TITLE: GENOMIC ANALYSES OF METHICILLIN-RESISTANT *Staphylococcus aureus* STRAINS ASSOCIATED TO OUTBREAKS

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ABSTRACT

Methicillin-resistant *Staphylococcus aureus* (MRSA) is one of the most important bacterial pathogens causing human infections due to its significant morbidity and mortality rates worldwide. Successful treatment of a MRSA infection is contingent upon timely and appropriate antimicrobial treatment. Additionally, the success of MRSA is, at least in part, related to the organism`s array of virulence factors. The ability to distinguish between high and low toxic MRSA can steer therapeutic treatment and facilitate the clearance of potentially persistent infections. The prediction of antimicrobial resistance (AMR) and virulence phenotype based on genome analysis has potential to facilitate more reliable and fast characterization of MRSA strains. Recently, our research group developed and validated a nanopore-based whole genome sequencing protocol for surveillance and outbreak investigation using 42 MRSA strains belonging to 4 different lineages. To perform complementary characterization of those genomes, the current study aims to evaluate AMR-related and virulence-related genes, comparing the results between Oxford Nanopore (ONT) and Illumina sequencing technologies. So far, the detection of AMR and virulence genes were performed using the ResFinder and VirulenceFinder, respectively, from Center of Genomic Epidemiology. As expected, the *mecA* gene was found in all the 42 MRSA genomes (100% identity). Other genes conferring AMR were also found, being the *blaZ* and *aac(6')-aph(2")* the most frequently among the lineages. The profile of virulence genes was mostly lineage-dependent, where each MRSA lineage showed a particular pattern of toxins and exoenzymes genes. Both AMR and virulence repertoire were also partially correlated among outbreaks identified previously. When comparing the results from the genomes sequenced by ONT and Illumina, 98,75% of the genes were found in both technologies, although some of them presented variable percentages of identity. Those differences will be further investigated. The study will also investigate mobile genetic elements and the influence of different times of ONT sequencing (20 and 48h). In addition, the AMR-related genes detected will also be compared with conventional phenotypic antimicrobial susceptibility testing. So far, MRSA characterization based on genome analysis looks to be a promising alternative in the effort to provide rapid and accurate complementary diagnostic.

Keywords: Genome sequencing; MRSA; Oxford Nanopore Technology; Resistance; Virulence.

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