LEPTOSPIRA ACQUIRES VITRONECTIN VIA THE SURFACE PROTEINS LIGA AND LIGB TO OVERCOME HOST INNATE IMMUNITY

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Over the last years functional characterization of some *Leptospira* immune evasion proteins has been reported. Identification of specific host ligands and definition of the mechanisms of complement inactivation have been accomplished for certain leptospiral outer membrane proteins present only in pathogenic species. Given the ability of certain bacterial surface proteins to bind multiple host molecules, the present study investigated the binding of Leptospiral Immunoglobulin-like protein A (LigA) and Leptospiral immunoglobulin-like protein B (LigB) to vitronectin, a regulator of the terminal pathway of the complement system. Vitronectin has three heparin binding domains and one plasminogen activator inhibitor-1 (PAI-1) binding domain.Our group has previously shown that the Lig proteins are capable of binding the complement regulators C4b Binding Protein (C4BP) and Factor H (FH).Binding of LigA and LigB to vitronectin was assessed by ligand affinity blot. Competitive binding assays and mapping of the sites involved in the interactions were performed by ELISA.Competition assays indicated that these proteins interact with C4BP, FH and vitronectin through distinct sites.Moreover,LigA and LigB interact with human vitronectin through their C-terminus. Co-incubation with heparin blocked the interactionsin a dose-dependent manner thus indicating that binding occurs through the heparin binding domains of vitronectin,and does not involveits PAI-1 domain. With regard to the role of ionic forces, NaCl at 250 to 1000 mM could partially inhibit vitronectin binding to Ligs proteins. These findings indicate that high salt concentrations may partially impair the interactions.Successful colonization of hosts by pathogenic microorganisms can be attributed to the ability of these microorganisms to disrupt complement effector functions, thus compromising the first line of defense of the host innate immune response. So taken together, our findings indicate these proteins may play a role in leptospiral immune evasion.

Keywords: Leptospirosis, *Leptospira*, Complement System, Vitronectin.

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