V 38 Identification of a novel plasminogen-binding protein of *Borrelia burgdorferi*

Arno Koenigs[a], Claudia Hammerschmidt[a], Diana Barthel[b], Christine Skerka[b], Reinhard Wallich[c], Peter F. Zipfel[b,d], Peter Kraiczy[a]

[a] Institute of Medical Microbiology and Infection Control, University Hospital of Frankfurt, Paul-Ehrlich-Str. 40, D-60596 Frankfurt/M., Germany
[b] Dept. of Infection Biology, Leibniz Institute for Natural Product Research and Infection Biology, Beutenbergstr. 11a, D-07745 Jena, Germany
[c] Institute of Immunology, University of Heidelberg, Im Neuenheimer Feld 305, D-69120 Heidelberg, Germany
[d] Friedrich Schiller University, Jena, Germany

Borrelia burgdorferi, the aetiological agent of Lyme disease exploits versatile strategies to establish infection and to overcome the host immune system. Immune escape mechanisms comprise interactions of spirochaetes with diverse host proteins including plasminogen, extracellular matrix proteins, and complement regulators. A number of genetically unrelated outer surface proteins, i.e. OspA, OspC, CspA (CRASP-1), ErpA (CRASP-5), ErpC (CRASP-4), and ErpP (CRASP-3) have been identified as ligands for host-derived plasminogen. Here, we report the identification of a novel protein, termed PbpA for plasminogen-binding protein A of *B. burgdorferi*. In comparison to other borrelial proteins, PbpA displayed the strongest binding capacity for plasminogen. Bound plasminogen is converted to proteolytically active plasmin in the presence of urokinase type plasminogen activator (uPA) and subsequently cleaved the chromogenic substrate D-valyl-leucyl-lysine-p-nitroanilide dihydrochloride as well as the natural substrate fibrinogen. Employing diverse truncated proteins, the plasminogen-interacting site has been mapped within the C terminus of PbpA. Lysine residues located within this particular alpha-helical C-terminal domain appeared to be crucial to binding of plasminogen, as the lysine analogue tranexamic acid significantly inhibited these interactions. By utilizing several plasminogen constructs containing single or multiple Kringle domains, it was determined that Kringle domain 4 most likely represents the major PbpA interaction site. Finally, RT-PCR analyses revealed that spirochaetes expressed the PbpA-encoding gene under in vitro conditions. Taken together, binding of plasminogen/plasmin endows *B. burgdorferi* with the capability of resisting opsonization and to degrade components of the extracellular matrix.