Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

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Literature references


Reactome database release: 79

This document contains 1 pathway and 42 reactions (see Table of Contents)
Regulation of Complement cascade

Stable identifier: R-HSA-977606

Compartments: plasma membrane, extracellular region

Two inherent features of complement activation make its regulation very important:

1. There is an inherent positive feedback loop because the product of C3 activation forms part of an enzyme that causes more C3 activation.

2. There is continuous low-level activation of the alternative pathway (see Spontaneous hydrolysis of C3 thioester).

Complement cascade activation is regulated by a family of related proteins termed the regulators of complement activation (RCA). These are expressed on healthy host cells. Most pathogens do not express RCA proteins on their surface, but many have found ways to evade the complement system by stably binding the RCA that circulates in human plasma (Lambris et al. 2008); trapping RCA is by far the most widely employed strategy for avoiding the complement response. RCA recruitment is common in bacteria such as E. coli and streptococci (Kraiczy & Wurzner 2006) and has also been described for viruses, fungi and parasites. RCA deposition and the complement system also have an important role in tissue homeostasis, clearing dead cells and debris, and preventing damage from oxidative stress (Weismann et al. 2011).

RCA proteins control complement activation in two different ways; by promoting the irreversible dissociation (decay acceleration) of complement convertases and by acting as cofactors for Complement factor I (CFI)-mediated cleavage of C3b and C4b.

Decay accelerating factor (DAF, CD55), Complement factor H (FH), Membrane Cofactor Protein (MCP) and Complement receptor 1 (CR1) are composed of arrays of tandem globular domains termed CCPs (complement control protein repeats) or SCRs (short consensus repeats). CR1, MCP and FH are cofactors for the CFI-mediated cleavage of C3b, generating iC3b. CR1 and MCP are also cofactors for C4b cleavage. C4BP is an additional cofactor for the CFI-mediated cleavage of C4b.

Literature references


## Editions

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C3 convertases spontaneously dissociate

**Location:** Regulation of Complement cascade

**Stable identifier:** R-HSA-981621