Proteomic Analysis of DNA Starvation/Stationary Phase Protection Proteins from Extended Spectrum β – Lactamase Producing *Escherichia coli*

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ABSTRACT

Escherichia coli, especially the extended-spectrum β-lactamase producing E. coli (ESBL-EC), is the most frequent cause of urinary tract infections. They are not only resistant to β - lactams, but also may be resistant to other drugs, such as ciprofloxacin (CIP). This study aims to identify the proteins related to its CIP resistance using proteomic analysis by isolating ESBL-EC from urine specimens, and comparing the significantly different intracellular proteins extracted from these high-resistant isolates, with or without ciprofloxacin. Among 2,072 uropathogenic E. coli that were screened, 1,644 (79.34%) were confirmed as ESBL-EC isolates. Based on the minimal inhibitory concentrations (MIC) of ceftazidime (CAZ) and ciprofloxacin, 193 isolates (12.12%) exhibited high-level resistance ($CAZ^{HR}CIP^{HR}$). Fourteen isolates of ($CAZ^{HR}CIP^{HR}$) and a representative isolate each of intermediate resistance ($CAZ^{I}CIP^{I}$) and resistance ($CAZ^{R}CIP^{R}$) were selected to detect the different protein bands. They were cultured in Mueller Hinton broth (MHB) with various concentrations of CIP or without CIP. Intracellular protein of each selected isolate was separately extracted, detected, and compared by SDS – PAGE. Interestingly, we found a distinct intracellular protein band at approximately 19 kDa in the presence of ciprofloxacin after extracting from the MHB culture. Comparative analysis by 2-D gel revealed 10 protein spots at an interesting range of molecular weight; these were selected and further analyzed with LC-MS/MS. Proteomic identification showed that two of these protein spots matched a DNA starvation/stationary phase protection protein. This protein is responsible for protecting DNA from damage by ciprofloxacin. This protein may play a role in maintaining ciprofloxacin tolerance in ESBL-EC when MIC of ciprofloxacin is increased.

Keywords: ESBL, *Escherichia coli*, Ciprofloxacin, DNA starvation/stationary phase protection proteins, Proteomic analysis