PRODUCTION OF α-BISABOLOL FROM METABOLICALLY ENGINEERED ESCHERICHIA COLI

Ju-Eon Park, Institute of Agriculture and Life Science, Gyeongsang National University, Korea
pachajueoi@gmail.com
Chonglong Wang, School of Biology and Basic Medical Sciences, Soochow University, Suzhou, People's Republic of China
Hyo-Jung Han, Division of Applied Life Science (BK21 Plus), PMBBRC, Gyeongsang National University, Korea
Sinyoung Kim, Division of Applied Life Science (BK21 Plus), PMBBRC, Gyeongsang National University, Korea
Seon-Won Kim, Division of Applied Life Science (BK21 Plus), PMBBRC, Gyeongsang National University, Korea

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α-Bisabolol is a natural-occurring sesquiterpenoid with applications in cosmetics as whitening and soothing agent. It is synthesized from the universal precursors, isopentenyl pyrophosphate (IPP) and dimethylallyl pyrophosphate (DMAPP), which are generated either through the mevalonate (MVA) pathway or the 2C-methyl-D-erythritol-4-phosphate (MEP) pathway. Farnesyl pyrophosphate (FPP) synthase (IspA) then catalyzes the condensation of IPP and DMAPP to the linear FPP, which is rearranged and cyclized to α-bisabolol by bisabolol synthases.

Here, we compared the capacity of 5 α-bisabolol synthases from *Lippia dulcis*, *Streptomyces citricolor*, *Santalum spicatum*, *Matricaria recutita*, and *Artemisia annua* for α-bisabolol production. MVA pathway and FPP synthase were also overexpressed to supply sufficient FPP for bisabolol synthesis in the recombinant *E. coli*. Bisabolol synthase from *M. recutita* (MrBBS) shows the highest activity of bisabolol synthesis, and 75 mg/L/OD_{600} of bisabolol was produced in a test-tube culture. We further optimized the expression level of IspA and MrBBS by modulation their RBS strength. The 24 bisabolol synthesis operons with different RBSs were assessed for their performance on bisabolol synthesis. By this approach, the best strain is able to produce bisabolol with a capacity of 220mg/L/OD_{600} in a test tube culture. The consequence of host strain optimization led to an increase in bisabolol production to 300 mg/L/OD_{600}, which presents a 4-fold increase over the initial engineered strain. This work was supported by a grant (NRF-2016R1A2B2010678) from the National Research Foundation, MSIP, Korea.