# Metabolic engineering of curcumin production in *Saccharomyces cerevisiae*

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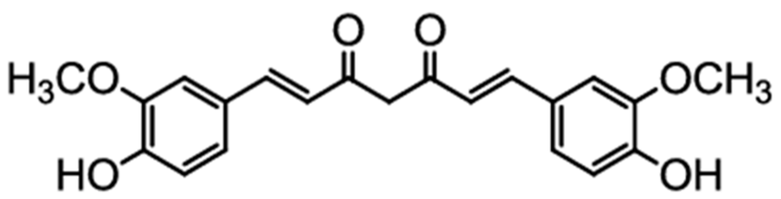
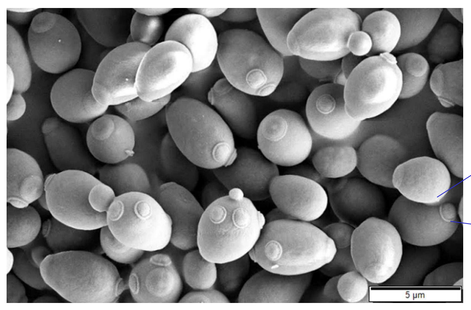
## Introduction




**Curcumin**

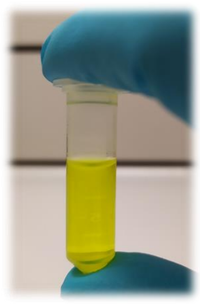
- Difficult and expensive to isolate
- Hard to chemically synthesize

To overcome that




**Genetic modified** *Saccharomyces cerevisiae*

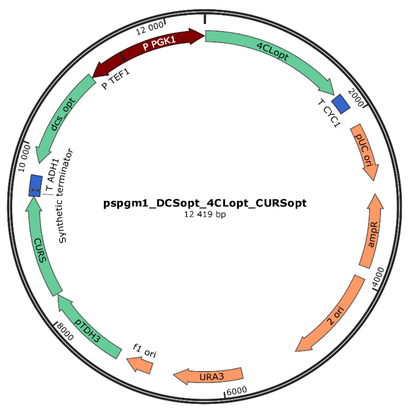
Therapeutic properties → Anticancer, Antioxidant, Anti-inflammatory → Are required → **High purity curcumin extracts**



Constructed pathways

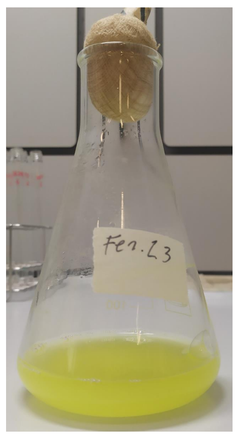
Ferulic acid —(**4CL/FerA**; SH-CoA)→ Feruloyl-CoA —(**DCS/CUS**; Malonyl-CoA)→ Feruloyl-diketide-CoA —(**CURS/CUS**; Feruloyl-CoA)→ **Curcumin**

## Methods



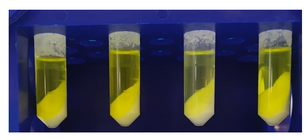

YEP harbouring curcumin **biosynthetic pathway**

Transformed into *S. cerevisiae* wild type BY4741

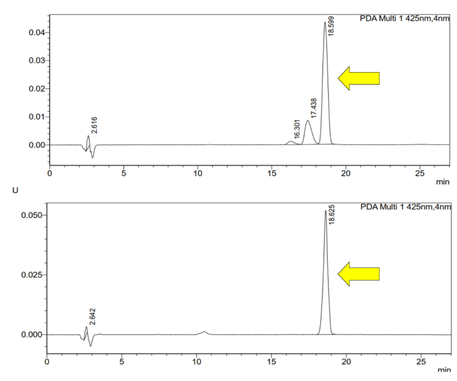



**Flask cultivation** of mutants w/ supplemented ferulic acid

Curcumin extracted from cells with **methanol**



UHPLC quantification




## Results

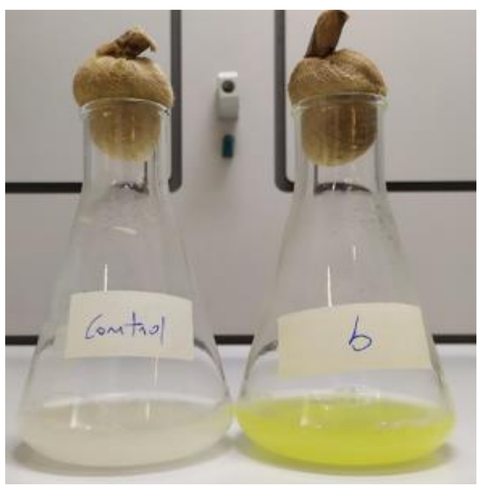
Heterologous pathway combinations tested:

A - **4CL1** (4-coumarate-CoA ligase) from *Arabidopsis thaliana* and **CUS** (curcuminoid synthase) from *Oryza sativa* (capable of one-pot synthesis of curcumin from feruloyl-CoA)

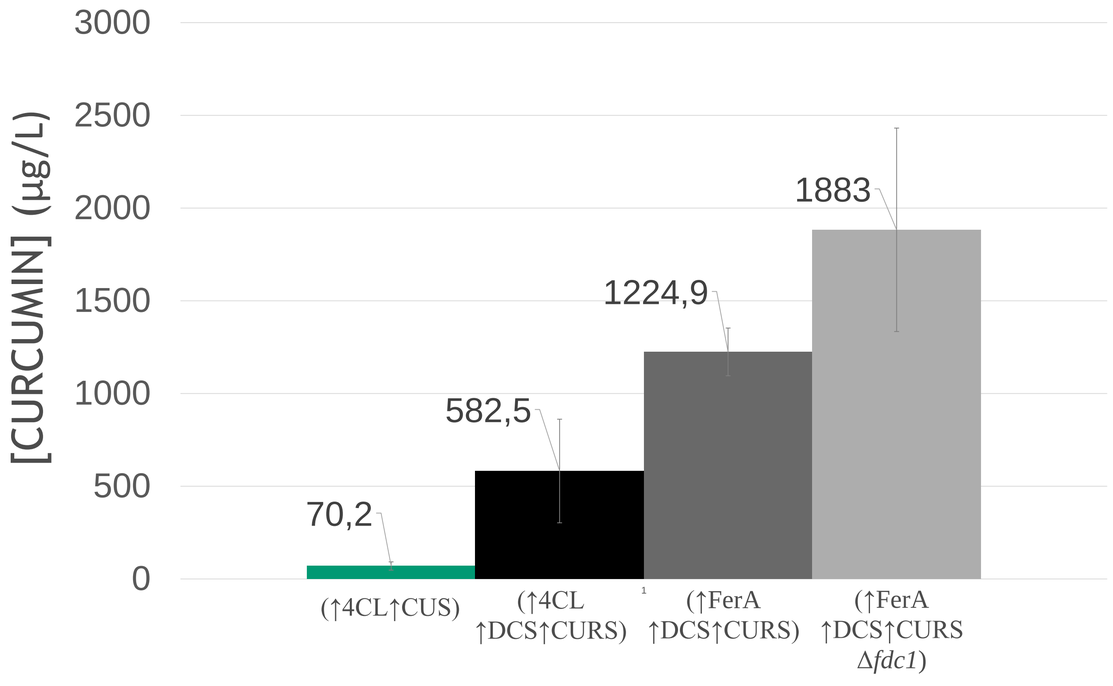
B - **4CL1** from *A. thaliana*, **DCS** (diketide-CoA synthase) and **CURS** (curcumin synthase) from *Curcuma longa*

C – **FerA** (feruloyl-CoA synthetase) from *Pseudomonas paucimobilis*, **DCS** and **CURS** from *C. longa*

D - **FerA** from *P. paucimobilis*, **DCS** and **CURS** from *C. longa*, *fdc1* (ferulic acid decarboxylase) knock-out strain




**Left flask**: No ferulic acid was added to the culture media; **Right flask**: 16 mg/L of ferulic acid were added to the media at 24 h of fermentation




## Conclusions

- Engineered *S. cerevisiae* expressing type III PKS (DCS and CURS) from *C. longa* produced more curcumin than when CUS from *O. sativa* was expressed;
- FerA from *P. paucimobilis* resulted in more curcumin than 4CL from *A. thaliana*;
- Deletion of *fdc1* improved curcumin production;

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