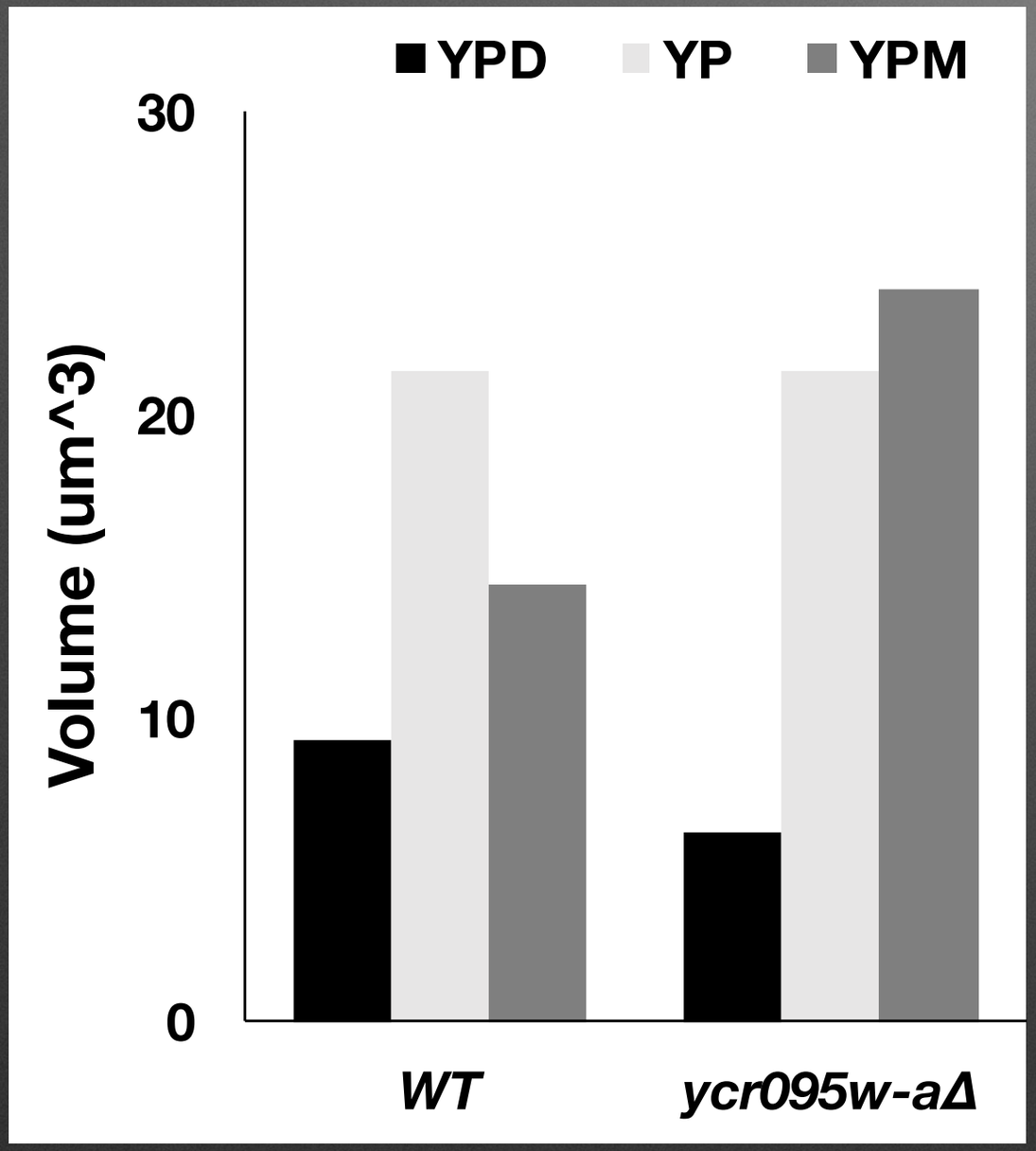


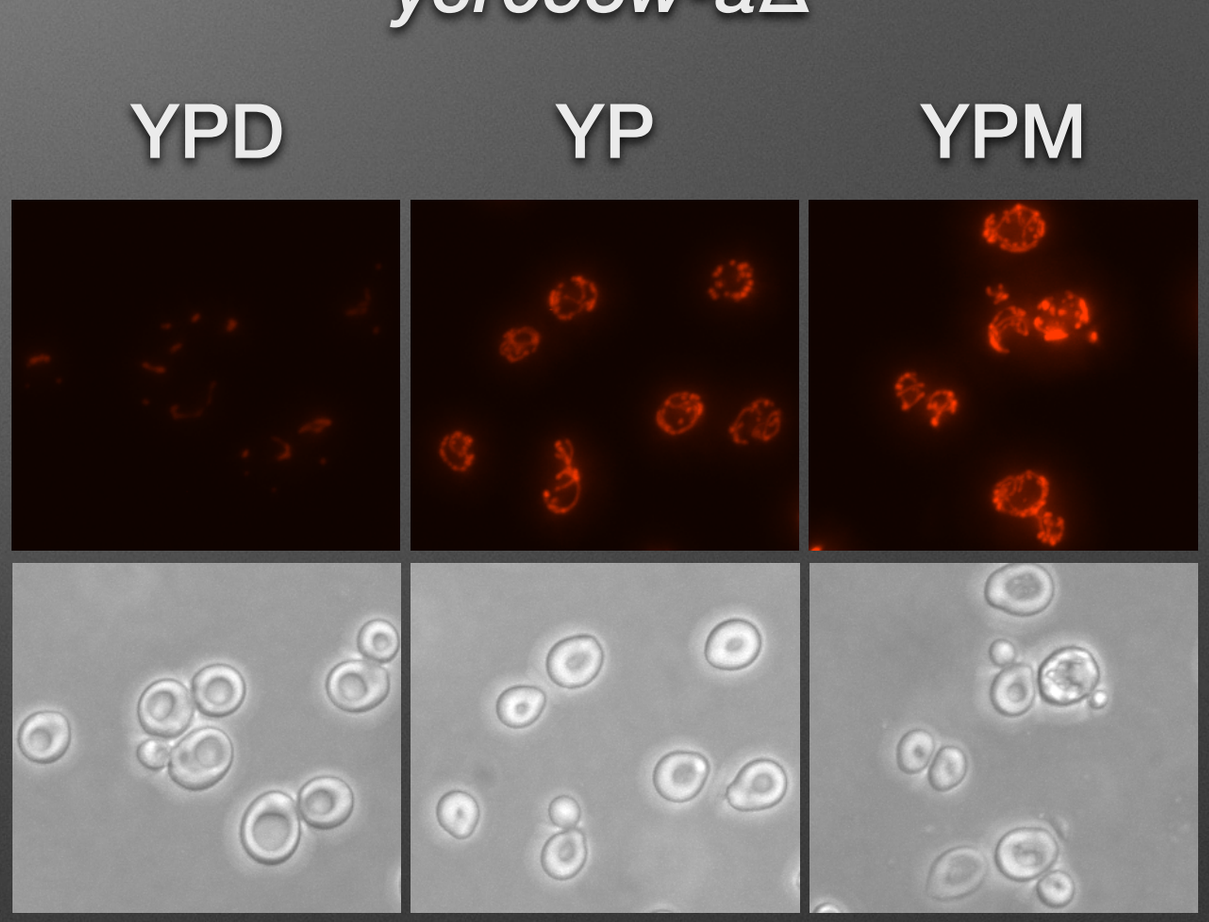
* - 10s expo time

Mucin increases mitochondrial volume in a *ycr095w-aΔ*

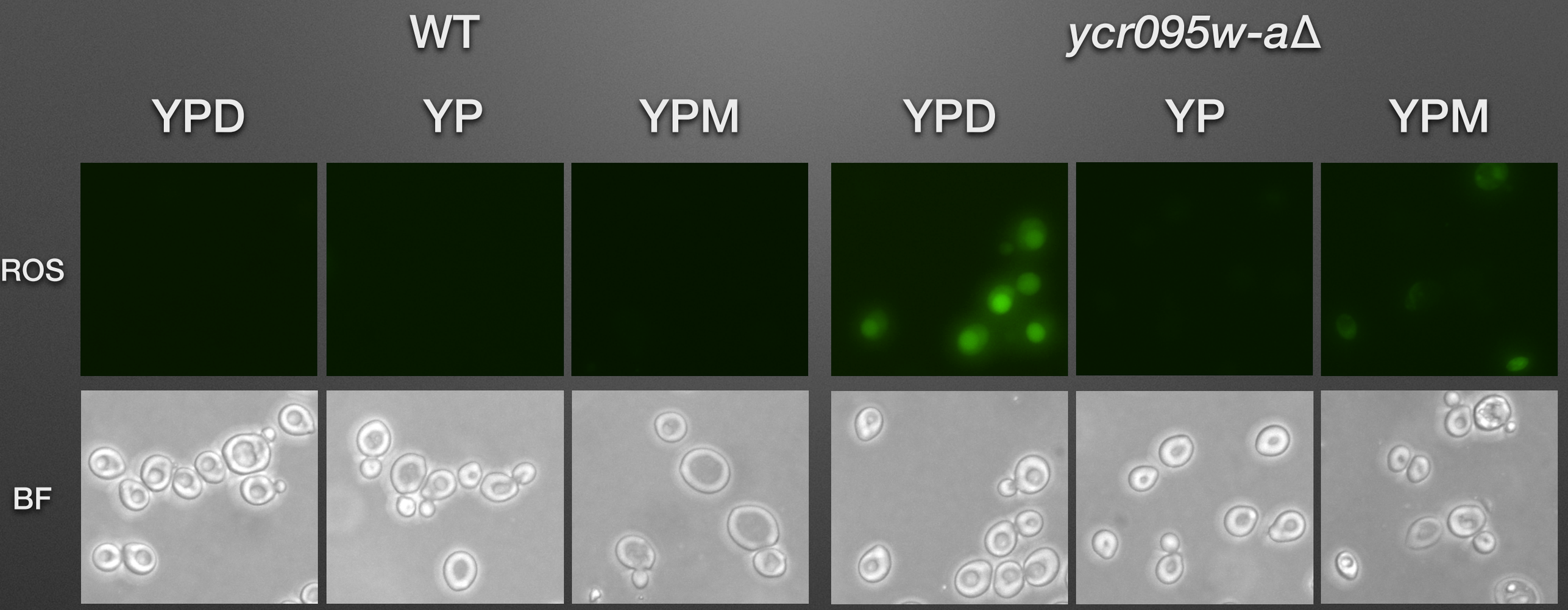


Mucin increases mitochondrial volume in a *ycr095w-aΔ*





ycr095w-aΔ increases ROS accumulation



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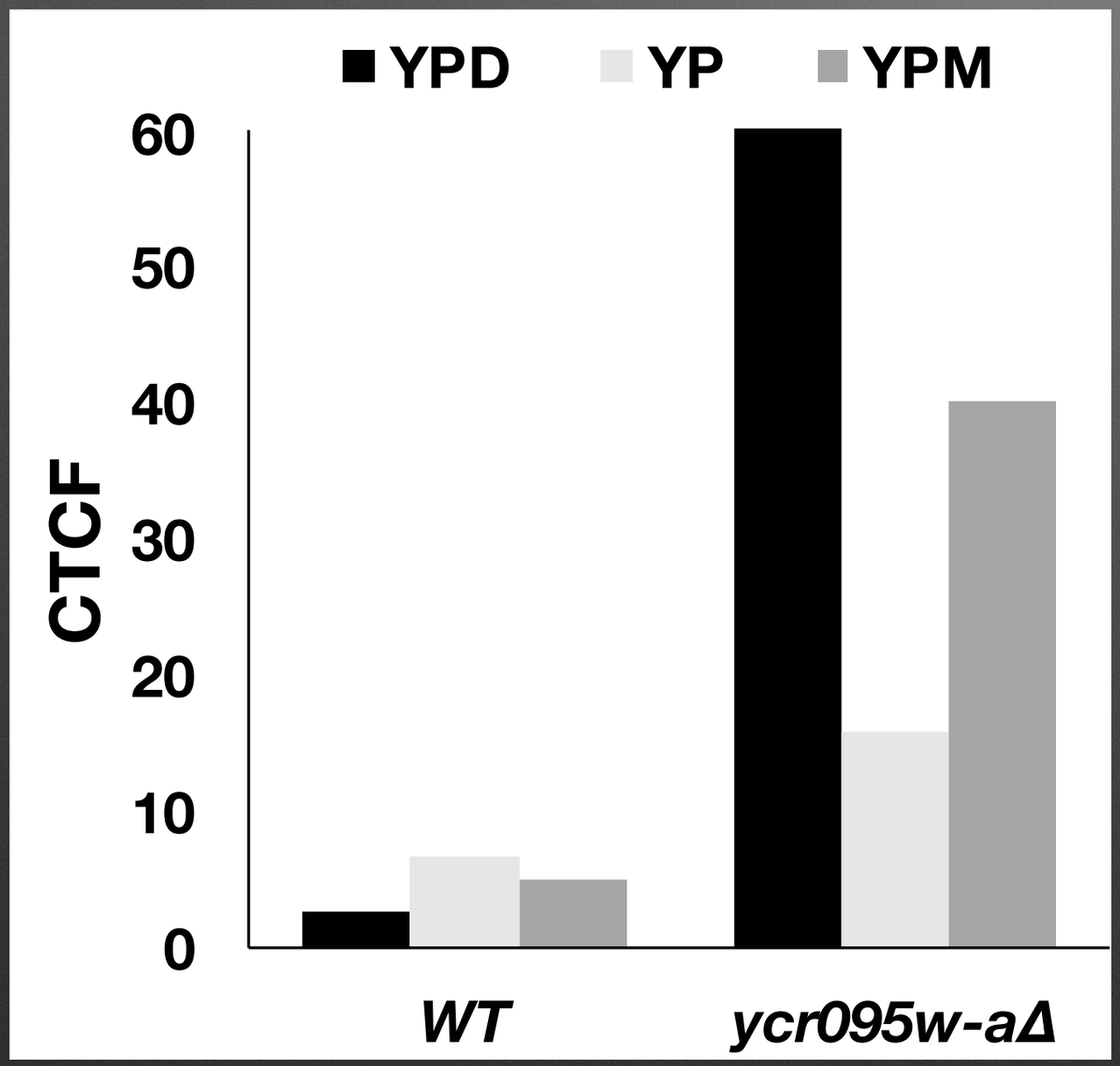
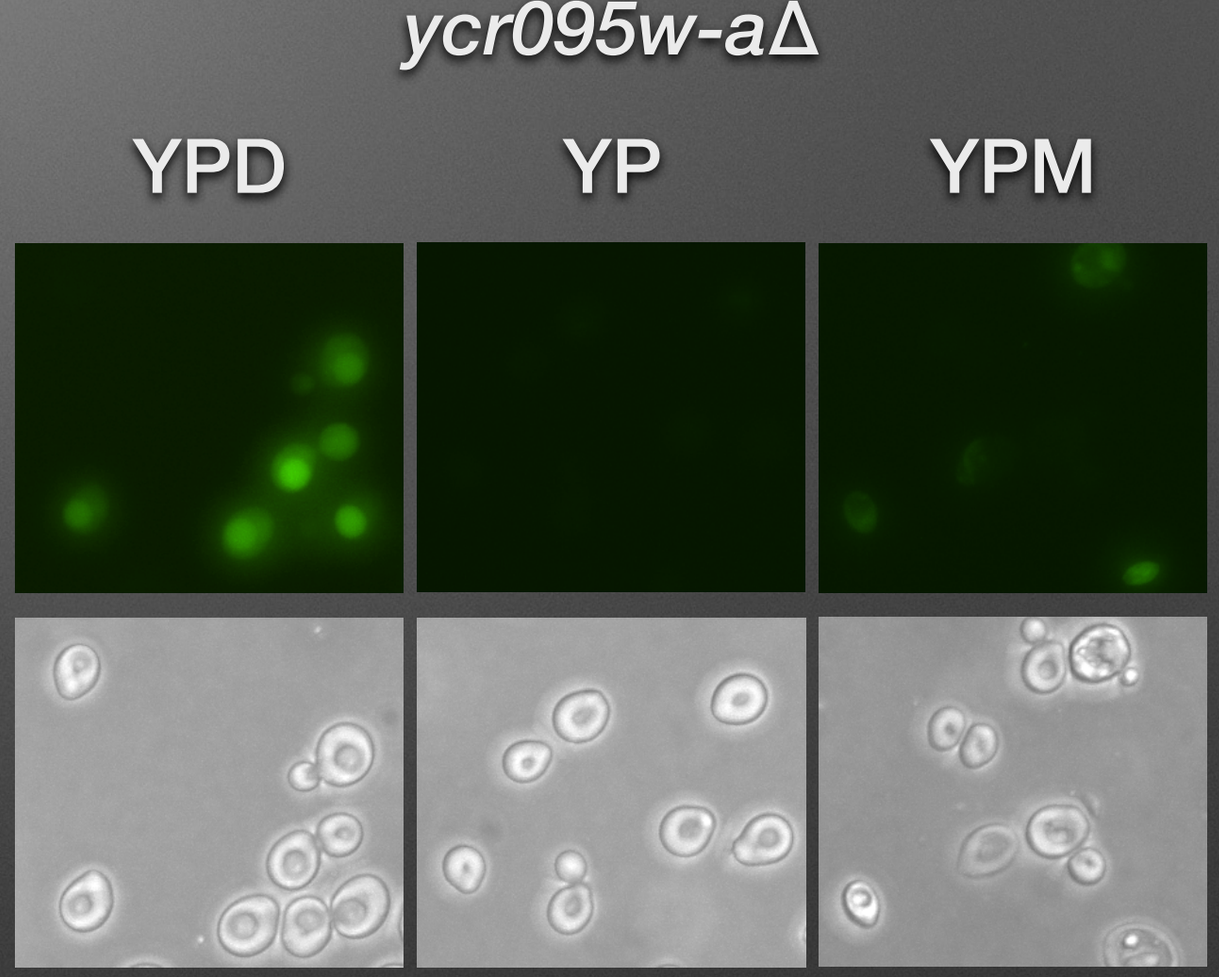
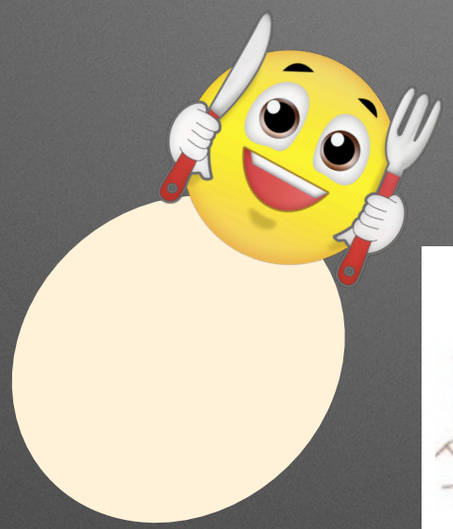
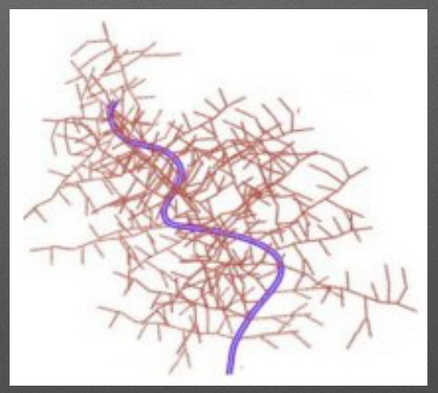




Conclusions

Can grow and adapt to mucin





Yapsins induced in mucin

Mitochondrial functionality play an integral role for growth on mucin

Future Directions: Transcriptome

1

Yeast grown in YP

2

Yeast grown in YPM

Acknowledgements

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TECHNOMISE

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Faculty of Medicine

NSERC
CRSNG

Ottawa Institute of Systems Biology
L'institut de la Biologie des Systèmes d'Ottawa
University of Ottawa / Université d'Ottawa

Thank you!

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