論 文 要 旨

Genome-wide transcriptome analysis of fluoroquinolone resistance in clinical isolates of *Escherichia coli*

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Objectives: Coincident with their worldwide use, resistance to fluoroquinolones in *Escherichia coli* has increased. To identify the gene expression profiles underlying fluoroquinolone resistance, we carried out genome-wide transcriptome analysis of fluoroquinolone-sensitive *E. coli*.

Methods: Four fluoroquinolone-sensitive *E. coli* and five fluoroquinolone-resistant *E. coli* clinical isolates were subjected to complementary deoxyribonucleic acid microarray analysis. Some upregulated genes' expression was verified by real-time polymerase chain reaction using 104 *E. coli* clinical isolates, and minimum inhibitory concentration tests were carried out by using their transformants.

Results: A total of 40 genes were significantly upregulated in fluoroquinolone-resistant *E. coli* isolates ($P < 0.05$). The expression of phage shock protein operons, which are involved in biofilm formation, was markedly upregulated in our profile of fluoroquinolone-resistant *E. coli*. One of the phage shock protein operons, *pspC*, was significantly upregulated in 50 fluoroquinolone-resistant *E. coli* isolates ($P < 0.0001$). The expression of type I fimbriae genes, which are pilus operons involved in biofilm formation, were markedly downregulated in fluoroquinolone-resistant *E. coli*. Deoxyribonucleic acid adenine methyltransferase (*dam*), which represses type I fimbriae genes, was significantly upregulated in the clinical fluoroquinolone-resistant *E. coli* isolates ($P = 0.007$). We established pspC- and dam-expressing *E. coli* transformants from fluoroquinolone-sensitive *E. coli*, and the minimum inhibitory concentration tests showed that the transformants acquired fluoroquinolone resistance, suggesting that upregulation of these genes contributes to acquiring fluoroquinolone resistance.

Conclusions: Upregulation of *psp* operones and *dam* underlying pilus operons downregulation might be associated with fluoroquinolone resistance in *E. coli*.