

DECIPHERING THE INTRICACIES OF LIPID BIOSYNTHESIS IN *UMBELOPSIS ISABELLINA*: A SYSTEMS BIOLOGY PERSPECTIVE.

Learn more
about our work!



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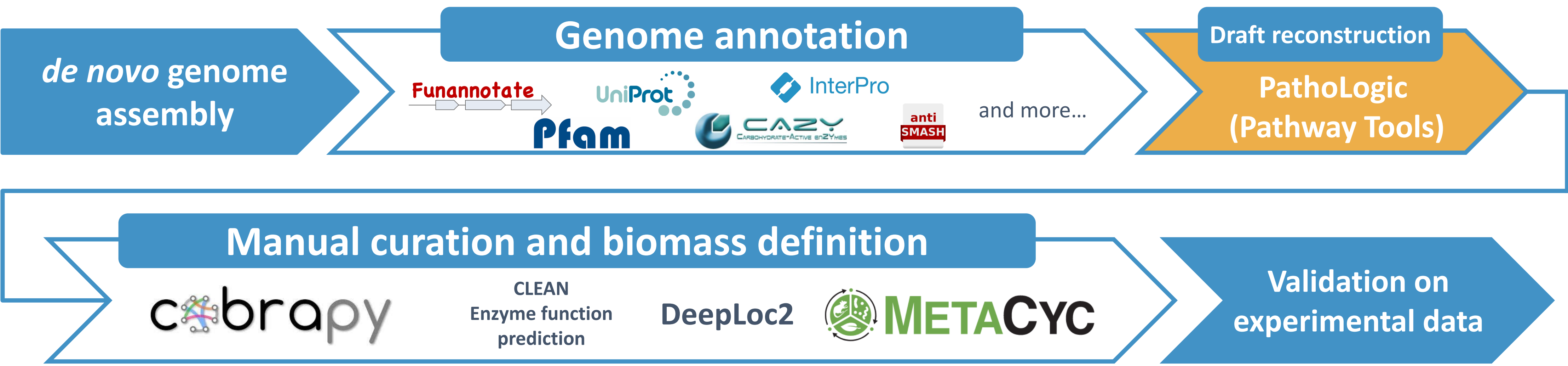
Introduction

Umbelopsis isabellina, a member of Mucoromycota, has been studied for over 20 years due to its high lipid production, reaching up to 80% of its dry mass. Despite its oleaginity and growth on low-cost carbon sources, further optimization is hindered by limited genetic tools and *in silico* insights. This study presents the first *in silico* metabolic model of *U. isabellina*, emphasizing genome and model annotation for enhanced utility. The model has been used to identify potential gene targets for optimizing lipid production, demonstrating its potential for guiding future metabolic engineering efforts.

Methods

Metabolic model reconstruction pipeline.

The genome of *U. isabellina* WA50703 was sequenced, quality-controlled, and assembled using SPAdes, with quality and completeness assessed via QUAST, BUSCO, and CheckM2. Structural and functional annotation involved the Funannotate pipeline, incorporating multiple gene prediction tools and reference databases. The draft metabolic model was reconstructed with Pathway Tools, manually curated, and aligned with SBML standards. Experimental growth data were collected from literature, focusing on carbon substrate utilization.

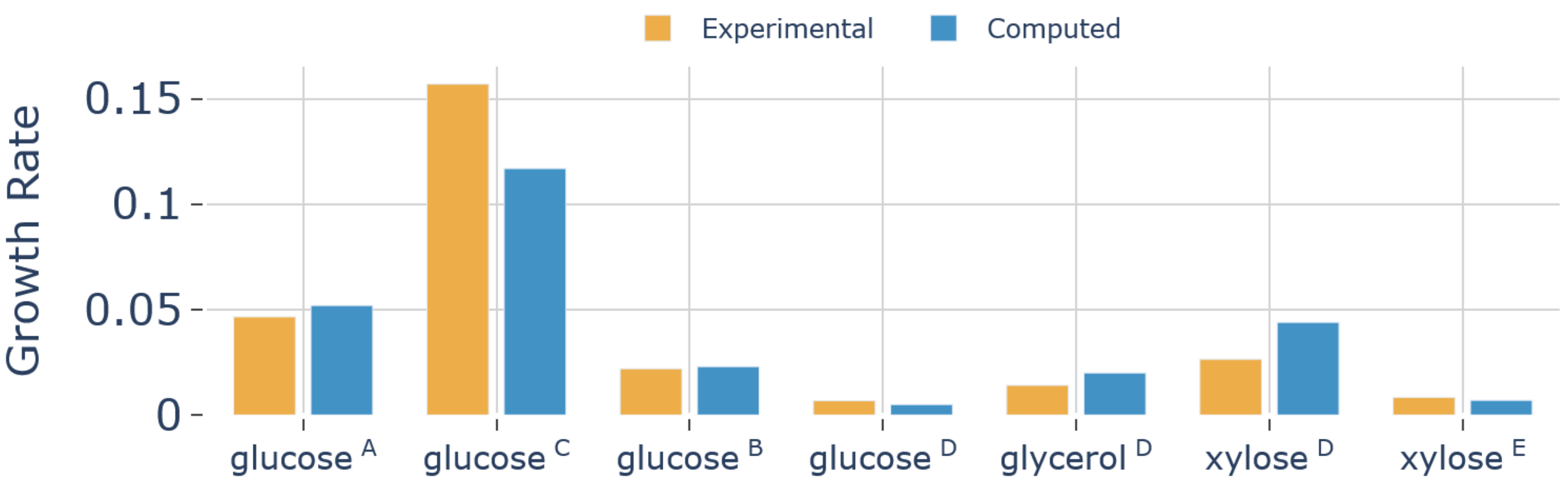


Model validation

Experimental data	
Model simulations	Growth
	No growth
Growth	49
No growth	8

Model predictions vs Biolog carbon phenotypic microarrays

U. isabellina growth has been tested on 95 different carbon sources using the Biolog phenotypic microarray. Out of the 95 carbon sources tested, the MD1629 model produced incorrect results for only 18 of them.



Model predictions vs experimental growth rates

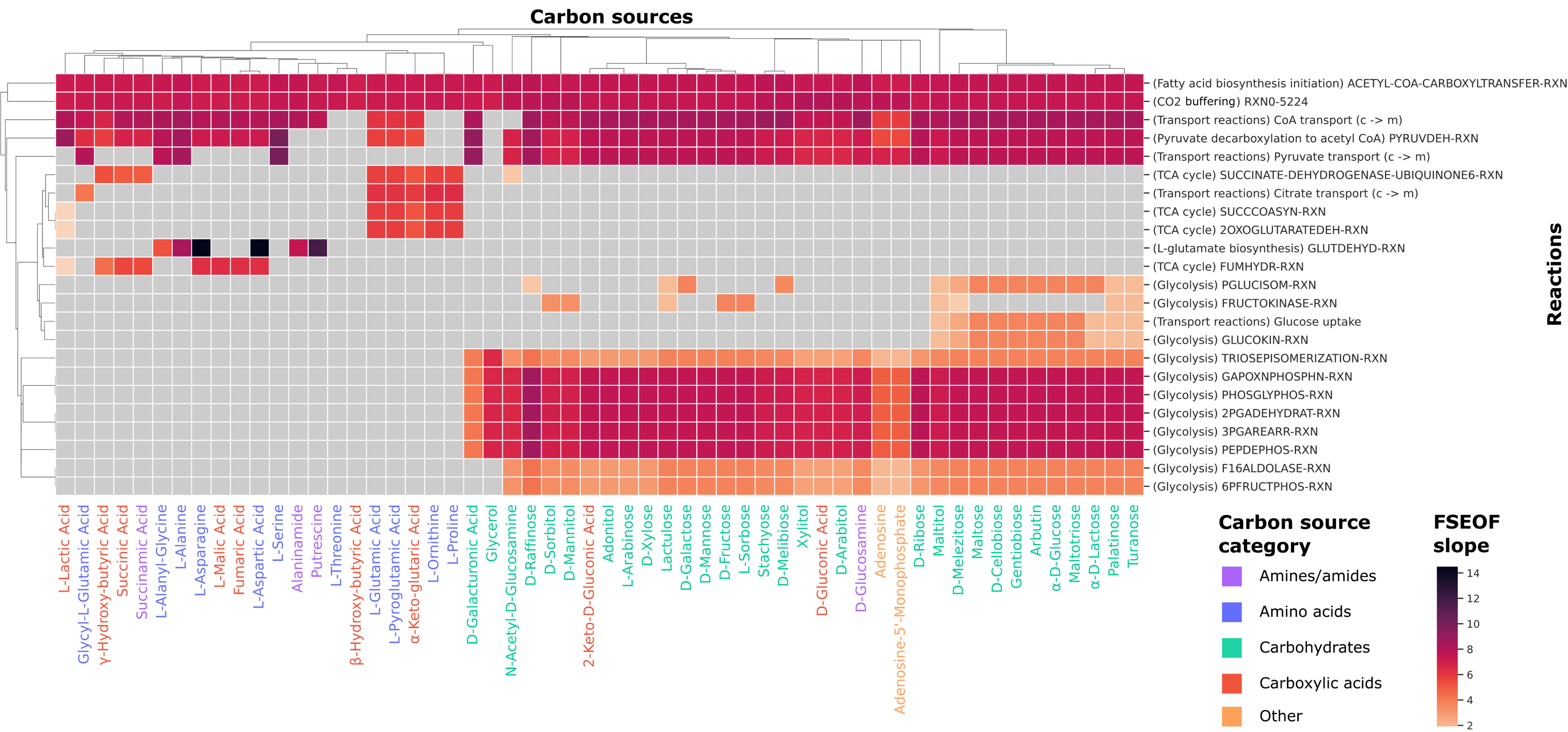
Model simulations exhibited high concordance with the growth curves reported in the literature for *U. isabellina* grown on various carbon sources. A-E superscript – different experimental data sources.

Results

The synthesis of malonyl-CoA by acetyl-CoA carboxylase (ACC) is the primary reaction to target for improving lipid production in *U. isabellina*.

Overexpression of ACC should be coupled with carbonic anhydrase overexpression to ensure adequate bicarbonate levels for optimal function.

Strategies for optimizing lipid production are highly dependent on the type of the main carbon source.



Flux scanning based on enforced objective flux (FSEOF) results. The heatmap illustrates reactions that are positively correlated with the enhanced production of long-chain fatty acids. Although the identified reactions (Y-axis) vary significantly based on different carbon source types (X-axis), the top of the heatmap highlights reactions that, if increased in flux, should boost lipid production regardless of the primary substrate type.

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