Complement activation

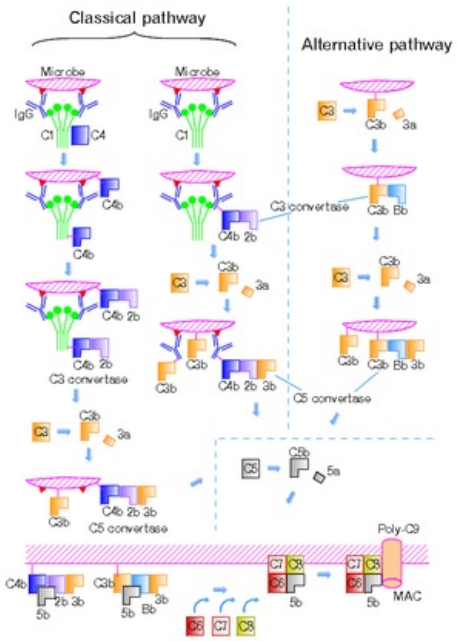
The classic way of complement activation

More on *Classic Complement Activation Path page.*

The classic pathway of complement activation is developmentally younger than the alternative pathway.

Started on surfaces where **antibodies** are bound (IgG, IgM). Binding to the surface (e.g.: bacteria) changes the conformation of the antibody molecule → the binding site for **C1** is revealed. It begins by binding **C1q** to the **Fc** fragment of the immunoglobulin. **C1** (= C1q + x C1r + 2xC1s) also changes shape after binding to the antibody and acquires proteolytic activities → **C4** and **C2** begin to cleave. **C4b** and **C2a** bind to the surface of the infected microorganism → forming a ***classical C3-convertase*** → it cleaves a lot of C3 into C3a and C3b. Then another enzyme is formed - ***classical C5-convertase*** (**C4bC3bC2a**) → cleaves C5 into **C5a** and **C5b**.

Pentraxins can also start the classic pathway: CRP, serum amyloid P (acute phase reactants).



Classical and alternative ways of complement activation

The terminal (lytic) phase of the complement cascade

C5b forms a complex with other components - **C6**, **C7**, **C8**. This complex sinks into the lipid membrane surface of the attacked cell and attaches to it in a ring of **13-18 C9 molecules**. **Pores** form in the membrane - cytoplasmic components escape, osmotic balance is disturbed, and cells can lyse.

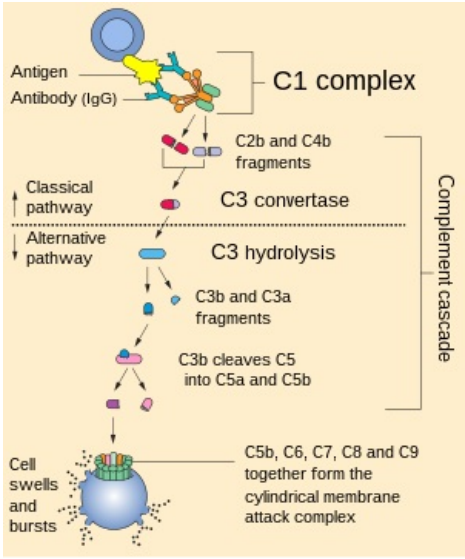
Most microorganisms are **resistant** (CM protection).

An alternative way of complement activation

More on *Alternative Complement Activation Path.*

An alternative way of complement activation is a non-adaptive, non-specific immune response, which begins in C3 by direct contact with chemicals, *endotoxins*, bacterial walls, etc. It is older than classical activation.

The key component of complement (**C3**) cleaves spontaneously with low frequency into a larger fragment **C3b** and a smaller **C3a**. The resulting C3b reveals a reactive cyclic **thioester group** that reacts rapidly with hydroxy and amino groups in the vicinity. If these groups lie on the surface of the organism's own cells or on the microorganism, C3b binds covalently. Usually, the thioester group reacts with water to inactivate. C3b is inactivated by factors **H** and **I**.



Classical and alternative ways of complement activation

C3b bound to the particle surface initiates a cascade of further reactions. Serum **factor B** protein is added. It is cleaved by a serum protease called **factor D** (dependent on the presence of magnesium ions) to **Ba** and **Bb**. The C3bBb complex is stabilized by **factor P** (properdin). It acts as an ***alternative C3-convertase***. It cleaves C3 very efficiently into C3a and C3b.

The resulting C3b fragments are covalently captured on the surface around the enzyme-active complex - they serve as important **opsonins**. Some of them form additional C3-convertases (multiple amplification of the original stimulus). **C3a** acts chemotactically on phagocytes. Some C3-convertase molecules form more complex C3bBbC3b complexes (different enzymatic activity). It cleaves C5 into C5b and smaller C5a (strong chemotactic effects). **C3bBbC3b** (resp. C3bnBb) = ***alternative C5-convertase***.

The formation of C5b begins the **terminal** (lytic) **phase** of the complement cascade common to both pathways.

These events are initiated in a spontaneous, non-specific manner. It can happen both on the surface of foreign particles (useful) and on the surface of one's own cells (self-harm).

Therefore, several **protective regulatory proteins** (plasma and membrane inhibitors) on the surface of their own cells prevent the development of the cascade.

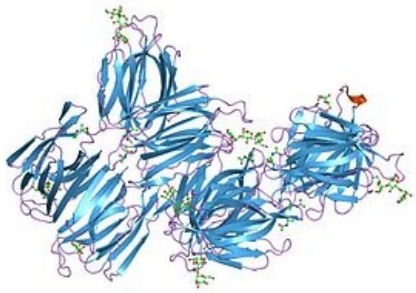
The lectin pathway of complement activation

More on *Lectin Complement Activation Path.*

The lectin pathway of complement activation:

Initiated with serum lectin **MBL** (mannose-binding lectin). MBL binds to the carbohydrate structures of the surfaces of some microbes directly (independent of antibodies). Its structure and function are similar to C1 - after binding to the microbial surface it cleaves C4 and C2.

See also the Terminal (lytic) phase of the complement cascade.



Mannose-binding lectin

Links

Related articles

- Complement
- Mannose - Lectins

References

- HOŘEJŠÍ, Václav and Jiřina BARTŮŇKOVÁ. *Basics of immunology.* 3rd edition. Prague: Triton, 2008. pp. 280. ISBN 80-7254-686-4.