Bilevel Optimization of gene amplification for enhanced lycopene production of *Escherichia coli* using metabolic flux analysis

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Lycopene is a red-colored open-chain unsaturated carotenoid, which is predominantly found in red fruits and vegetables, and widely used as an antioxidant, anti-cancer agent. Combinatorial engineering for direct synthesis of desired products and systems biology to interfere rational metabolic design from complete genome of *Escherichia coli* have been emerged to enhance lycopene production. In this study gene amplification for balancing precursors i.e. pyruvate and glyceraldehydes-3-phophate in central metabolism are evaluated by bilevel-optimization with enhanced gene modification and lycopene flux using constrained- based FBA and MOMA. As a result of metabolic redesign, metabolic engineered strain produced more lycopene contents. Systematic approach by dual optimization using metabolic flux analysis is indispensable for enhanced lycopene production. (Acknowledgement:This work was financially supported by the Korean Systems Biology Research program (M10309090000-03B5002-00000) of the Korean Ministry of Science and Technology (MOST), and LG chemicals Chair Professorship. Hardware for computational analysis supported by the IBM-SUR program.)