Engineering *Escherichia coli* for Increased Productivity of Serine-Rich Proteins Based on Proteome Profiling

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Variations in proteome profiles of *Escherichia coli* in response to the overproduction of human leptin, a serine-rich (11.6% of total amino acids) protein, were examined by 2-dimensional gel electrophoresis. The levels of heat shock proteins increased while those of protein elongation factors, 30S ribosomal protein, and some enzymes involved in amino acid biosynthesis decreased after leptin overproduction. Most notably, the levels of enzymes involved in the biosynthesis of serine family amino acids significantly decreased. Based on this information, we designed a strategy to enhance the leptin productivity by manipulating the *cysK* gene, encoding cysteine synthase A. By the co-expression of the *cysK* gene, we were able to increase the cell growth rate by ca. twofold. Also, the specific leptin productivity could be increased by four-fold. In addition, we found that *cysK* co-expression can improve the production of another serine-rich protein, interleukin-12 β chain, suggesting that this strategy may be useful for the production of other serine-rich proteins as well. The approach taken in this study should be useful in designing a strategy for improving recombinant protein production.

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