## Functional expression of *Yarrowia lipolytica* acetyl-CoA carboxylase in *Saccharomyces cerevisiae*

## Humberto Pereira, Paulo Silva, Flávio Azevedo, Björn Johansson

CBMA—Centre of Molecular and Environmental Biology, Department of Biology, University of Minho, Campus de Gualtar, Braga 4710-057, Portugal

Malonyl coenzyme A (Malonyl-CoA) is an important precursor for a range of economically valuable compounds such as biodiesel, 3-hydroxypropionic acid, fatty alcohols, flavonoids, stilbenoids and polyketides. Even though Saccharomyces cerevisiae is one of the most used cell factories for the production of a variety of compounds, it is limited in its ability to generate malonyl-CoA and derived products. In this yeast, the only source of malonyl-CoA is the ATP-dependent carboxylation of acetyl coenzyme A (acetyl-CoA) catalyzed by acetyl-CoA carboxylase (ACC), the rate-limiting step in fatty acid biosynthesis. In this work, expression of Yarrowia lipolytica ACC in S. cerevisiae was attempted with the objective of establishing an alternative malonyl-CoA production system in this yeast. A S. cerevisiae strain with a tetracycline repressible ACC1 was used for functional testing. Since ACC1 is an essential gene, this strain is not capable of growing in medium supplemented with tetracycline. Expression of S. cerevisiae or Yarrowia lipolytica ACC1 from a plasmid complemented the conditional phenotype and enabled growth in tetracycline containing medium. Expression of ACCs from plasmids caused prolonged lag phase, and specific growth rates were considerably lower than the ones obtained for the wild type strain. This result is consistent with previous studies where ACC activity was increased and likely results from the metabolic imbalance this increase might cause. Results of in-vivo measurements of malony-CoA levels in the recombinant strain will be discussed.

This work was supported by the Fundacão para a Ciência e Tecnologia Portugal (FCT) through Project FatVal POCI-01-0145-FEDER-032506. CBMA was supported by the strategic programme UID/BIA/04050/2013 (POCI-01-0145-FEDER-007569) funded by national funds through the FCTI.P. and by the ERDF through the COMPETE2020 - Programa Operacional Competitividade e Internacionalização (POCI).