

GENOME SCALE MODEL RECONSTRUCTION OF THE METHYLOTROPHIC YEAST *OGATAEA* *POLYMORPHA*

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Ogataea polymorpha is a thermotolerant, methylotrophic yeast with significant industrial applications. It is a promising host to generate platform chemicals from methanol, derived e.g. from carbon capture and utilization streams. Full development of the organism into a production strain requires additional strain design, supported by metabolic modeling on the basis of a genome-scale metabolic model. However, to date, no genome-scale metabolic model is available for *O. polymorpha*. To overcome this limitation, we used a published reconstruction of the closely related yeast *Pichia pastoris* as reference and corrected reactions based on KEGG annotations. Additionally, we conducted phenotype microarray experiments to test *O. polymorpha*'s metabolic capabilities to grown on or respire 192 different carbon sources. Over three-quarter of the substrate usage was correctly reproduced by the model. However, *O. polymorpha* failed to metabolize eight substrates and gained 38 new substrates compared to the *P. pastoris* reference model. To enable the usage of these compounds, metabolic pathways were inferred from literature and database searches and potential enzymes and genes assigned by conducting BLAST searches.

To facilitate strain engineering and identify beneficial mutants, gene-protein-reaction relationships need to be included in the model. Again, we used the *P. pastoris* model as reference to extend the *O. polymorpha* model with this relevant information.

The final metabolic model of *O. polymorpha* supports the engineering of synthetic metabolic capabilities and enabling the optimization of production processes, thereby supporting a sustainable future methanol economy.