

TITLE: PROSPECTION OF VACCINE TARGETS FOR DIFTERIA FROM THE CORYNEBACTERIUM ULCERANS CORE EXOPROTEOME BY REVERSE VACCINOLOGY

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ABSTRACT: *Corynebacterium ulcerans* is an emerging pathogen responsible for attacking humans and animals with diphtheria, an acute infection of lethal potential that exhibits local and systemic manifestations, being able to develop in the respiratory tract and skin of infected hosts. Through the major virulence factor associated with the disease, diphtheria toxin, a toxoid for immunization against the pathogen was developed. However, this approach is not completely effective, and there may be other determinant factors not elucidated yet. Thus, this research carried out an *in silico* prospection through reverse vaccinology for targets that exhibit antigenic potential against diphtheria. For the analysis, the reference genome of the *C. ulcerans* strain FRC11 was used. From the bacterial core genome, 237 surface-exposed or secreted proteins, constituting the core exoproteome, were selected due to their higher potential for exposure to the host after infection. These were subjected to analyses of antigenicity (MED 1.0 Server) and pathogenicity potentials (MP3), besides search for homology with virulence factors (VFDB). In addition, proteins instability indexes (ProtParam) were calculated. In the search for antigenic targets, the highest MED Score was 19.64 and the lowest value was 1.51. Most of these proteins had a high MED Score, suggesting an antigenic role. The great majority was also defined as pathogenic (73.8%). Furthermore, many of these proteins were stable under normal conditions (instability index <40), what would facilitate *in vitro* analyzes. It was possible to identify 10 genes related to virulence factors of *Corynebacteria*, all of which are responsible for the maintenance of bacterial pathogenesis. Among these factors, the following stand out: bacterial *pili*, anchorage function to the host cell surface, genes related to iron uptake, and exotoxin. The identification of antigenic targets through this study is important for opening up experimental *in vitro* tests with predicted proteins in order to validate the obtained computational data.

Keywords: *Corynebacterium ulcerans*, diphtheria, antigenicity, virulence factors.

Development Agency: FAPESPA