Development of acquired resistance by *Staphylococcus aureus* to a big-defensin

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Abstract

The ever-increasing resistance to antibiotics is a global health issue. Thanks to their cationic properties that promote their binding to the negatively charged bacterial surface, cationic antimicrobial peptides (CAMPs) represent an alternative to conventional antibiotics. To explore the therapeutic potential of *Cg*-BigDef1, a promising CAMP active against methicillin resistant *Staphylococcus aureus* (MRSA) clinical strain [1], we studied a possible development of resistance by bacteria after a 14-day exposure to this peptide. The results show the development of both acquired and adaptive resistance by MRSA and non-MRSA strains. Genomic analyses were performed and several mutations were found in resistant clones. Constructions of mutants are currently underway to verify the role of these mutations in acquired resistance. For one selected resistant clone carrying mutations on several genes including a frame shift on the gene *lyrA* (or *spdC*), transcriptomic study was realized to determine the mechanism of resistance. Interestingly, we observed an up-regulation of *dlta* gene, implicated in the addition of positive charges on teichoic acid of *S. aureus*, and known to modulate the action of CAMPs on *S. aureus*. The capsule operon was also up regulated. Studies are currently underway to examine the possible implication of capsule production in the observed resistance. This study highlights the need to examine the possibility of CAMPs to induce bacterial resistance before the development of clinical trials.

Références :

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