# ENGINEERED INDUSTRIAL YEAST FOR RESVERATROL DE NOVO PRODUCTION FROM WINE WASTE

**Molecular Biotechnology, Systems Biology and Metabolic Engineering**

## OP - (442) - ENGINEERED INDUSTRIAL YEAST FOR RESVERATROL DE NOVO PRODUCTION FROM WINE WASTE

**Costa, Carlos E.** (Portugal)[1]; Møller-Hansen, Iben (Denmark)[2]; Romaní, Aloia (Spain)[3]; Teixeira, José A. (Portugal)[1]; Borodina, Irina (Denmark)[2]; Domingues, Lucília (Portugal)[1]

1 - CEB - Centre of Biological Engineering, University of Minho, 4710-057 Braga, Portugal; 2 - The Novo Nordisk Foundation Center for Biosustainability, Technical University of Denmark, Kgs. Lyngby, Denmark; 3 - Department of Chemical Engineering, Faculty of Science, University of Vigo (Campus Ourense), As Lagoas, 32004 Ourense, Spain

### Body

The yeast *Saccharomyces cerevisiae* is widely used as a cell factory to produce several chemicals of interest, from biofuels to high-value natural products. Resveratrol is a polyphenolic compound with strong antioxidant activity, naturally present in plants such as grapes, that can be synthesized by fermentation. Its microbial biosynthesis is a valuable alternative to its plant extraction or chemical synthesis, both complex and unsustainable. Nevertheless, its biosynthesis is mostly attained from expensive substrates such as *p*-coumaric acid. Therefore, there is a demand for cheaper substrates, namely carbon sources. Portugal and Spain are two of the largest wine manufacturers in the world, and this vast production generates a substantial amount of wine wastes like grape pomace or wine lees. Wine lees, consisting of residual fermentative microorganisms and other particles, have high organic content and ethanol, among other components. They have been previously proposed as economic nutrients for microbial production of biochemical products but could also be used as substrate. Furthermore, there is a significant surplus of grape must that is not used for wine production, which could serve as a carbon source for biotechnological processes that generate value-added products. Here, a robust industrial diploid strain engineered with the resveratrol biosynthetic pathway[1] via CRISPR/Cas9 was used for resveratrol production from carbon sources. Initially, overexpression of genes from the Pentose Phosphate Pathway coupled with the expression of *AtATR2* and *ScCYB5* for enhancement of cytochrome P450 activity increased resveratrol titre by 55%. Subsequently, resveratrol production using wine waste as substrate was assessed. Grape must fermentation, using glucose and fructose as carbon sources, led to a production of 259 mg/L of resveratrol. In addition, fermentation of wine lees achieved a titre of 264 mg/L of resveratrol using ethanol as sole carbon source. To the best of our knowledge, this is the first report of resveratrol production exclusively from ethanol. The use of wine wastes expands the palette of feedstocks available for the establishment of sustainable processes in a circular bioeconomy.

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### References

[1] Resveratrol production from hydrothermally pretreated eucalyptus wood using recombinant industrial *Saccharomyces cerevisiae* strains, Costa, C.E., Møller-Hansen, I., Romaní, A., Teixeira, J.A., Borodina, I., Domingues, L., *ACS Synthetic Biology,* 10, 8, 1895–1903 (2021)

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