Factor H-related protein 1 (CFHR-1) inhibits complement C5 convertase activity and terminal complex formation.

Heinen S, Hartmann A, Lauer N, Wiehl U, Dahse HM, Schirmer S, Gropp K, Enghardt T, Wallich R, Hälbich S, Mihlan M, Schlötzer-Schrehardt U, Zipfel PF, Skerka C (2009) Factor H-related protein 1 (CFHR-1) inhibits complement C5 convertase activity and terminal complex formation. *Blood* 114(12), 2439-2447. PubMed

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Projects

Complement evasion of human pathogenic microorganisms
Details

Abstract

Homozygous deletion of a 84-kb genomic fragment in human chromosome 1 that encompasses the CFHR1 and CFHR3 genes represents a risk factor for hemolytic uremic syndrome (HUS) but has a protective effect in age-related macular degeneration (AMD). Here we identify CFHR1 as a novel inhibitor of the complement pathway that blocks C5 convertase activity and interferes with C5b surface deposition and MAC formation. This activity is distinct from complement factor H, and apparently factor H and CFHR1 control complement activation in a sequential manner. As both proteins bind to the same or similar sites at the cellular surfaces, the gain of CFHR1 activity presumably is at the expense of CFH-mediated function (inhibition of the C3 convertase). In HUS, the absence of CFHR1 may result in reduced inhibition of terminal complex formation and in reduced protection of endothelial cells upon complement attack. These findings provide new insights into complement regulation on the cell surface and biosurfaces and likely define the role of CFHR1 in human diseases.

Identifier

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