

Overexpression of acetyl-CoA carboxylase in *Aspergillus terreus* to increase lovastatin production

ABSTRACT

The present work describes the application of homologous recombination techniques in a wild-type *Aspergillus terreus* (ATCC 20542) strain to increase the flow of precursors towards the lovastatin biosynthesis pathway. A new strain was generated to overexpress acetyl-CoA carboxylase (ACCCase) by replacing the native ACCCase promoter with a strong constitutive PadhA promoter from *Aspergillus nidulans*. Glycerol and a mixture of lactose and glycerol were used independently as the carbon feedstock to determine the degree of response by the *A. terreus* strains towards the production of acetyl-CoA, and malonyl-CoA. The new strain increased the levels of malonyl-CoA and acetyl-CoA by 240% and 14%, respectively, compared to the wild-type strain. As a result, lovastatin production was increased by 40% and (+)-geodin was decreased by 31% using the new strain. This study shows for the first time that the metabolism of *Aspergillus terreus* can be manipulated to attain higher levels of precursors and valuable secondary metabolites.

Keyword: Acetyl-CoA carboxylase; *Aspergillus terreus*; Homologous recombination; Lovastatin; Overexpression