Precise precursor rebalancing for isoprenoid production by fine control of gapA expression in *Escherichia coli*

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Biosynthesis of isoprenoids via the DXP pathway requires equimolar glyceraldehyde 3-phosphate and pyruvate to divert carbon flux toward the products of interest. Here, we demonstrate that precursor balancing is one of the critical steps for the production of isoprenoids in *E.coli*. First, the implementation of the synthetic lycopene production pathway as a model system and the amplification of the native DXP pathway were accomplished using synthetic promoters and redesigned 5′-UTRs. Next, fine-controlled precursor balancing was investigated by tuning phosphoenolpyruvate synthase (PpsA) or glyceraldehyde 3-phosphate dehydrogenase (GAPDH). The results showed that tuning-down of gapA improved the specific lycopene content by 46% compared to the overexpression of ppsA. The lycopene in the strains with downregulated gapA increased by 96% compared to that in the parental strain. Our results indicate that gapA is the best target for precursor balancing to increase biosynthesis of isoprenoids.