TITLE: STUDY OF THE CORE GENOME OF *Corynebacterium pseudotuberculosis* TO NEW THERAPEUTIC TARGETS PROSPECTION

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ABSTRACT:

Corynebacterium pseudotuberculosis is a Gram-positive microorganism, pleomorphic, facultative intracellular and etiologic agent of veterinary relevance diseases, such as caseous lymphadenitis and ulcerative lymphangitis, affecting different animal species which causes damage to the global agribusiness. The virulence factors of this bacterium are well characterized, like phospholipase D and mycolic acids. However, there are still no completely effective treatment methods to overcome the impacts of this pathogen. Due to the importance of this organism, several strains have been sequenced, and the increase of genomes deposited on public databases allowed studies related to comparative genomics, specially, the pan-genomic approach, that is composed of three parts: core genome, accessory genome and strain-specific genes. The core genome consists in genes that are shared by all strains analyzed, and they usually encode proteins that are essential to mechanisms of maintenance of cellular activities, and this characteristic makes them interesting objects of research for new therapeutic targets. Furthermore, a transcriptomic study was realized to analyze the gene expression of this pathogen under acid (pH 5), osmotic (2M) and thermal (50ºC) stress conditions. The aim of this study was obtain the core genome of *C. pseudotuberculosis* and investigate the differential transcriptomic profile in three stress conditions of strain 1002 (biovar *ovis*), available on public databases, to identify new therapeutic targets. PGAP software was used to analyze the pan-genome of 57 strains available on NCBI. The differentially expressed genes were identified by the protocols of Tophat and Cufflinks, considering a minimum expression alteration of two fold (fold change ≥ 2). The functional annotation by gene ontology of the core genome was performed by GO feat. The pan-genome of this species has 6243 genes, which 896 (14,3%) of them belong to the core genome. We identified *panC* (fold change = 2,82 in acid and 2,25 in osmotic stress), that encodes a protein involved in pantothenate and coenzyme A metabolism, which has been described as a valuable drug target against *Mycobacterium tuberculosis*; *tlyC* (fold change = 2,66 in osmotic and 2,24 in thermal stress), a hemolysin related to virulence mechanisms in members of *Rickettsia* genus, and *dps* (fold change = 6,16 in acid stress) involved in DNA protection during starvation, as potential therapeutic targets in *C. pseudotuberculosis*.

Keywords: *Corynebacterium pseudotuberculosis*, core genome, transcriptomics, therapeutic targets

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