TITLE: ANALISYS OF RESISTOME OF *Mycobacterium abscessus* SUBSP. *massiliense* BY NEXT GENERATION SEQUENCING

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ABSTRACT:
Mycobacterium abscessus complex (MABC) belongs to a group of rapidly growing mycobacteria which cause various diseases including skin and respiratory infections. This complex is composed of 3 related species: *M. abscessus* subsp. *abscessus, M. abscessus* subsp. *massiliense,* and *M. abscessus* subsp. *bolletii.* MABC is one of the most drug resistant mycobacteria, being naturally resistant to many antibiotics, including the first-line tuberculostatic drugs and was related to outbreaks in several regions of Brazil. This study aimed to analyze the resistome of *M. abscessus* subp. *massiliense* (termed myco1POA) in Rio Grande do Sul. The resistome of myco1POA was compared to other 3 MABC belonging to Brazilian outbreaks from different regions. The DNA was extracted by boiling and ultrasonic bath and a final step of purification was performed with ReliaPrep™ gDNA Tissue Miniprep System (PROMEGA). The library was made with the Nextera® XT DNA Sample Preparation Kit (Illumina, San Diego, CA), followed by quantification on TapeStation (Agilent) and sequenced in the MiSeq Platform (Illumina, San Diego, CA). The genome was trimmed with Trim Galore! and assembled with SPAdes Genome Assembler. After assembly, the sequences were annotated on Patrick server and detailed analyzes were made in the Geneious and Bioedit softwares. Susceptibility profile was determined by broth microdilution, according CLSI (M24-A2). The draft genome comprised 4.622,780 bp with an average G-C content of 64.18%. Our results showed high homology between myco1POA resistance related genes and the genes present in the following isolates: GO-06 (GO), CRM0020 (RJ) and INQCS_00594 (PA). The myco1POA presented one silent point mutation in the *rrl* gene (T116C) and in the *rrs* gene (C988T); multiple silent point mutations in *gyr*A and *gyr*B were also found; on the other hand, the *erm*(41) gene presented one point mutation which lead to one amino acid exchange (R282H). The minimum inhibitory concentration was 16 µg/mL for clarithromycin, 0.5 µg/mL for ciprofloxacin, 2 µg/mL for amikacin. Despite the fact that the isolate was resistant to clarithromycin, it was not possible to identify the mutation(s) responsible for this profile when compared to the literature. The latter indicates that the resistance determinants which lead to clarithromycin resistance in this isolate may be novel and not described in the literature as yet.

Keywords: *Mycobacterium abscessus* complex, Next Generation Sequencing, Resistome

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