FHR3 Blocks C3d-Mediated Coactivation of Human B Cells.

Buhlmann D, Eberhardt HU, Medyukhina A, Prodinger WM, Figge MT, Zipfel PF, Skerka C (2016) FHR3 Blocks C3d-Mediated Coactivation of Human B Cells. *J Immunol* , PubMed

ILRS Authors

Denise Buhlmann Hannes Eberhardt

Abstract

The autoimmune renal disease deficient for complement factor H-related (CFHR) genes and autoantibody-positive form of hemolytic uremic syndrome is characterized by the presence of autoantibodies specific for the central complement regulator, factor H, combined with a homozygous deficiency, mostly in CFHR3 and CFHR1 Because FHR3 and FHR1 bind to C3d and inactivated C3b, which are ligands for complement receptor type 2 (CR2/CD21), the aim of the current study was to examine whether FHR3-C3d or FHR1-C3d complexes modulate B cell activation. Laser-scanning microscopy and automated image-based analysis showed that FHR3, but not FHR1 or factor H, blocked B cell activation by the BCR coreceptor complex (CD19/CD21/CD81). FHR3 bound to C3d, thereby inhibiting the interaction between C3d and CD21 and preventing colocalization of the coreceptor complex with the BCR. FHR3 neutralized the adjuvant effect of C3d on B cells, as shown by inhibited intracellular CD19 and Akt phosphorylation in Raji cells, as well as Ca(2+) release in peripheral B cells. In cases of CFHR3/CFHR1 deficiency, the FHR3 binding sites on C3d are occupied by factor H, which lacks B cell-inhibitory functions. These data provide evidence that FHR3, which is absent in patients with the autoimmune form of hemolytic uremic syndrome, is involved in B cell regulation.

Identifier

doi: 1600053 PMID: 27279373