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Lipoamide dehydrogenase (Lpd) is a surface expressed protein of Pseudomonas aeruginosa that binds Factor H, Factor H related protein 1 (CFHR1) and Plasminogen

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The complement system is the first line of defence and is an essential part of the innate immune system. Activation of complement leads to a cascade of protein activation and C3b deposition on the surface of the pathogen, and further formation of the terminal complement complex (TCC). Pathogenic microbes acquire human host plasma proteins and complement inhibitors to evade host innate immune attack. *Pseudomonas aeruginosa* is an oppurtunistic human pathogen that can cause a wide range of infections, particularly in immunocompromised patients. This Gram-negative bacterium utilizes Factor H, the inhibitor of the alternative pathway and surface attached Factor H has a protective effect for immune and complement escape. Upon incubation in Factor H-depleted complement active human serum, survival of *P. aeruginosa* was decreased as compared to normal human serum. Thus, demonstrating a specific role of surface attached Factor H for complement evasion. Here we identified Lipoamide dehydrogenase (Lpd) of *P. aeruginosa* as a new Factor H-binding protein that was isolated using a Factor H affinity matrix. Lpd is a surface exposed protein that binds Factor H via two regions that are located within short consensus repeat (SCR) domains 6-7 and 19-20. Factor H bound to surface-attached Lpd displays cofactor activity as shown by C3b degradation. Lpd also binds Factor H related protein 1 (CFHR1) mainly via SCR domains 3-5. Factor H and CFHR1 are colocalized on the surface of intact *P. aeruginosa* as shown by electron microscopy. Furthermore, Lpd also bound plasminogen, and Lpd-bound plasminogen was converted by urokinase plasminogen activator to active plasmin. Attached to Lpd, activated plasmin cleaved a chromogenic substrate, as well as the natural substrate fibrinogen. In summary, Lpd is a surface protein of the human pathogen *P.aeruginosa* and a virulence factor that binds multiple host effector proteins and uses attached host regulators for complement control and tissue invasion.

Keywords: P. aeruginosa, evasion, the complement system, complement regulators