Engineering the lactococcal mevalonate pathway for increased sesquiterpene production

ABSTRACT

Isoprenoids are a large, diverse group of secondary metabolites which has recently raised a renewed research interest due to genetic engineering advances, allowing specific isoprenoids to be produced and characterized in heterologous hosts. Many researches on metabolic engineering of heterologous hosts for increased isoprenoid production are focussed on Escherichia coli and yeasts. E. coli, as most prokaryotes, use the 2-C-methyl-D-erythritol-4-phosphate (MEP) pathway for isoprenoid production. Yeasts on the other hand, use the mevalonate pathway which is commonly found in eukaryotes. However, Lactococcus lactis is an attractive alternative host for heterologous isoprenoid production. Apart from being food-grade, this Gram-positive prokaryote uses the mevalonate pathway for isoprenoid production instead of the MEP pathway. Previous studies have shown that L. lactis is able to produce sesquiterpenes through heterologous expression of plant sesquiterpene synthases. In this work, we analysed the gene expression of the lactococcal mevalonate pathway through RT-qPCR to successfully engineer L. lactis as an efficient host for isoprenoid production. We then overexpressed the mvk gene singly or co-expressed with the mvaA gene as an attempt to increase ɓ-sesquiphellandrene production in L. lactis. It was observed that co-expression of mvk with mvaA doubled the amount of ɓ-sesquiphellandrene produced.

Keyword: Isoprenoid; Lactococcus lactis; Metabolic engineering; Mevalonate pathway; RT-qPCR; Sesquiterpene