In silico design of *Saccharomyces cerevisiae* strains for production of industrial compounds derived from TCA cycle

Hélder Lopes[1], Paulo Maia[2], Kiran R. Patil[3], Isabel Rocha[1*]

* Correspondence: irocha@deb.uminho.pt

[1]Centre of Biological Engineering, University of Minho, 4710-057 Campus de Gualtar, Braga, Portugal; [2] SilicoLife, Lda, Braga, Portugal; [3] European Molecular Biology Laboratory, 69117 Heidelberg, Germany.

Saccharomyces cerevisiae is one of the most widely used cell factories in industrial biotechnology. However, the development of optimized yeast strains for the production of novel compounds is a costly and time-consuming process, mainly due to the unavailability of suitable chassis cells. This work was developed under the scope of the ERA-IB DeYeastLibrary project and aimed to design *in silico* pre-optimized strains capable of overproducing organic acids originating from the TCA cycle, based on the fact that these compounds are derived from the same metabolic precursors. The iMM904 genome-scale metabolic model was used during the optimization procedures, which were performed simulating aerobic conditions and using glucose as a carbon source, setting as targets four organic acids for maximization: fumarate, succinate, malate and itaconate. The mutant phenotypes were predicted using the pFBA method. Following this procedure, other yeast metabolic models and simulation methods were used to test the robustness of the obtained solutions, using Optflux.

Despite some discrepancies observed between the results using different models and simulation methods, we identified several possible solutions that may constitute suitable chassis strain candidates for metabolic engineering towards the overproduction of the compounds of interest.

Acknowledgments: CEB, MIT-PT/FCT (SFRH/BD/52336/2013), ERA-IB DeYeastLibrary Project (ERA-IB-2/0003/2013)