Streptococcus pneumoniae from patients with hemolytic uremic syndrome binds human plasminogen via the surface protein PspC and uses plasmin to damage human endothelial cells.

Meinel C, Spartà G, Dahse HM, Hörhold F, König R, Westermann M, Cseresnyés Z, Coldewey SM, Figge MT, Hammerschmidt S, Skerka C, Zipfel PF (2018) *Streptococcus pneumoniae* from patients with hemolytic uremic syndrome binds human plasminogen via the surface protein PspC and uses plasmin to damage human endothelial cells. *J Infect Dis* 217(3), 358-370.

Abstract

Pneumococcal hemolytic uremic syndrome (HUS) in children is caused by infections with *Streptococcus pneumoniae.* Because endothelial cell damage is a hallmark of HUS, we studied how HUS-inducing pneumococci derived from infant HUS patients during the acute phase disrupt the endothelial layer. HUS pneumococci efficiently bound human plasminogen. These clinical isolates of HUS pneumococci efficiently bound human plasminogen via the bacterial surface proteins Tuf and PspC. When activated to plasmin at the bacterial surface, the active protease degraded fibrinogen and cleaved C3b. Here, we show that PspC is a pneumococcal plasminogen receptor and that plasmin generated on the surface of HUS pneumococci damages endothelial

cells, causing endothelial retraction and exposure of the underlying matrix. Thus, HUS pneumococci damage endothelial cells in the blood vessels and disturb local complement homeostasis. Thereby, HUS pneumococci promote a thrombogenic state that drives HUS pathology.

Beteiligte Forschungseinheiten

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