Role of *Mar* Operon in Acquisition of Resistance to Quaternary Ammonium Compounds in *Escherichia Coli*

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Abstract: In the modern societies, various techniques to control harmful microbes, such as using biocides, are essential to enjoy our comfortable life. Quaternary ammonium compounds (QAC), cationic surfactants, have been widely used as biocides for medical, industrial and domestic purposes because of their low toxicity or wide antimicrobial spectrum. However, such a repetition of daily use has also brought about spreading of resistant bacteria. Therefore, this study was done to clarify the resistance mechanism to QAC and to get resistant bacteria under control. *Escherichia coli* NBRC12713 resistant to a QAC, *N*-dodecylpyridinium iodide (P-12), was bred in the laboratory and characterized comparing with a normal strain. As for the resistant strain, the cell surface was more hydrophilic, and the amount of lipopolysaccharide of outer membrane was increased. It was suggested that *E. coli* acquired the resistance to QAC by controlling the adsorption/binding reaction between cell and QAC. The proteomic analysis showed that QAC leads to over expression of drug efflux pumps and the proteins related to organic solvent resistance. Then, the role of *mar* operon that closely relates to multidrug resistance or expression of stress proteins, in resistance to QAC in *E. coli* was studied. Minimum inhibitory concentration (MIC) of P-12 against the MarA (transcription activator)-over expressing clone (80.0 μ M) was higher than MIC of the host (*E. coli* BL21 DE3) without a vector (26.2 μ M). Therefore, it was indicated that over expression of *marA* closely relates to resistance to QAC. Furthermore, since a point mutation to stop protein synthesis was found in *marR* gene of the resistant strain, it is implied that *marR* (transcription repressor) inactivation leads to high-level resistance to QAC. In order to elucidate how mutation in *marR* affects the binding to QAC and resultantly to discuss what a role *mar* operon plays in acquiring biocide-resistance, bioinformatic analysis is now in progress.

Key words: Quaternary ammonium compounds (QAC), cationic surfactants, biocides, medical, industry, domestic purposes.