論 文 要 旨

An alternative nisin A resistance mechanism affects virulence in *Staphylococcus aureus*

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Abstract

Nisin A is a bacteriocin produced by *Lactococcus lactis* and is widely used as a food preservative. *Staphylococcus aureus* has the BraRS-VraDE system that provides resistance against low concentrations of nisin A. BraRS is a two-component system that induces the expression of the ABC transporter VraDE. Previously, we isolated a highly nisin A-resistant strain with increased VraDE expression due to a mutation in *braRS*. In this study, we isolated *S. aureus* MW2 mutants with BraRS-VraDE-independent nisin A resistance. These mutants, designated SAN2 (*S. aureus* nisin resistant) and SAN469, had a mutation in *pmtR*, which encodes a transcriptional regulator responsible for the expression of the *pmtA-D* operon. As a result, these mutants exhibited increased expression of PmtA-D, a transporter responsible for the export of phenol soluble modulin (PSM). Characterization of the mutants revealed that they have decreased susceptibility to human β defensin-3 (hBD3) and LL37, which are innate immune factors. Additionally, these mutants showed higher hemolytic activity than the original MW2 strain. Furthermore, in a mouse bacteremia model, the SAN2 strain exhibited a lower survival rate than the original MW2 strain.

These results indicate that the increased expression of *pmtA-D* due to *pmtR* mutation is an alternative nisin A resistance mechanism that also affects virulence in *S. aureus*.