

TITLE: *IN SILICO* GENOMIC ANALYSIS OF MULTIPLE *CORYNEBACTERIUM ULCERANS* STRAINS

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ABSTRACT: *Corynebacterium ulcerans* is an emerging zoonotic pathogen that causes respiratory and cutaneous diphtheria, characterized by the appearance of cutaneous lesions, pulmonary nodules, among other symptoms. Many cases of diphtheria caused by *C. ulcerans* have been described worldwide, inducing severe infections in both humans and animals. Despite its the medical and veterinary relevance, the biological mechanisms of virulence have not been fully elucidated yet. Due to the evolution of sequencing technologies and the emergence of new bioinformatics tools, there has been an increase in research related to comparative genomics. This area allows the direct comparison of the genetic material between organisms, in order to identify if the differences and similarities are able to influence phenotypic changes. Thus, in this study, a comparative analysis was performed among 14 strains of *C. ulcerans*. The complete genomes were obtained from NCBI and standardized through RAST database. A pan-genomic analysis was performed through the PanWeb platform, using the GF method, with 0.00001 *e-value*, 80% identity and 90% coverage. A phylogenetic tree, based on the maximum likelihood method of the MEGAX program, was constructed from the multiple alignment of 16S rRNA gene sequences, using as external group three different strains: *Mycobacterium tuberculosis* H37Rv, *Nocardia farcinica* W6977 and *Rhodococcus fascians* D188. The structural comparison of the genomes was visualized by the BRIG tool. The pan-genome of *C. ulcerans* has 4683 genes, of which 1531 are part of the core genome, 1158 belong to the genome accessory and 1994 are strain-specific genes. In the phylogenetic analysis, the 14 strains were clustered in the same clade, as expected, which suggests a high similarity between them. Among the external group, *M. tuberculosis* H37Rv showed greater similarity when compared to the *C. ulcerans* strains. According to the genomic map, in which the *C. ulcerans* FRC11 strain was used as reference, the isolates showed a clonal-like behavior, due to high similarity of genomic architecture. The comparative genomics approach contributed to a better understanding of differences and similarities among the studied strains, which may help future research to evaluate if these particularities may interfere in the biological mechanism of the pathogen.

Keywords: *Corynebacterium ulcerans*, diphtheria, pan-genome, phylogeny.

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