IMPROVEMENT OF RETINOIDS PRODUCTION IN RECOMBINANT *E. COLI* USING GLYOXYLIC ACID

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Isoprenoids are the most chemically diverse compounds found in nature. They are present in all organisms and have essential roles in membrane structure, redox chemistry, reproductive cycles, growth regulation, signal transduction and defense mechanisms. In spite of their diversity of functions and structures, all isoprenoids are derived from the common building blocks of isopentenyl diphosphate (IPP) and its isomer dimethylallyl diphosphate (DMAPP). Optimization of IPP synthesis pathway is of benefit to mass production of various isoprenoids. There are two pathways of 2-C-Methyl-D-erythritol-4-phosphate (MEP) and mevalonate (MVA) for IPP synthesis. Prokaryotes including *E. coli* generally use MEP pathway whereas MVA pathway is used in eukaryotes.

To improve isoprenoid production, it was performed the deletion of genes in *E. coli,* which are involved in both formation of fermentation by-products such as organic acids and alcohols, and consumption of precursors of MEP and MVA pathways, pyruvate and acetyl-CoA. As a result, we were able to develop a strain with improved fermentation productivity and carbon source utilization efficiency, the mutant strain was called AceCo. Higher lycopene production was achieved in the AceCo strain compared to the wild type MG1655 strain due to no formation of the inhibitory by-products. However, retinoids production of AceCo strain decreased to a half of that of MG1655 strain.

The decrease of retinoids production was presumed to be related to glyoxylate cycle. Glyoxylic acid was thus added in various concentrations into the culture media. It increased the retinoids production in the AceCo strain by up to 80% after 72 hours when 10g/L glyoxylic acid was added. In MG1655 strain, the supplementation of 1g/L glyoxylic acid improved the retinoids production by 3-folds at 24 hours. This work was supported by the grant (NRF-2016R1A2B2010678 and NRF-2016M1A2A2924237) from the National Research Foundation, Korea.

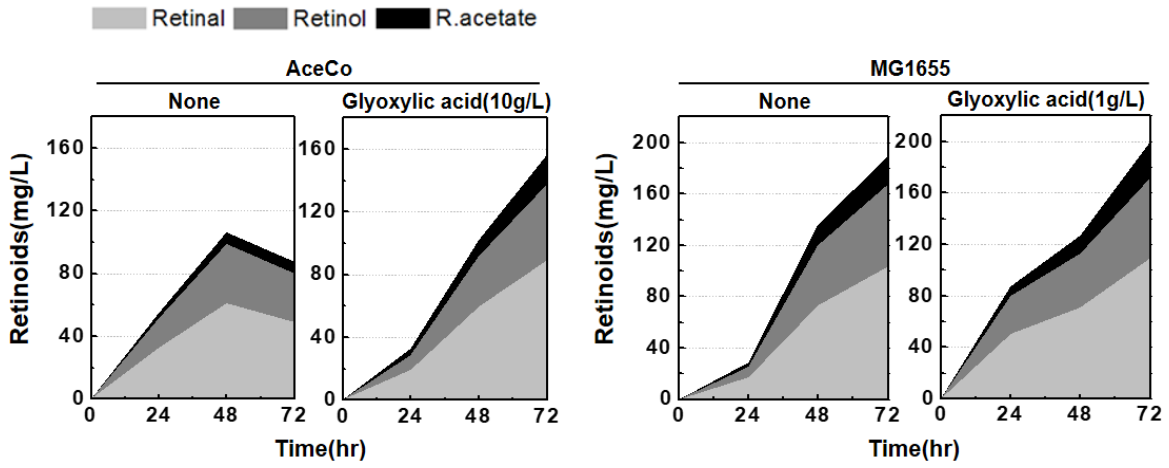

Figure 1 – Production of Retinoids from AceCo and MG1655 strain harboring pT-DHBSR and pSNA with or without supplementation of glyoxylic acid. Culture was carried out at 30℃ for 72 hours in 2YT medium containing, 2% (v/v) glycerol, and 0.2% (w/v) arabinose with overlay of 5mL dodecane.