

## 362. Resveratrol production by recombinant robust yeast strains for valorisation of wine waste

Carlos E. Costa<sup>1</sup>, Iben Møller-Hansen<sup>2</sup>, Aloia Romani<sup>1</sup>, José A. Teixeira<sup>1</sup>, Irina Borodina<sup>2</sup>,  
Lucília Domingues<sup>1</sup>

<sup>1</sup> Centre of Biological Engineering, University of Minho, Braga, Portugal

<sup>2</sup> The Novo Nordisk Foundation Center for Biosustainability, Technical University of Denmark, Kgs. Lyngby, Denmark

The Iberian Peninsula is an exceptional territory to produce a wide variety of wines, with both Portugal and Spain being amongst the main wine producers on the planet. This extensive manufacture generates large quantities of wastes like grape pomace or wine lees. Wine lees (residual fermentative yeast and other particles) have a high organic content, including acids, phenols, and ethanol, among others. They have been previously proposed as economic nutrients for microbial production of biochemical products but could also be used as substrate. Additionally, there is a substantial surplus of grape must that is not used for wine production that could be an interesting carbon source for biotechnological processes for value-added products generation. The establishment of a sustainable bioeconomy is highly dependent on the valorisation of these industrial wastes. Resveratrol is a polyphenolic compound with strong antioxidant activity, naturally present, e.g., in grapes. Its known anti-inflammatory and anti-ageing properties, among others, makes it suitable for several applications in health, diet, and cosmetics. Microbial biosynthesis of resveratrol is a valuable alternative to its plant extraction or chemical synthesis, both complex and unsustainable. Nevertheless, its biosynthesis is mostly attained from expensive substrates as *p*-coumaric acid. The yeast *Saccharomyces cerevisiae* is widely used as a cell factory to produce several chemicals of interest, from biofuels to high-value natural products. Industrial yeast strains are known for their higher fermentation capacity and their ability to cope with harsh fermentation conditions (e.g. low pH). Here, a robust industrial diploid strain was engineered with the resveratrol biosynthesis pathway<sup>[1]</sup> coupled with overexpression of genes for the Pentose Phosphate Pathway, and used for resveratrol production with glucose as carbon source. In batch fermentation of synthetic media, a resveratrol titre up to 440 mg/L was attained from 70 g/L of glucose. Resveratrol production using wine wastes as substrates was subsequently assessed. A titre of 222 mg/L of resveratrol was obtained from a media with 50% of wine lee, with supplementation of grape must, using glucose, fructose, and ethanol simultaneously as carbon source. This is

the first report of resveratrol production from wine wastes, expanding the possible uses of these feedstocks for the development of sustainable processes in a circular bioeconomy.

[1] Costa et al. (2021) *ACS Synth. Biol.*, 10, 8, 1895–1903

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