

The Complement Immune System (CIS)

An Approach with Systems Biology Graphic Notation Process Description

System Biology Graphical Notation

The goal of the Systems Biology Graphical Notation (SBGN) is to standardize the graphical/visual representation of biochemical and cellular processes: signaling pathways, metabolic networks, and gene regulatory networks amongst communities of biochemists, biologists, and theoreticians.

SBGN is made up of three orthogonal languages for representing different views of biological systems: Process Descriptions, Entity Relationships and Activity Flows. Each language defines a comprehensive set of symbols with precise semantics, together with detailed syntactic rules regarding the construction and interpretation of maps.

The SBGN Process Description (PD) language shows the temporal courses of biochemical interactions in a network. It can be used to show all the molecular interactions taking place in a network of biochemical entities.

SBGN References

<http://sbgn.github.io/sbgn/>
<http://co.mbine.org/specifications/sbgn.pd.level-1.version-1.3.pdf>

Proteins

The HUGO Gene Nomenclature Committee (HGNC) is a committee of the Human Genome Organisation (HUGO) that sets the standards for human gene nomenclature. The HGNC approves a unique and meaningful name for every known human gene, based on a query of experts. Each name within this paper is based on the HGNC nomenclature.

B, Ba, Bb

Factor B circulates in the blood as a single chain polypeptide. Upon activation of the alternative pathway, it is cleaved by complement factor D yielding the noncatalytic chain Ba and the catalytic subunit Bb. The active subunit Bb is a serine protease that associates with C3b to form the alternative pathway C3 convertase. Bb is involved in the proliferation of preactivated B lymphocytes, while Ba inhibits their proliferation.

C1, C1q, C1r, C1s

The multiprotein complex C1 (cca. 790 kDa) initiates the classical pathway of complement activation on binding to antibody-antigen complexes, pathogen surfaces, apoptotic cells, and polyanionic structures. It is composed of C1q, a protein with a bouquet-like architecture, together with a tetramer assembled from two copies each of the serine proteases C1r and C1s, which activate when C1q binds to a pathogen surface.

C2, also known as C02; ARMD14

Component C2 is a serum glycoprotein that functions as part of the classical pathway of the complement system. Activated C1 cleaves C2 into C2a and C2b. The serine protease C2a then combines with complement factor 4b to create the C3 or C5 convertase.

C3, also known as ASP; C3a; C3b; C3bBb; AHUS5; ARMD9; CPAMD1

Complement component C3 plays a central role in the activation of complement system. Its activation is required for both classical and alternative complement activation pathways. The encoded preproprotein is proteolytically processed to generate alpha and beta subunits that form the mature protein, which is then further processed to generate numerous peptide products. The C3a peptide, also known as the C3a anaphylatoxin, modulates inflammation and possesses antimicrobial activity.

C4, C4a, C4b, C4b2b, also known as RG; C4S, C04; C4A2; C4A3; C4A4

C4 encodes the acidic form of complement factor 4, part of the classical activation pathway. The protein is expressed as a single chain precursor which is proteolytically cleaved into a trimer of alpha, beta, and gamma chains prior to secretion.

C5, C5a, C5b67, C5b678, C5b6789, also known as C5D; C5a; C5b; ECLZB; CPAMD4

Encodes a component of the complement system, a part of the innate immune system that plays an important role in inflammation, host homeostasis, and host defense against pathogens. The encoded preproprotein is proteolytically processed to generate multiple protein products, including the C5 alpha chain, C5 beta chain, C5a anaphylatoxin and C5b. The C5 protein is comprised of the C5 alpha and beta chains, which are linked by a disulfide bridge.

C6

This gene encodes a component of the complement cascade. The encoded protein is part of the membrane attack complex (MAC) that can be incorporated into the cell membrane and cause cell lysis. The 105 kDa serum glycoprotein shows significant homology to the other late components, C7-C9. C6 is a polypeptide chain cross/linked by 32 disulfide bonds.

C7

Encodes a serum glycoprotein that forms a membrane attack complex together with complement components C5b, C6, C8, and C9 as part of the terminal complement pathway of the innate immune system. The protein encoded by this gene contains a cholesterol-dependent cytolysin/membrane attack complex perforin-like (CDC/MACPF) domain and belongs to a large family of structurally related molecules that form pores involved in host immunity and bacterial pathogenesis. This protein initiates Membrane Attack Complex formation by binding the C5b-C6 subcomplex and inserts into the phospholipid bilayer, serving as a membrane anchor.

C8

The C8 protein involved in the complement system (part of the immune system). It is part of the Membrane Attack Complex (MAC). C5b, C6, C7, C8 and C9 together form the cylindrical membrane attack complex. C8 is a heterotrimer, consisting three different subunits, encoded by the genes C8a, C8b and C8g respectively.

C9, also known as C9D, ARMD15

The gene encodes the final component of the complement system. It participates in the formation of the Membrane Attack Complex (MAC). The MAC assembles on bacterial membranes to form a pore, permitting disruption of bacterial membrane organization.

CD46, also known as MCP; TLX; AHUS2; MIC10; TRA2.10

The protein encoded by this gene is a type I membrane protein and is a regulatory part of the complement system. The encoded protein has cofactor activity for inactivation of complement components C3b and C4b by serum factor I, which protects the host cell from damage by complement. The protein encoded by this gene may be involved in the fusion of the spermatozoa with the oocyte during fertilization.

CD55, also known as CR; TC; DAF; CROM; CHAPLE

This gene encodes a glycoprotein involved in the regulation of the complement cascade. Binding of the encoded protein to complement proteins accelerates their decay, thereby disrupting the cascade and preventing damage to host cells.

CD59, also known as 1F5; EJ16; EJ30; EL32; G344; MIN1; MIN2; MIN3; M1RL; HRF20; MACF; MEM43; MIC11; MSK21; 16.3A5; HRF-20; MAC-IP

Encodes a cell surface glycoprotein that regulates complement-mediated cell lysis, and it is involved in lymphocyte signal transduction. This protein is a potent inhibitor of the complement membrane attack complex, whereby it binds complement C8 and/or C9 during the assembly of this complex, thereby inhibiting the incorporation of multiple copies of C9 into the complex, which is necessary for osmolytic pore formation.

Fc

Fc is a fragment of immunoglobulins. They are large, Y-shaped proteins produced mainly by plasma cells that is used by the immune system to neutralize pathogens. The classical pathway is initiated when immune complexes are formed after immunoglobulin G level or M level binding to pathogens or to other foreign and non-self antigens. The C1 complex, a multimeric complex consisting of C1q, C1r and C1s molecules then binds to the Fc portion of the IgG or IgM immune complex. Activation of C1s and C1r occurs as a consequence of C1q binding to the exposed Fc portion of IgG or IgM. C1s then cleaves C4 and C2 to form the classical pathway C3 convertase, C4bC2a.

He4

Encodes a protein that is a member of the WFDC (Whey Acidic Protein four disulfide core domain) family. The WFDC domain, or Whey Acidic Protein Signature motif, contains eight cysteines forming four disulfide bonds at the core of the protein, and functions as a protease inhibitor in many family members. This gene is expressed in pulmonary epithelial cells, and was also found to be expressed in some ovarian cancers.

CIS References

<https://www.genenames.org/>
[https://www.nlm.nih.gov/research/umls/sourcereleasedocs/current/HGNC/E.Nieschlag,H.M.Behre,S.Nieschlag\(Editors\)Andrology-MaleReproductiveHealthandDysfunction,3rdEdition,Springer-VerlagBerlinHeidelberg2010.e-ISBN:978-3-540-78355-8](https://www.nlm.nih.gov/research/umls/sourcereleasedocs/current/HGNC/E.Nieschlag,H.M.Behre,S.Nieschlag(Editors)Andrology-MaleReproductiveHealthandDysfunction,3rdEdition,Springer-VerlagBerlinHeidelberg2010.e-ISBN:978-3-540-78355-8)

