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Differential daptomycin resistance development in *Staphylococcus aureus* strains with active and mutated *gra* regulatory systems

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ABSTRACT

The first-in-class lipopeptide antibiotic daptomycin (DAP) is highly active against Gram-positive pathogens including β -lactam and glycopeptide resistant strains. Its molecular mode of action remains enigmatic, since a defined target has not been identified so far and multiple effects, primarily on the cell envelope have been observed. Reduced DAP susceptibility has been described in *S. aureus* and enterococci after prolonged treatment courses. In line with its pleiotropic antibiotic activities, a unique, defined molecular mechanism of resistance has not emerged, instead non-susceptibility appears often accompanied by alterations in membrane composition and changes in cell wall homeostasis. We compared *S. aureus* strains HG001 and

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