Título: UNEXPECTED ROLES OF *LEPTOSPIRA* ENOLASE

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Resumo:

Leptospirosis is a zoonosis caused by spirochetes of the genus *Leptospira.* The disease is widespread throughout developing countries, posing a significant health problem. Leptospires have the ability to adhere to renal tubule cells, and to extracellular matrix components, which facilitates invasion and host colonization. They have also developed strategies to evade host´s complement system. Enolases are cytosolic metalloenzymes that catalyze the conversion of 2-phosphoglycerate to phosphoenolpyruvate. Despite lacking a classical membrane anchor sequence, they are found in the surface of a variety of eukaryotic and prokaryotic cells, where they are able to interact with plasminogen. Recent published data have shown that enolase from *Leptospira interrogans* is secreted to the extracellular medium and then reassociates with the bacterial surface by interacting with outer membrane proteins. As shown for many other bacteria, membrane-anchored leptospiral enolase displays plasminogen-binding activity. In the present work, the functional consequences of plasminogen binding to leptospiral enolase were assessed and the interaction of this particular protein with other host molecules was evaluated. The enolase gene was amplified by PCR and the protein was expressed and purified by nickel-affinity chromatography. The interaction of enolase with host molecules was evaluated by Far Western blot or ELISA. Here we demonstrate that plasminogen bound to enolase is converted to plasmin, which in turn degrades natural substrates including fibrinogen and vitronectin. Moreover, leptospiral enolase binds laminin and the complement regulator Factor H. Bound-FH remains functional, acting as a cofactor for Factor I in the cleavage of C3b. Taken together, our data suggest that enolase may contribute to leptospiral pathogenesis.

Key words: *Leptospira*, enolase, plasminogen, factor H

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