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Metabolic Flux and Resource Balance in the Oleaginous Yeast *Rhodotorula toruloides*

Background/Objective

The yeast *R. toruloides* is a promising bioproduction organism due to its high lipid yields and ability to grow on cheap and abundant substrates. Quantitative, systems-level assessment of its metabolic activity is accordingly merited. Resource-balance analysis (RBA) models capture both reaction stoichiometry and enzyme requirements for catalysis, providing valuable tools for understanding metabolic trade-offs and optimizing engineering strategies. We present systems-level measurements of its metabolic flux based on isotope tracing and metabolic flux analysis.

Approach

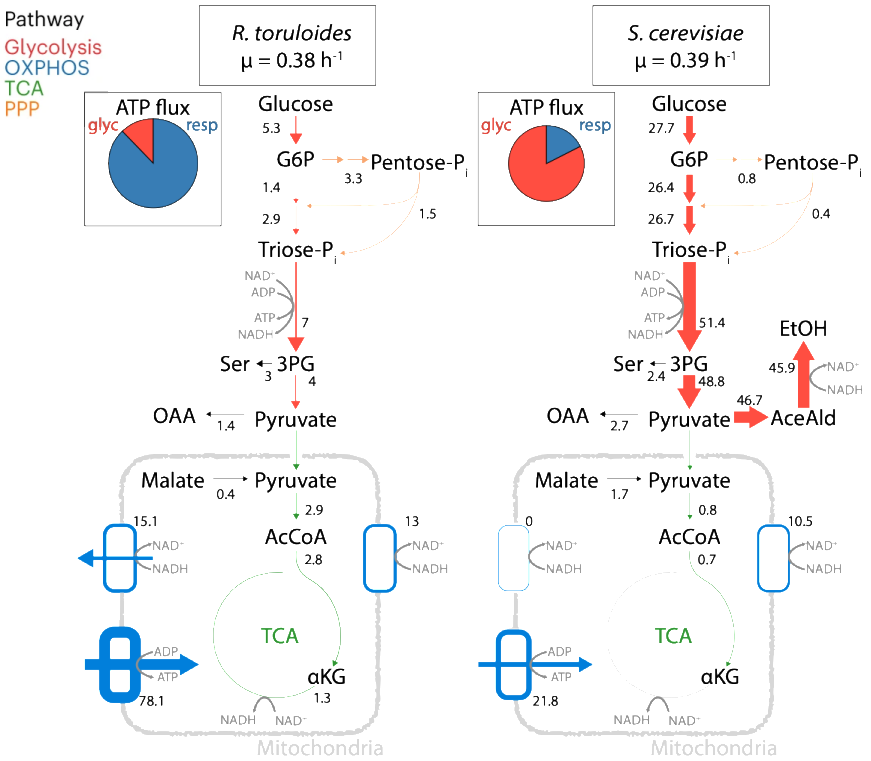
We combined ^{13}C metabolic flux analysis with proteomics to quantify *in vivo* fluxes and protein abundances in *R. toruloides* under defined growth conditions. These flux data were used to parameterize a genome-scale resource balance model 'rtRBA'. The rtRBA model, and an updated 'scRBA' model for *S. cerevisiae,* were used to predict growth phenotypes, proteome allocation, and theoretical yields for industrial chemicals.

Results

We found that *S. cerevisiae* and *R. toruloides* grew at similar rates but use distinct central metabolic strategies, with *R. toruloides* consuming one-fifth as much glucose and favoring the pentose phosphate pathway and TCA cycle over glycolysis. Yet, protein abundances were more conserved than metabolic flux for both yeasts. RBA models predicted higher theoretical yields but lower productivities in *R. toruloides* than *S. cerevisiae* for industrial chemicals.

Significance/Impacts

RBA models inform metabolic engineering strategies to improve industrial chemical yields.



Best-fit flux solutions determined from ^{13}C labeling data.

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