



**P 61 Molecular analysis of the interaction of *Borrelia recurrentis* with the complement regulatory proteins CFH, CFHR-1, C4bp, and C1-INH**

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*Borrelia (B.) recurrentis* is the agent of louse-borne relapsing fever and causes a severe septic disease associated with high mortality in humans. While spirochetes are present in blood, they must evade the immune defense systems. To control complement attack on their surface, many pathogens recruit host complement regulators. In this study, we identified and characterized 2 outer surface proteins of *B. recurrentis*, HcpA (human complement regulators and plasminogen-binding protein) and CihC (C1-inhibitor and C4b-binding protein) that bind human complement regulators of the alternative pathway of complement activation, CFH (complement factor H), and CFHR-1 (complement factor H-related-1), and of the classical pathway, C1-INH (C1 esterase inhibitor) and C4bp (C4b-binding protein), respectively. CFH interacts with HcpA via its C-terminal domain CCP20, and HcpA-bound CFH retains cofactor activity for factor I-mediated C3b inactivation. Simultaneously, recombinant HcpA acquires the host protease plasminogen via distinct non-overlapping domains. *B. recurrentis*-associated plasminogen is converted by uPA to proteolytically active plasmin and exhibits anti-opsonic properties as indicated by the removal of C3b molecules from the bacterial surface. Most importantly, ectopic expression of HcpA in a serum-sensitive *B. burgdorferi* B313 strain confers resistance to complement-mediated killing. C4bp is recruited to the spirochetal surface via CihC and maintains its cofactor activity for factor I-mediated C4b inactivation. In addition, recombinant CihC acquires the major regulator of the classical complement cascade, C1-INH. By examining complex formation of C1-INH and C1s protease, we demonstrate that C1-INH attached to *B. recurrentis* exhibits anticomplement activity. By recruiting multiple complement regulators via surface-expressed molecules, HcpA and CihC, *B. recurrentis* organisms use versatile strategies to simultaneously evade complement attack, to resist opsonization, and to degrade extracellular matrix components.