Versatile roles of CspA orthologs in complement inactivation of serum-resistant Lyme disease spirochetes.

Hammerschmidt C, Koenigs A, Siegel C, Hallström T, Skerka C, Wallich R, Zipfel PF, Kraiczy P (2014) Versatile roles of CspA orthologs in complement inactivation of serum-resistant Lyme disease spirochetes. *Infect Immun* 82(1), 380-392.

Abstract

CspA of the Lyme disease spirochete Borrelia burgdorferi represents a key molecule in immune evasion, protecting borrelial cells from complement-mediated killing. As previous studies focused almost exclusively on CspA of B. burgdorferi, here we investigate the different binding capacities of CspA orthologs of Borrelia burgdorferi, B. afzelii, and B. spielmanii for complement regulator factor H and plasminogen and their ability to inhibit complement activation by either binding these host-derived plasma proteins or independently by direct interaction with components involved in formation of the lethal, pore-like terminal complement complex. To further examine their function in serum resistance in vivo, a serum-sensitive B. garinii strain was used to generate spirochetes, ectopically producing functional CspA orthologs. Irrespective of their species origin, all three CspA orthologs impart resistance to complement-mediated killing when produced in a serum-sensitive B. garinii surrogate strain. To analyze the inhibitory effect on complement activation and to assess the potential to inactivate C3b by binding of factor H and plasminogen, recombinant CspA orthologs were also investigated. All three CspA orthologs simultaneously bound factor H and plasminogen

but differed in regard to their capacity to inactivate C3b via bound plasmin(ogen) and inhibit formation of the terminal complement complex. CspA of B. afzelii binds plasmin(ogen) and inhibits the terminal complement complex more efficiently than CspA of B. burgdorferi and B. spielmanii. Taken together, CspA orthologs of serum-resistant Lyme disease spirochetes act as multifunctional evasion molecules that inhibit complement on two central activation levels, C3b generation and assembly of the terminal complement complex.

Beteiligte Forschungseinheiten

Infektionsbiologie Peter F. Zipfel Mehr erfahren

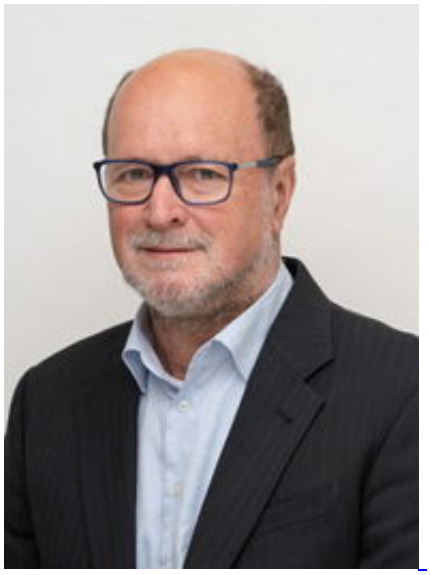
Leibniz-HKI-Autor*innen

Teresia Hallström

Details

Christine Skerka

Details



Peter F. Zipfel

Details

Identifier

doi: 10.1128/IAI.01094-13

PMID: 24191298