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.

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.

Involved units

Infection Biology Peter F. Zipfel Read more

Molecular and Applied Microbiology Axel Brakhage Read more

Applied Systems Biology Marc Thilo Figge Read more

Leibniz-HKI-Authors

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