Design and construction of a new biosynthetic pathway for the production of curcuminoids in Escherichia coli

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Curcuminoids are natural pigments from plants that have been reported as potential cancer-fighting drugs. The aim of this work is to engineer an artificial biosynthetic pathway for curcuminoids production by Escherichia coli. Starting from the substrate tyrosine, the curcumin pathway involves several enzymatic steps: conversion of tyrosine to p-coumaric acid; conversion of p-coumaric acid to caffeic acid; production of caffeoyl-CoA from caffeic acid; production of feruloyl-CoA from caffeoyl-CoA; and finally the production of curcumin from feruloyl-CoA and possibly other curcuminoids, due to enzyme promiscuity. The enzymes involved in the two first enzymatic steps are tyrosine ammonia lyase from Rhodotorula glutinis, P450 CYP199A2 from Rhodopseudomonas palustris, and the redox partners pdr from Pseudomonas putida and pux from R. palustris. These two steps were successfully accomplished. Two CoA ligases from different sources are being explored for the conversion of the different carboxylic acids into their corresponding CoA esters. Different combinations of these enzymes and caffeoyl-CoA 3-methyl transferase may lead to the production of different curcuminoids. For the last step of the pathway two approaches are being studied: the use of diketide-CoA synthase and curcuminoid synthase from Curcuma longa, and curcumin synthase from Oryza sativa that itself catalyzes both steps. Successful construction of the curcuminoids biosynthetic pathway would mark a significant step forward in the in situ production of these poorly soluble, anti-carcinogenic compounds.