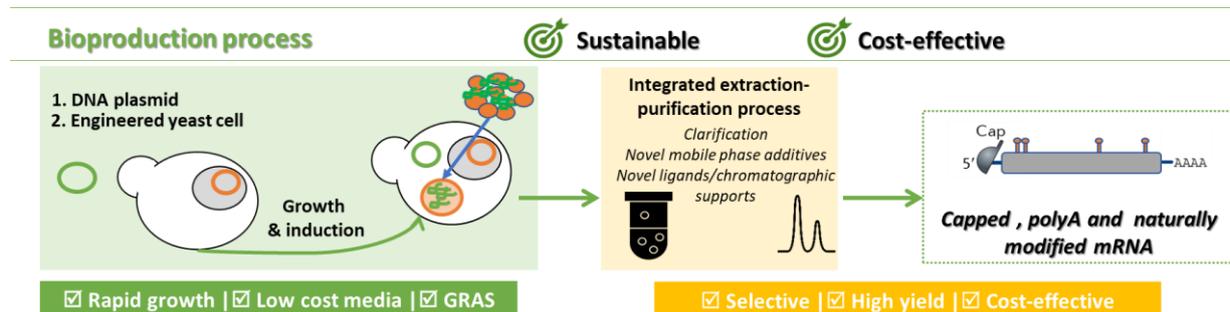


Yscript – engineering yeast for RNA production

Orléans, 1 April 2022 – The Yscript consortium sets out to develop a tailor-made yeast-based messenger RNA (mRNA) factory platform for large-scale and cost-effective manufacturing of mRNA therapeutics. Messenger RNA vaccines have become a game-changer in the fight against COVID-19, and mRNA is considered for a vast array of therapeutic applications. Currently, *in vitro* transcription (IVT) is the only available technology for mRNA production, however, it relies on a complex supply chain and a costly purification process. This is a major problem hampering large-scale IVT production and high production costs are a problem for low-income countries. Within Yscript, eight partners from five countries are working together over the next three years to overcome this obstacle. The EU has selected the consortium, which is led by Prof. Chantal Pichon from CNRS and University of Orléans, for funding in the first round of the new Horizon Europe framework as part of the EIC Pathfinder programme.

The Yscript consortium aims to establish a specific mRNA bioproduction process in yeast. Although yeast has been employed for the production of several biopharmaceuticals, RNA production has never been attempted. The challenge is to express mRNA for a gene-of-interest (GOI) on demand and to separate it from yeast's own mRNA. The project attempts to do this by assembling mRNA-of-interest in specialised compartments, from where it could be specifically purified. “*Development of a specific mRNA-bioproduction and purification process in yeast would be groundbreaking*”, Prof. Pichon sums up the vision of the project.



Objectives of Yscript

- 1) The development of a robust and scalable yeast-bioprocess for the production of different lengths of mRNA.
- 2) The design of innovative and cost-effective extraction and purification processes for bio produced mRNA.

Yeast has innovation potential

Yeast cells share many processes with human cells. They combine the advantages of high expression levels, fast growth, easy maintenance and easy scale-up in low-cost growth media. Furthermore, they are generally recognised as safe (GRAS) for human applications, and have been used for decades for the biosynthesis of high-value compounds in medical applications. Accordingly, powerful yeast engineering tools are available and a robust infrastructure already exists for yeast bioproduction at industrial scale.

Advantage of yeast over *in vitro* transcription

As a living organism, yeast synthesises all components required for producing mature mRNA from its nutrients, whereas the dependency on synthetic reagents and materials is highly reduced compared to IVT.

The future of mRNA therapeutics

The yeast factory set up in Yscript will be flexible and rapidly adjustable for manufacturing any mRNA therapeutic at a scale and cost that enables global delivery and accessibility. If the approach works, the mRNA production supply chain and costs will be reduced by at least 10 times, while keeping mRNA efficacy. With this setup, *“the project will be a gamechanger in the fight against many diseases”*, says project coordinator Prof. Chantal Pichon.

Overall societal impact

“Yscript will promote the development of affordable mRNA therapeutics that are available to everyone and hence will foster the well-being and health of citizens all over the world”, Prof. Pichon is convinced. The project has the potential to provide Europe with a cost-effective approach to defend itself against future infection outbreaks, but also to expand its arsenal to treat chronic diseases, which are on the rise due to population aging. Thus, the project will have a positive impact not only on health, but also on economy and society.

International consortium

Yscript brings together world-class expertise in mRNA therapeutics and yeast RNA biology, yeast engineering and bioproduction, in extraction, purification and stabilisation of biomolecules as well as in scientific management consulting.

Health sciences, molecular biology, biophysics:

- CNRS (France)
- TRON gGmbH (Germany)
- IBCH PAS (Poland)

Biotechnology:

- INRAE-TWB (France)

Materials chemistry, computational chemistry and chemical engineering:

- UAVR (Portugal)
- UBI (Portugal)
- BIA Sep (Slovenia)

Project management, communication:

- EURICE (Germany)

Yscript key facts

Acronym	Yscript
Title	Yeast cell factory for mRNA bioproduction
Project duration	April 2022 - March 2025
Budget	€ 3,078,249.75
Coordination	CNRS, University of Orléans, Prof. Chantal Pichon
Partners	CNRS, INRAE-TWB, UAVR, UBI, TRON gGmbH, EURICE, IBCH PAS, BIASEP
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