

Genetic diversity of the *Staphylococcus aureus* efflux pump gene *norA*

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Efflux pumps are capable of extruding multiple antimicrobial compounds from the cell, contributing to the development of resistance phenotypes. In *Staphylococcus aureus* one of the most well studied efflux pumps is NorA, which has been related to reduced susceptibility to fluoroquinolones and biocides. Earlier studies described two alleles of NorA encoding gene, *norAI* and *norAII*. However, the relevance of each *norA* allele in the clinical setting is scarcely documented. In our study, the promoter region and structural *norA* gene sequences were analyzed in representatives of a collection of clinical *S. aureus* isolates and in the reference strain ATCC25923, in order to ascertain the occurrence of each *norA* allele and establish a correlation between the *norA* alleles and susceptibility phenotypes to different antimicrobial compounds.

Among the isolates carrying *norAI*, three types of alterations were found, namely an insertion downstream of the -10 consensus promoter sequence and the mutations Gly147Ser and Gly291Asp. The *norAII* allele showed a higher number of mutations when compared to the *norAII* allele described earlier, of which only one resulted in an aminoacid substitution, Asn200Asp. RT-qPCR assays and MIC determinations showed no direct correlation between *norA* alleles and the strain susceptibility profile towards fluoroquinolones and biocides. Further characterization of *norA* diversity should clarify the importance of the different NorA variants and their interplay with the remaining *S. aureus* efflux pumps.