

Dihydrolipoamide dehydrogenase of *Pseudomonas aeruginosa* is a surface-exposed immune evasion protein that binds three members of the factor H family and plasminogen.

Hallström T, Mörgelin M, Barthel D, Raguse M, Kunert A, Hoffmann R, Skerka C, Zipfel PF (2012) Dihydrolipoamide dehydrogenase of *Pseudomonas aeruginosa* is a surface-exposed immune evasion protein that binds three members of the factor H family and plasminogen. *J Immunol* 189(10), 4939-4950.

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Abstract

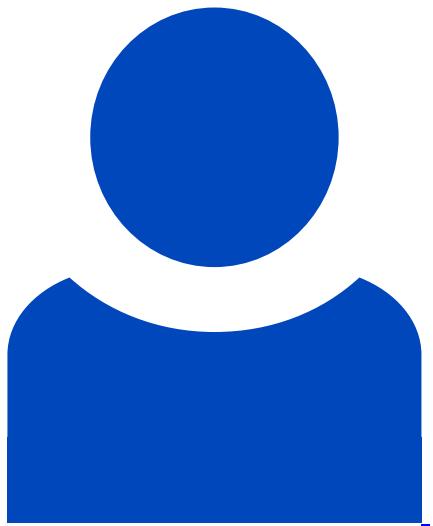
The opportunistic human pathogen *Pseudomonas aeruginosa* causes a wide range of diseases. To cross host innate immune barriers, *P. aeruginosa* has developed efficient strategies to escape host complement attack. In this study, we identify the 57-kDa dihydrolipoamide dehydrogenase (Lpd) as a surface-exposed protein of *P. aeruginosa* that binds the four human plasma proteins, Factor H, Factor H-like protein-1 (FHL-1), complement Factor H-related protein 1 (CFHR1), and plasminogen. Factor H contacts Lpd via short consensus repeats 7 and 18-20. Factor H, FHL-1, and plasminogen when bound to Lpd were functionally active. Factor H and FHL-1 displayed complement-regulatory activity, and bound plasminogen, when converted to the active protease plasmin, cleaved the chromogenic substrate S-2251 and the natural substrate fibrinogen. The lpd

of *P. aeruginosa* is a rather conserved gene; a total of 22 synonymous and 3 nonsynonymous mutations was identified in the *Lpd* gene of the 5 laboratory strains and 13 clinical isolates. *Lpd* is surface exposed and contributes to survival of *P. aeruginosa* in human serum. Bacterial survival was reduced when *Lpd* was blocked on the surface prior to challenge with human serum. Similarly, bacterial survival was reduced up to 84% when the bacteria was challenged with complement active serum depleted of Factor H, FHL-1, and CFHR1, demonstrating a protective role of the attached human regulators from complement attack. In summary, *Lpd* is a novel surface-exposed virulence factor of *P. aeruginosa* that binds Factor H, FHL-1, CFHR1, and plasminogen, and the *Lpd*-attached regulators are relevant for innate immune escape and most likely contribute to tissue invasion.

Beteiligte Forschungseinheiten

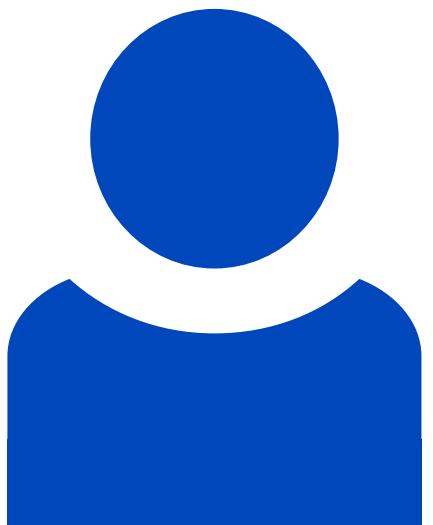
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Identifier

doi: 10.4049/jimmunol.1200386

PMID: 23071278