

**Title:** Origin, evolution, and zoonotic potential of livestock-associated methicillin-resistant *Staphylococcus aureus* found in US swine farms - NPB #14-124

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**Scientific Abstract:** Since its first detection associated with swine industry, livestock associated methicillin-resistant *S. aureus* (LA-MRSA) has drawn concern from the public health community for two main reasons. The first reason is that these isolates are the single largest reservoir of MRSA outside of hospitals settings and secondly, similar to all MRSA strains, LA-MRSA strains tend to contain a high number of antimicrobial resistance genes. The adaption and evolution of *S. aureus* is largely due to the acquisition of large segments of DNA referred to as mobile genetic elements (MGEs) that carry genes encoding factors enabling *S. aureus* to cause disease and antimicrobial resistance (AMR). The first sequence type (ST) of LA-MRSA associated with swine is ST398. Studies have demonstrated a genetic basis for reduced human infection with ST398. In the US, MRSA ST5 is more commonly being found in swine facilities. Genetic studies similar to the ones performed on ST398 strains have not been conducted on these MRSA ST5 strains. The objectives of this study were to 1) obtain draft whole-genome sequences of 110 ST5 strains isolated from human, animal, and environmental samples collected from swine farms in the U.S. 2) compare the draft genome sequences obtained for these strains to each other and to other MSSA and MRSA publicly available genome sequences to generate a more comprehensive assessment of the origin, evolution, and zoonotic potential of these strains. 3) use *in vitro* binding assays to test the capacity of these strains, which draft genome sequence information will be obtained, to adhere to human and porcine keratinocytes. To date we have obtained whole-genome sequence for 155 ST5 strains encompassing both MSSA and MRSA strains from both human and swine related sources. Additionally, we have chosen a subset of these strains that encompasses the diversity based on spa type, host, and origin or location of isolation and used these strains in *in vitro* binding assays. The genome assemblies for the ST5 strains is now complete along with the phylogenetic and other comparative genomic analyses. One of the comparative genomic analyses that is now completed is the screening of these ST5 isolates for the prevalence of the IEC genes carried by  $\beta$ -hemolysin converting bacteriophages, whose absence in LA-MRSA ST398 is thought to contribute to reduced rates of human infection and transmission associated with this lineage. We found IEC genes absent from any of the ST5 strains from agricultural sources and the  $\beta$ -hemolysin gene was intact in these strains, indicating the bacteriophage's absence. In contrast, the prevalence of the  $\beta$ -hemolysin converting bacteriophage in ST5 strains from humans with no exposure to swine was 90.4%. The absence of  $\beta$ -hemolysin converting bacteriophage in LA-MRSA ST5 isolates is consistent with previous reports evaluating ST398 strains and provides genetic evidence indicating LA-MRSA ST5 isolates may harbor a reduced capacity to cause severe disease in immunocompetent humans.

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