Enolase from *Aspergillus fumigatus* is a moonlighting and immune evasion protein that binds the human plasma complement proteins factor H, FHL-1, C4BP, and plasminogen.

Dasari P, Koleci N, Shopova I, Wartenberg D, Beyersdorf N, Dietrich S, Sahagun-Ruiz A, Figge MT, Skerka C, Brakhage AA, Zipfel PF (2019) Enolase from *Aspergillus fumigatus* is a moonlighting and immune evasion protein that binds the human plasma complement proteins factor H, FHL-1, C4BP, and plasminogen. *Front Immunol* 10, 2573.

Details

PubMed
OPEN ACCESS
PAPER

Abstract

The opportunistic fungal pathogen *Aspergillus fumigatus* can cause severe infections, particularly in immunocompromised individuals. Upon infection, *A. fumigatus* faces the powerful and directly acting immune defense of the human host. The mechanisms on how *A. fumigatus* evades innate immune attack and complement are still poorly understood. Here, we identify *A. fumigatus* enolase, AfEno1, which was also characterized as fungal allergen, as a surface ligand for human plasma complement regulators. AfEno1 binds factor H, factor-H-like protein 1 (FHL-1), C4b

binding protein (C4BP), and plasminogen. Factor H attaches to AfEno1 via two regions, via short conserved repeats (SCRs) 6–7 and 19–20, and FHL-1 contacts AfEno1 via SCRs 6–7. Both regulators when bound to AfEno1 retain cofactor activity and assist in C3b inactivation. Similarly, the classical pathway regulator C4BP binds to AfEno1 and bound to AfEno1; C4BP assists in C4b inactivation. Plasminogen which binds to AfEno1 via lysine residues is accessible for the tissue-type plasminogen activator (tPA), and active plasmin cleaves the chromogenic substrate S2251, degrades fibrinogen, and inactivates C3 and C3b. Plasmin attached to swollen *A. fumigatus* conidia damages human A549 lung epithelial cells, reduces the cellular metabolic activity, and induces cell retraction, which results in exposure of the extracellular matrix. Thus, *A. fumigatus* AfEno1 is a moonlighting protein and virulence factor which recruits several human regulators. The attached human regulators allow the fungal pathogen to control complement at the level of C3 and to damage endothelial cell layers and tissue components.

Beteiligte Forschungseinheiten

Infektionsbiologie Peter F. Zipfel Mehr erfahren

Molekulare und Angewandte Mikrobiologie Axel Brakhage Mehr erfahren

Angewandte Systembiologie Marc Thilo Figge Mehr erfahren

Leibniz-HKI-Autor*innen



Axel A. Brakhage

Details



Prasad Dasari

Details



Stefanie Dietrich

Details



Marc Thilo Figge

Details



Naile Koleci

Details



Iordana Shopova

Details



Christine Skerka

Details



Dirk Wartenberg

Details



Peter F. Zipfel

Details

Identifier

doi: 10.3389/fimmu.2019.02573

PMID: 31824478