Engineering *Aspergillus terreus* Metabolic Pathways to Increase Lovastatin Production via Metabolic Engineering and Fermentation Approaches

Hanan Hasan[1], Muhammad Hafiz Abd Rahim[1], Leona Campbell[2], Dee Carter[2], Ali Abbas[2,3], and Alejandro Montoya[3]

[1]University Putra Malaysia
[2]University of Sydney
[3]The University of Sydney

June 23, 2020

Abstract

This study explores the application of metabolic engineering in *Aspergillus terreus* to re-route the precursor flow towards the lovastatin biosynthetic pathway by simultaneously overexpressing the gene for acetyl-CoA carboxylase (*acc*) to increase the precursor and eliminating (+)-geodin biosynthesis (competing metabolite), by knocking out emodin anthrone polyketide synthase (*gedC*). Alterations to metabolic flux in the double mutant ($\gamma\epsilon\delta\tilde{}\Delta*a\varsigma\varsigma o\xi$) strain and the effects of using two different substrate formulations were examined. Cultivation of $\gamma\epsilon\delta\tilde{}\Delta*a\varsigma\varsigma o\xi$ strain with a mixture of glycerol and lactose, had greatly increased levels of precursors malonyl-CoA (48%) and acetyl-CoA (420%), complete inhibition of (+)-geodin biosynthesis and a maximum production of lovastatin (152 mg/L), 143% more than the wild-type (WT) strain. This study demonstrates the manipulation of *A. terreus* metabolic pathways to increase the efficiency of carbon flux towards lovastatin, elevating its production. It provides a framework for new opportunities to synthesize valuable compounds using cheap and renewable carbon sources.

Hosted file

`Hasan et. al 2020 Manuscript.docx` available at https://authorea.com/users/336007/articles/461829-engineering-aspergillus-terreus-metabolic-pathways-to-increase-lovastatin-production-via-metabolic-engineering-and-fermentation-approaches