Monomeric CRP contributes to complement control in fluid phase and on cellular surfaces and increases phagocytosis by recruiting factor H.

Mihlan M, Stippa S, Józsi M, Zipfel PF (2009) Monomeric CRP contributes to complement control in fluid phase and on cellular surfaces and increases phagocytosis by recruiting factor H. *Cell Death Differ* 16(12), 1630-1640. PubMed

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Projects

Interaction of complement proteins and acute phase proteins in inflammatory processes
Details

Abstract

Complement forms the first defense line of innate immunity and has an important role in the non-inflammatory clearance of apoptotic and necrotic cells. Factor H is one essential complement inhibitor that binds to the acute phase reactant C-reactive protein (CRP). By using recombinant proteins, calcium-independent binding of Factor H to monomeric CRP (mCRP), but not to pentameric CRP (pCRP), was shown. In addition to the two known CRP-binding sites, a novel third site was localized within the C-terminus. This region is frequently mutated in the hemolytic uremic syndrome and the mutant proteins show reduced mCRP binding. In this study, we show that mCRP directs Factor H to the surface of apoptotic and necrotic endothelial cells and identify phosphocholine as one binding moiety for this complex. Factor H-mCRP complexes enhance C3b inactivation both in the fluid phase and on the surface of damaged cells and inhibit the production of pro-inflammatory cytokines. By recruiting the soluble complement inhibitor Factor H to the surface of damaged cells, mCRP blocks the progression of the complement cascade beyond the step of the C3 convertase, prevents the formation of inflammatory activation products, and thus contributes to the safe removal of opsonized damaged cells and particles.

Identifier

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