VAC_21 - Identification of naturally immunogenic B-cell epitopes in *Leptospira* secreted metalloproteases: novel and promising targets to multi-epitopes vaccines against leptospirosis

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Introduction: Leptospirosis is the most widespread zoonosis in the world, caused by pathogenic bacteria of the genus *Leptospira*, affects more than 1 million people, and causes 60,000 deaths per year. In Brazil, leptospirosis affects more than 3,500 people annually, of which about 75% progress to hospitalization and result in a lethality rate of 11%. Despite the impact on public health, the high number of *Leptospira* species able to infect humans and their immunogenic properties hamper the development of protective vaccines. In this context, due to the ability to degrade complement factors, thermolysins are critical to the evasion of pathogenic *Leptospira* from the host immune system and emerge as novel vaccines targets against leptospirosis. However, the vast repertoire of *Leptospira* proteases makes it difficult to study them by classical methods, doing of the combination of immunoinformatics and synthetic biology, a promising strategy to identify protective epitopes and to hasten the vaccine development against leptospirosis.

Objective: To identify B-cell epitopes in the *Leptospira* thermolysins.

Methodology: Thermolysins predicted as antigenic and virulence-associated factors, were explored by immunoinformatic to predict their linear B-cell epitopes. Predicted epitopes were synthetized as single peptides and tested (ELISA) against samples of patients reactive to leptospirosis by MAT (LG, n=51), and subjects with other febrile cases, not reactive for leptospirosis (NC, n=39).

Results: Among studied thermolysins, LIC13321 and LIC10715 were evaluated as antigenic and virulence-associated proteins. These proteins presented two (LIC13321-E1; LIC13321-E2) and four (LIC10715-E1, LIC10715-E2, LIC10715-E3, LIC10715-E4) predicted B-cell linear epitopes. Regarding the natural immunogenicity of predicted epitopes, about 8% and 25% of LG presented antibodies against LIC13321-E1 and LIC13321-E2, respectively. Moreover, while only 6% of LG presented antibodies against LIC10715-E2, other LIC10715 epitopes were specifically recognized by more than 25% of studied individuals.

Conclusion: Four naturally immunogenic B-cell epitopes were identified in *Leptospira* thermolysins and will be evaluated about their protective potential to further compose novel multi-epitopes vaccines.

Keywords: Immunoinformatics; *Leptospira*; Vaccine