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# Differential regulation of Alpha-Toxin expression by SNPs in *Staphylococcus aureus* Isolates of Bovine Mastitis

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## Abstract

*Staphylococcus aureus* is a major human and animal pathogen that can cause a variety of diseases. The exported α-toxin (*hla*) is an important virulence factor in many S. aureusinfections. Although the complicated regulation of *hla*expression has been well studied in human *S. aureus* isolates, the mechanisms of *hla* regulation in bovine *S. aureus* isolates remain poorly defined. We found that many bovine *S. aureus* isolates generate tremendous amounts of α-toxin *in vitro*culture compared with human clinical *S. aureus* isolates. To explore potential regulatory mechanisms, we identified predominant single nucleotide polymorphisms (SNPs) at the *hla* promoter regions. Using bioinformatics, site-directed mutagenesis and *hla* promoter-*lux* reporter approaches, we identified and demonstrated that the SNPs contribute to the differential control of *hla* expression among bovine and human *S. aureus* isolates. Using a DNA affinity assay, gel-shift assays and a null mutant, we identified and revealed that an *hla*positive regulator, SarZ, mainly contributes to the involvement of the SNPs in mediating *hla*expression. In addition, we found that the hyper-production of α-toxin in these bovine S. aureus isolates may be partially attributable to higher transcription levels of *hla* positive regulators, including *agrA*, *saeR*, and *arlR*, but a lower expression level of *hla* repressor *rot* compared to the human *S. aureus* isolate. These findings provide new insights into the regulatory mechanisms of hlaexpression in S. aureus. Moreover, the identification of predominant SNPs in the*hla* promoter region may provide a novel method for genotyping the *S. aureus* isolates.

## Biography

Yinduo Ji is an associate professor of microbiology at the University of Minnesota, USA. He obtained his Ph.D. from the Chinese Center for Disease Control and Prevention in 1993 anddid his postdoctoral training at the University of MinnesotaMedical School from 1994 -1997.Then, he joined in the GlaxoSmithKline Pharmaceuticals Research & Development, USA, and performed basicanti-infective drug discovery. Since 2002, he has joined in the Department of Veterinary Biomedical Science at the University of Minnesota as a faculty member; his research focuses on the functional genomics, molecular and cellular pathogenesisof *Staphylococcusaureus*, and antibacterial drug discovery.