

TITLE: INSIGHTS ON MOLECULAR MECHANISMS INVOLVED IN INFECTIVENESS AND MULTI-DRUG RESISTANCE IN *CORYNEBACTERIUM STRIATUM* THROUGH PAN-GENOME ANALYSIS

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ABSTRACT

Corynebacterium striatum, which is a common constituent of the human skin microbiome, is now considered an emerging multidrug-resistant pathogen of immunocompromised and chronically ill patients. However, little is known about the molecular mechanisms involved in transition from colonization to the MDR invasive phenotype in clinical isolates. **AIM:** To perform a comprehensive pan-genomic analysis of *C. striatum*, including 'normal skin' and MDR clinical isolates, to gain insights into genetic factors contributing for infectiveness and multi-drug resistance in this species. **METHODS:** We generated 04 draft genomes sequences from MDR *C. striatum* clinical isolates from Brazil, using Ion Torrent NGS technology. Additionally, 24 complete or draft *C. striatum* genomes were retrieved from NCBI, including the ATCC6940 isolate from the Human Microbiome Project. Bacterial Pan Genome Analysis tool (BPGA v.1.3) was used to run pan-genome analyzes and to obtain COG functional annotations. Automated predictions of antimicrobial resistance (AMR) genes were performed in the Comprehensive Antibiotic Resistance Database (CARD) and the National Database of Antibiotic Resistant Organisms (NDARO). Additionally, virulence related genes were searched with VFAnalyzer, and genomic islands and prophages were annotated with IslandViewer4 and PHASTER. **RESULTS:** The species *C. striatum* presented an open pan-genome ($\alpha = 0.147197$) containing 3,816 gene-families, including 15 AMR genes and 32 putative virulence factors. The core and accessory genomes included 1,297 and 1,307 genes, respectively. The identified AMR genes are mostly associated with resistance to aminoglycosides and tetracyclines. Of these, 66.6% are present in genomic islands, and four genes are in regions associated to prophages, indicating extensive horizontal gene transfer (HGT). **CONCLUSION:** Species with an open pan-genome have extended ability to acquire new genes through HGT. Consistently, we found in the *C. striatum* isolates a high percentage of unique genes and the predominance of AMR and

virulence genes in genomic islands. Our results also demonstrate that *C. striatum* has a metabolism particularly adapted to invasive infections due to its high genomic plasticity.

Keywords: Genomic Island; Pathogenomics; Prophage; Virulence factor; Whole-genome sequencing

Development Agencies: FAPESB