Genome-scale Metabolic Reconstruction of the Non-model Yeast *Issatchenkia orientalis* SD108

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Project Goals: One goal of Genome Scale Engineering is to develop new genome-scale design and engineering tools and implement them on a biofoundry for non-model yeast organisms, including *Issatchenkia orientalis*, to produce high-levels of organic acids. The goal of the current work is to develop a genome-scale metabolic model for *I. orientalis* for use in designing these engineered pathways.

Microorganism can convert renewable biomass into organic acids, many of which are important platform chemicals. However, intolerance to typical biomass hydrolysate's low pH conditions remains a challenge for their industrial production. *Issatchenkia orientalis* is a promising host for industrial production owing to its tolerance of acidic conditions down to pH 2.5. In this work, we describe the development of a genome-scale metabolic model for *I. orientalis* SD108 covering 1,022 genes. The model accounts for reported growth viability on a number of carbon substrates and in-house experimentally measured macromolecular composition specific for this strain. We draw comparisons of the *I. orientalis* SD108 model with recent *Saccharomyces cerevisiae* genome-scale models and examine the network topology for growth on glucose, including proposed essential genes. We demonstrate use of the model by proposing specific genetic interventions for production pathways for the industrially-relevant succinic acid, employing OptKnock to discern modifications which link production of a targeted chemical to biomass production.

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