**TITLE:** THE MRSA CLONE ST105-SCC*mec*II-t002 DISPLAYS INCREASED ABILITY TO EVADE THE HOST IMMUNE SYSTEM

**AUTHORS:** VIANA, A.S.; BOTELHO, A.M.N.; ECHEVARRIA-LIMA, J.; FERREIRA-CARVALHO, B.T.; FIGUEIREDO, A.M.S.

**INSTITUTION:** INSTITUTO DE MICROBIOLOGIA PAULO DE GÓES, UNIVERSIDADE FEDERAL DO RIO DE JANEIRO (RUA CARLOS CHAGAS FILHO 373 - BLOCO I, CIDADE UNIVERSITÁRIA, RIO DE JANEIRO, RJ)

**ABSTRACT**:

Methicillin-resistant *Staphylococcus aureus* (MRSA) are major hospital pathogens that can be involved in life-threatening infections. In addition to the *S. aureus* ability to acquire antimicrobial resistances, they present a plethora of virulence factors; some of which enable them to escape the host immune system by subverting phagocytosis, reactive oxygen species and complement activation. MRSA clones are usually defined by SCC*mec* typing, MLST and *spa* polymorphisms. Recently, we have performed a large epidemiological panel study, in Rio de Janeiro State, with 600 MRSA isolates, which reveals clonal complex 5 (CC5) as the predominant MRSA nowadays. Among CC5 isolates, ST105-SCC*mec*II-t002 prevailed, accounting for about 50%, followed by ST5-SCC*mec*IV-t002 (approx. 20%). The aim of this study was to compare CC5 MRSA clones in a phagocytosis model, bacterial survival after interaction with monocytes, and a virulence model using *Caenorhabditis elegans*. Phagocytosis assays were carried out using fluorescent-marked bacteria and the monocytes lineage THP-1 (MOI 10) and then measured by flow-cytometry. Additionally, after 30 min-interaction with monocytes, the survival of extracellular bacteria was determined by CFU counting. CC5 strains were used to feed adult *C. elegans* and nematode survival curves determined by daily counting for 3 days, using inverted microscopy. The genome sequencing of CC5 isolates was carried out using Illumina MiSeq system. Our data revealed a drop of 91.7% ($p$=0.0005) in the phagocytosis rate for the dominant ST105-SCC*mec*II-t002 in relation to ST5-SCC*mec*IV-t002. Also, the survival rate of ST105-SCC*mec*II-t002, after interaction with monocytes, was 10-fold higher than that of ST5-SCC*mec*IV-t002 ($p$=0.0422). Finally, no significant difference was observed in the *C. elegans* survival curves for ST105 and ST5 strains. Taken together, these results suggest that, although both clones showed comparable virulence in the nematoid model, ST105-SCC*mec*II-t002 appear to evolved toward increased capability of immune evasion, which may have contributed for their success as a hospital pathogen. In fact, a non-conservative mutation, occurred only in ST105-SCC*mec*II-t002 genomes, in the *aur* gene encoding aureolysin, a protease that cleaves host factors of the immune system, might be implicated in these evasion mechanisms.

**KEYWORDS**: Immune evasion; Phagocytosis; *Staphylococcus aureus*; Virulence

**DEVELOPMENT AGENCIES**: CNPq, CAPES, Bill and Melinda Gates Foundation, FAPERJ