TITLE: *IN SILICO* STUDIES OF THE DISTRIBUTION OF TOXIN-ANTITOXIN VapBC MODULES IN SAPROPHYTIC, PATHOGENIC AND INTERMEDIATE-PATHOGENIC *LESPTOSPIRA*

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ABSTRACT:

Pathogenic *Leptospira* species are the etiological agents of leptospirosis, a zoonotic disease affecting humans and a wide range of animals worldwide with significant impact. The genus *Leptospira* includes at least 21 species and comprises saprophytic, pathogenic and intermediate-pathogenic species. The high diversity among *Leptospira* species provides an array to look for important mediators involved in pathogenesis. Toxin-antitoxin (TA) systems represent an important mechanism of bacteria survival during stress conditions, such as starvation or antibiotic pressure. TA systems have been involved in potentially harmful aspects of an infection, such as antimicrobial resistance, persistence and biofilm formation. They are based in the conditional modulation of its toxic component, which leads to slow growth and cell death. Type II TA modules are grouped into different families according to the toxin structure and protein sequence similarity. *vap*BC family *loci* have been found in nearly thousand genomes corresponding to about 40% of known TAs. In the present study, we used TA database and BLASTp to search and compare the putative *vapBC* operons of the whole sequenced genomes of pathogenic *L. interrogans* and *L. borgpetersenii*, intermediate-pathogenic *L. licerasiae* and saprophytic *L. biflexa* strains within 20 *Leptospira* species. Our analysis identified significant differences in the number of putative *vap*BC modules distributed in pathogenic, saprophytic and intermediate strains: 4 in *L. interrogans*, 3 in *L. borgpetersenii*, 8 in *L. biflexa* and 15 in *L. licerasiae*. VapC toxins show low identity among amino acid sequences within the species. The distribution of *vap*BC operons among *Leptospira* species through the analysis of the conservation of their toxic element showed that some VapC toxins appear to be exclusively conserved in unique species, others appear to be conserved among pathogenic or saprophytic strains and some are distributed apparently at random. The data shown here emphasizes the importance of the discussion on how the distribution of these modules relate to bacterial adaptation and it indicates that these modules evolved in a very complex manner, highlighting the strong need to identify and characterize new TAs as well as to understand their regulation nets and the possible roles of TA systems in pathogenic bacteria.

Keywords: Leptospira, Toxin-antitoxin, VapBC, VapC

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