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Sterols and carotenoids overproduction by expressing the transcriptional activation domain of Sre1 (Sre1N) in the carotenogenic yeast *Xanthophyllomyces dendrorhous*

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The yeast Xanthophyllomyces dendrorhous is one of the few known natural sources of the carotenoid astaxanthin. Mutant strains incapable of producing ergosterol, the main sterol in yeasts, overproduce carotenoids and sterols, having increased transcript levels of several genes controlling both pathways. Considering that the synthesis of carotenoids and sterols share the same precursors that derive from the mevalonate pathway, the main goal of this work was to study the mechanism that regulates the biosynthesis of both type of metabolites in *X. dendrorhous*. Sterol Regulatory Element Binding Proteins (SREBPs) are a family of membrane-bound transcription factors that activate the transcription of target genes depending on sterol and oxygen levels. These proteins have been recently identified in fungi and named as Sre1. Under low oxygen or ergosterol levels, Sre1 is proteolytically cleaved by Stp1 releasing the N-terminal activation domain (Sre1N) that activates gene expression at the nucleus. Our recent studies indicate that X. dendrorhous has an orthologous sterol regulated SREBP activation pathway regulating sterol and carotenoid biosynthesis as production of both types of metabolites is affected in sre1 and stp1 mutant strains. In this study, we analyzed the effect of the Sre1N constitutive expression in *X. dendrorhous*. Strains CBS 6938 (wild-type), CBS.sre1- and CBS.SRE1N were included. Strain CBS. SRE1N was obtained by replacing through homologous recombination, the endogenous SRE1 gene by a module designed to express just Sre1N and an antibiotic resistance marker. Strains were cultured with constant agitation in YM medium at 22 °C and samples were taken to extract carotenoids and sterols to evaluate their content (measured at 465 or 280 nm, respectively) and composition (analyzed by RP-HPLC). SRE1N expression increased sterol and carotenoid production, suggesting that Sre1 is responsible for the carotenoid and ergosterol overproducing phenotype in mutants unable to produce ergosterol.

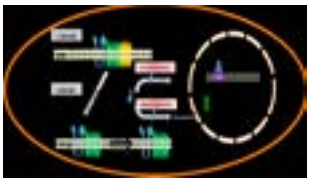

Figure: SREBP Pathway: The Sre1 (in yeast) transcriptional activator is synthesized as an inactive precursor that is bound to the endoplasmic reticulum (ER) membrane through two transmembrane helices.

Biography

Maria Soledad Gutierrez was graduated in Molecular Biotechnology Engineering from University of Chile in 2014, studying the alternative electron donor in P450s systems of the carotenogenic yeast *Xanthophyllomyces dendrorhous*.

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