TITLE: COMPARATIVE GENOMICS OF METHICILLIN-RESISTANT *Staphylococcus aureus* ISOLATES OF ST239 LINEAGE BELONGING TO THE BRAZILIAN EPIDEMIC CLONE.

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Abstract:

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a bacterial pathogen associated with both community and hospital infections. Isolates of the Brazilian epidemic clone (BEC), belonging to the ST239-SCC*mec*III lineage, are widely disseminated in hospitals located in Brazil and in other countries. In this study, genomic tools were used aiming to compare the Brazilian ST239 isolates with previously sequenced international ST239 strains. Whole-genome sequencing was performed in seven Brazilian ST239 isolates collected from different infection sites or from the nose of colonized patients. Sequencing was performed using a 454 platform (Roche), genomes were assembled (Celera and Newbler softwares) and annotated (Sabia platform). Phylogenetic analysis based on single nucleotide polymorphism showed that the Brazilian isolates clustered within a same clade, separately from the international strains. The analysis of mobile genetic element (MGE) shows that five of the Brazilians carry a transposase element upstream *mgrA* (TEu*mgrA*) coding sequence, which was absent in international ST239 isolates. The PCR screening showed that 58% of the isolates in a collection of 100 BEC had this TEu*mgrA*. In addition, a statistical correlation was found between isolates collected from infection sites and presence of TEu*mgrA* (p<0.01). We also found another transposase element that was unique for all ST239 isolates sequenced so far (Brazilians and international); however, this element could not be found when searched in other *S. aureus* genomes on public databases, suggesting that this transposase element is a marker for the ST239 lineage. Bacteriophage analysis showed that the Brazilian and international isolates carry 4-6 phage elements and only two phages in common: phiNM3 and PT1028, although some differences could be observed on their sequences. Brazilian isolates lack some enterotoxin-like genes, but *chp* gene was exclusively found among the Brazilians. The *chp* gene codifies for a chemotaxis inhibitory protein, being involved in evasion mechanisms, possibly favoring infection development. Concluding, our data suggest that differences in virulence gene content and the insertion of a transposase element near *mgrA* promoter region might have contributed to the widespread of the BEC isolates in this country.

Key-words: Methicillin-resistant *Staphylococcus aureus*, ST239, comparative genomics.