TITLE: FUNCTIONAL AND STRUCTURAL CHARACTERIZATION OF A PENICILLIN BINDING PROTEIN OF *LEPTOSPIRA INTERROGANS*

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ABSTRACT:

Leptospirosis is a widespread zoonotic disease caused by pathogenic spirochetes of the genus *Leptospira*; these bacteria have a high prevalence in tropical and subtropical regions significantly impacting public health. The transmission of leptospirosis has been associated with exposure of individuals to wild or domestic animals. Recently, the disease became prevalent in cities with sanitation problems and large populations of urban rodents, the latter of which contaminate the environment through their urine. Historically, antibiotics have been used to treat leptospirosis: penicillin was the first drug used to fight leptospirosis. Other antibiotics like doxycycline, cephalosporins, chloramphenicol, and azithromycin have also been tested in clinical trials. Despite the use of antibiotics in the treatment of leptospirosis, their role is still not completely clear due to the lack of effective diagnostic, particularly for severe cases of the disease. Here we present the crystal structure of Lsa45, previously characterized as putative adhesin and plasminogen binding protein of *L. interrogans*. Our study revealed that this protein is a bifunctional enzyme that has two domains: a large α/β domain and a small α-helix domain. The structure allowed us to understand the functionality of

Lsa45; the protein was genome annotated as Penicillin Binding Protein (PBP) with weak affinity to β-lactams. Additionally, an esterase functionality of Lsa45 was characterized with a greater affinity for the *p*-nitrophenyl acetate substrate. These findings are important to understanding the mechanism of antibiotic actions in the treatment of leptospirosis.

Keywords: *Leptospira interrogans*, antibiotics, β-Lactamase, Structural biology

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