Antisense Regulation of Acetate Pathway in *E. coli* for improved recombinant protein production

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A problem using *Escherichia coli* to produce foreign proteins is that although endogenously produced acetate is physiologically indispensable, it inhibits protein expression. We firstly employed an antisense strategy as an elaborate metabolic engineering tool to partially block biosynthesis of acetate pathway enzymes, pta and ackA. Three recombinant plasmids containing antisense genes targeting either or both of pta and ackA were compared to control without any antisesne genes to find out their effects on the acetate pathway and foreign protein(GFP) productivity in *E. coli* BL21. We found the antisense method partially reduced mRNA, activity levels of target enzyme and lowered the concentration of acetate in all antisense-regulated strains. Notably, total production of GFP was enhanced 1.6- to 2.1-fold in antisense-regulated strains, even though the degree of acetate reduction was not significantly large. It was revealed acetate pathway has more critical roles in cellular physiology than expected in the previous reports. When the culture scale increased, enhancement of protein production became larger, demonstrating this antisense strategy can be successfully applied to practical large-scale protein production processes.