Leptospira interrogans BatA and BatB proteins are pro-coagulant, impair platelet aggregation and cleave human fibrinogen *in vitro*

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Leptospirosis is one of the most widespread and prevalent zoonosis worldwide, caused by pathogenic spirochetes of the genus *Leptospira*. Leptospirosis is (re)emerging globally and several outbreaks were reported during the past decade. The hemostatic impairment is frequently observed in the severe leptospirosis patients, evidenced by bleeding complications, thrombocytopenia, activation of coagulation and enhanced fibrinolysis. Nevertheless, the molecular mechanisms of *Leptospira* spp. virulence and leptospirosis pathophysiological processes are poorly understood. The von Willebrand factor (vWF) is a multimeric glycoprotein which plays an important role in blood coagulation and primary hemostasis. The vWF A domains exhibit multiple binding sites which contribute to vWF's hemostatic function. In the genome of *L. interrogans* serovar Copenhageni, we identified two proteins, annotated as BatA and BatB, which are predicted to contain von Willebrand factor A domains. Therefore, we hypothesized that BatA/BatB could be involved in host-pathogen interactions and have a role in the hemostatic impairment observed during leptospirosis. We have cloned and expressed leptospiral BatA and BatB in *E. coli*. As the recombinant proteins were expressed as inclusion bodies, they were solubilized with guanidine and then purified by metal chelating chromatography with on column refolding. The influence of recombinant BatA and BatB on different *in vitro* hemostatic assays evaluating plasma coagulation, platelet aggregation and Fg integrity was investigated. We show that BatA/BatB shorten the coagulation time in human citrated plasma, interfere with normal platelet aggregation induced by thrombin and vWF/ristocetin and are able to cleave human fibrinogen. Our results suggest an important role of BatA/BatB in the hemostatic dysfunction observed during leptospirosis and contribute to the understanding of leptospirosis pathophysiological mechanisms.

Keywords: Leptospirosis; von Willebrand factor; Host-pathogen Interaction; Hemostasis.

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