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Binding of the human complement regulators FH and C4BP to pathogenic *Leptospira* species is mediated by the leptospiral surface protein LcpA

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Leptospirosis, an emerging global infectious disease, is caused by spirochetes belonging to different pathogenic species of the genus *Leptospira*. After penetrating the host, *Leptospira* have the ability to disseminate and to trigger a specific immune response. Like other pathogens, they have evolved strategies to evade innate immune defense systems, thereby causing severe disease. One strategy adopted by pathogenic *Leptospira* to resist hosts' innate immunity is their potential to acquire fluid phase complement regulators to their surfaces, particularly those of the alternative and the classical complement pathways such as factor H (FH), and C4b-binding protein (C4BP). Recently, we have shown that C4BP bound to *Leptospira* retains its cofactor activity, indicating that acquisition of this complement regulator may contribute to leptospiral serum resistance. After screening a number of putative leptospiral membrane proteins for their capacity to interact with human complement regulators, we found that a predicted membrane lipoprotein of 20 kDa, named LcpA (Leptospiral complement regulator-acquiring protein A), bound to both C4BP and FH, as assessed by ligand affinity blot analyses and ELISA. The gene coding for this 20-kDa lipoprotein is conserved among pathogenic leptospiral species. Moreover, *Leptospira* strains that resist, at least to a certain degree, complement-dependent killing by normal human serum express LcpA, whereas the serum-sensitive strain Patoc does not. LcpA was shown to be surface-exposed by a proteinase K accessibility assay and also by immunoelectron microscopy. To our knowlegde, this is the first description of a *Leptospira* protein that binds both C4BP and FH.

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