In silico design and modeling of new biosynthetic pathways: curcumin production in *Escherichia coli*

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Curcuminoids are produced by plants of the order Zingiberales, and often used in food additives and also in traditional Asian medicines due to their anti-tumour properties. Therefore, they constitute very attractive targets to metabolic engineering [1]. The aim of this work is to engineer a biosynthesis pathway for the production of curcumin in *Escherichia coli* by combining a systems biology approach with synthetic biology.

Synthetic biology provides an answer to the challenge of expanding the biological production capabilities of microorganisms through the incorporation in the host of engineered biosynthetic pathways for compounds of interest.

The design of biosynthetic pathways for both natural and unnatural compounds can be performed by assembling partial pathways recruited from different species [2,3], by engineering existing pathways and by the use of engineered enzymes exploring the natural diversity of enzyme-catalyzed reactions across several species. Key to this is the specification of gene sequences encoding enzymes that catalyze each reaction in the pathway and whose DNA sequences can be incorporated into devices that lead to functional expression of the molecules of interest [4,5].

To identify all the possible metabolic routes that allow the production of curcumin from metabolites that exist in native *E. coli* we used relevant databases like Kegg and MetaCyc. Then to each one of the identified reactions it was identified the species with the corresponding enzymes/genes. Afterwards, all the possible routes were incorporated in genome-scale stoichiometric models [6] coupled with the dynamic model to understand the likely limitations regarding the availability of the possible precursors. The inclusion of these possible set of pathways in a *in silico* model help to predict the cell behavior after their incorporation, such as product yield and cell growth, stoichiometric constraints and also to assess the potential of the successful implementation of a designed pathway by using other bioinformatics tools.

Further, the optimization of these synthetic biology modified strains using *in silico* metabolic models leads to the high-level production of specific metabolites in an industrial scale, while saving time and resources in laboratorial experimentation.

References

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