Engineering Escherichia coli for the production of Propionic Acid through the Wood-Werkman Cycle

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Propionic acid is a used primarily as a food preservative, but also for the production of fabrics, cosmetics and plastics. Compared to the current petrochemical production route, biological production of propionic acid is economically and environmentally attractive. Native producers Propionibacteria show promising yields and productivities, however we still lack of the genetic engineering tools to boost their metabolism to commercial levels. In this work, we have transferred the Propionibacteria’s pathway known as the Wood-Werkman cycle into Escherichia coli. First, we ran in silico simulations to evaluate the potential of E. coli for propionic acid production. Then, the optimized nucleotide sequences for the genes in the cycle were synthesized and cloned into synthetic operons. Four different promoters and two operon arrangements were tested. Our results showed the cycle to be functional in E. coli. Production of propionic acid and propanol was observed, reaching concentrations of up to 3.5 mM and 1 mM, respectively.

Figure 1: Recombinant system for the expression of the Wood-Werkman cycle in E. coli. A) Codon optimization P. acidipropionici genes from high GC content (70%, blue trend line) to average E. coli’s GC content (55%, yellow trend line). B) Structure of the synthetic operon. C) The Wood-Werkman cycle (red) coupled to E. coli’s central carbon metabolism (black). Reversible reaction of the TCA cycle are shown in blue.


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