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***Yarrowia lipolytica* the new workhorse for biotechnology in product development.**

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### **Abstract.**

*Yarrowia lipolytica* is a saccharomycetous oleaginous yeast with a long history of industrial use. Thanks to the increasingly advanced knowledge of its metabolic pathways, this yeast has had a great opening in the market, giving way to great business opportunities, becoming a great cellular factory.

*Y. lipolytica* meets all the requirements for the economic viability of a microbial bioprocess. Therefore, different companies such as Biocatalysts Ltd, Mayoly, DSM, Microbia Inc among others, have found a great potential to use it to produce different products such as citric acid, carotenoids and proteins, moving large millions of euros.

More companies are betting on the research and biotechnological application of *Y. lipolytica* thanks to its unique metabolic, genetic and physiological characteristics.

**Keywords:** *Yarrowia lipolytica*; Cellular manufacturing; Metabolic pathways; Biotechnological applications.

### 1. What is *Yarrowia lipolytica*

*Y. lipolytica* is a saccharomycetous oleaginous yeast with a long history of industrial use. Thanks to the development of numerous molecular and genetic tools, *Y. lipolytica* is now a recognized system for expressing heterologous genes and secreting the corresponding proteins of interest. Thanks to genomic and transcriptomic tools, knowledge of its metabolic pathways for use as a cell factory in various bioconversion processes has become available. Currently *Y. lipolytica* is developing as a workhorse for biotechnology, especially for the production of unicellular oil and the transformation of industrial waste into valuable products. (Madzak, 2018).

### 2. *Yarrowia lipolytica* and its suitability for industry

According to author (Julleson et al., 2015) the economic viability of a microbial bioprocess is usually related to three production metrics: titer, rate (also known as productivity) and yield. To achieve a higher yield from a microorganism, reduced by-product formation and high cell density growth (titer), varied and efficient feedstock conversion (yield), and rapid growth and production (rate) are required. The strain must be safe, genetically stable and controllable to maintain yield in the production phase and ensure reproducibility; another desirable characteristic is tolerance to low pH, which prevents bacterial contamination and reduces the need for pH neutralization. Thus, *Y. lipolytica* meets many of these requirements, making it a promising industrial host (Park and Amaro, 2022).

### 3. Commercial *Yarrowia lipolytica* products in industry

- Skotan SA started the production of single-cell protein (edible protein for human and animals from waste glycerol and registered the feed product in the EU. Microbial enzymes such as lipases already have their own market valued at US\$425 million in 2018 (Chandra et al., 2020). Commercial recombinant enzymes from *Y. lipolytica* are now available, such as the phospholipase enzyme Lipomod 833L2 by Biocatalysts Ltd., the lipase obtained by LIP2 gene overexpression by Mayoly, or the human acid  $\alpha$ -glucosidase OXY2810 by Oxyrane (Madzak, 2018)
- Citric acid is widely used by the food industry as additives, preservatives, anticoagulants, antimicrobial agents, fine chemicals, and so forth (Caballo et al., 2017). The global market volume of citric acid is greater than 2 million tons, and its value is estimated to reach US\$6.28 billion by 2030 (Citric Acid Market, 2022) Due to easy cultivation, high conversion rate, and tolerance to high product concentrations, *Y. lipolytica* has been proposed as an alternative citric acid producer to *Aspergillus niger* (Caballo et al., 2017). Several companies, such as DSM, Akad Wissenschaften DDR, and OrganoBalance GmbH, own approximately 40 patents on citric acid production by *Y. lipolytica*

- Carotenoids have a number of applications in the food processing, animal feed, pharmaceutical, and cosmetics industries. There is already an enormous global market, which is estimated to be US\$1.57 billion in 2022 and reach a valuation of US\$2.09 billion by 2027 (Global Carotenoids Market,2022) The production of carotenoids from *Y. lipolytica* has been described by numerous patents filed by DSM, E.I. DuPont de Nemours and Company, Amyris, and Microbia Inc., among others

### **Concluding remarks**

- In recent years, there has been an increase in new laboratories working with this organism to create tools that facilitate its manipulation. In the same way, many companies have started to choose *Y. lipolytica* as a production host.
- *Y. lipolytica* has become an organism of choice for microbial biotechnology research and applications in both academia and industry. This is mostly a consequence of its unique metabolic, genetic, and physiological features.
- In Spain, biotech companies have generated more than 10.1 billion of income, which represents 1% of the national PIB. Contributing with 117,700 jobs (AseBio,2022). That is why as researchers we must go to the next step to get a better match for great biotechnological potentials such as the yeast *Y. lipolytica*, taking all the research towards the creation of companies.

## References

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