Title: Comparative genomic of the methicillin-resistant *Staphylococcus aureus* isolates of the ST1-SCC*mec* IV lineage associated with community- or hospital-associated infections

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Abstract:

Methicillin-resistant *Staphylococcus aureus* (MRSA) of the ST1-SCC*mec*IV lineage have mainly been associated with community-acquired (CA) infections in USA, Canada and Australia. In Brazil, multiresistant ST1-SCC*mec*IV isolates have emerged in hospitals located in Rio de Janeiro, with high incidence of nosocomial bloodstream infections, while the North-American and Australian ST1 siblings have mainly been involved in skin/soft tissue infections affecting individuals from the community. These differences in clinical and epidemiological features suggest that ST1 isolates have diverged during their evolutionary paths to adapt as hospital or community pathogens. To gain some insights in the mechanisms involved in this divergence, the complete genome sequencing of seven ST1 isolates (two Americans, two Canadians, two Brazilians and one Australian) was performed using the Ion Torrent and 454 sequencing platforms. The genomes were assembled (Mauve and Newblersoftwares) and annotated (Sabia platform). In addition, we included in these analyses the genome of the ST1 isolate MW2, deposited in the GenBank with the accession no. BA000033. Our initial analyses showed that the great majority of the virulence genes were conserved in the different genomes; however, some genes were missing among the Brazilian isolates, including *lukFS*-PV, *fnbB*, and some superantigens. Additionally, despite the fact that all isolates carried the protease genes *splABCF*, only the Brazilians and Australians harbored *splDE.* Most of these genes were located in mobile genetic elements (MGE). It is interesting that the lack of a virulence gene was not accompanied by the absence of the associated MGE; high identity was found among MGE, independently on the presence or absence of the specific gene.Only the Brazilian isolates show resistance to ciprofloxacin [*grlA*(TCC (Ser-80) → TAC (Tyr)] and [*gyrA* (TCA (Ser-84) → TTA (Leu)], clindamycin and erythromycin (*ermC*), and to chloramphenicol (*cat*). A phylogenetic tree constructed based on SNPs (snpTree 1.1) suggested that the Brazilian isolates have more recently shaped their evolutionary adaptations, and seem to be more related to the Australian clone. New understanding of the mechanisms involved in the emergence of new bacterial clones might bring new insights into the evolutionary events associated with the clonal wave, and may help for predicting the spread of new epidemic and hipervirulent MRSA clone.

Keywords: MRSA, ST1 lineage, Comparative genomic, Whole genome sequencing

Sponsorship: CNPq, FAPERJ, CAPES