

RELATIONSHIP BETWEEN THE AdeABC EFFLUX SYSTEM GENE CONTENT, NETILMICIN SUSCEPTIBILITY AND MULTIDRUG RESISTANCE IN A GENOTYPICALLY DIVERSE POPULATION OF *ACINETOBACTER BAUMANNII*

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The AdeABC efflux system, encoded by three structural genes (*adeA*, *adeB*, *adeC*), has been associated with decreased susceptibility to aminoglycosides and other antibiotics in clinical strains of *Acinetobacter baumannii*. Up-regulation of this system has been ascribed to mutation in the regulatory genes *adeR* or *adeS*. This study assessed the occurrence of the AdeABC efflux system, and its association with antibiotic resistance, in a well-documented set of *A. baumannii* strains.

A genotypically and epidemiologically heterogeneous set of 120 *A. baumannii* strains was investigated. The strains were allocated to six multidrug resistant (MDR) clonal groups ($n=71$) or to unique genotypes ($n=49$) by AFLP analysis. PCR detection of the *adeA*, *adeB*, *adeR* and *adeS* genes was performed. Susceptibility to 11 antibiotics was tested by disk-diffusion. In addition, MICs to netilmicin, a possible phenotypical marker for up-regulation of the AdeABC system, was determined. Finally, PCR was used to detect two genes (*aacC2* and *aacA4*) which encode netilmicin-modifying enzymes and are commonly found in *A. baumannii*.

Ninety-nine (83%) strains, including all except one of the strains belonging to EU clones I - III, were positive for all four genes, while ten strains were positive for one to three genes. None of the genes were found in 11 strains, eight of which were fully susceptible (FS). Strains positive for all genes were MDR ($n=75$) or FS ($n=23$). Seven MDR strains were positive for *aacC2* or *aacA4*. All *A. baumannii* strains ($n=61$) with netilmicin MICs ≥ 4 mg/L, but without the netilmicin resistance genes, were both MDR and positive for all four genes, while strains with netilmicin MICs ≤ 2 mg/L ($n=52$) included all FS strains and those that tested negative for one or more efflux genes. The FS strains were genotypically highly heterogeneous as indicated by their AFLP profiles.

In conclusion, AdeABC is common in both MDR and FS *A. baumannii*, but may be absent in some strains. Strains with AdeABC genes present but not expressed, as indicated by susceptibility to netilmicin, are not uncommon and are usually susceptible to many other antibiotics. It is postulated that multidrug resistance in *A. baumannii* is generally associated with the presence of upregulated AdeABC.

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