COMPLEMENT COMPONENTS

Immune System Chemicals and Their Functions

© Elaine Moore

Complement refers to a family of immune system chemicals that are activated during the immune response. Complement abnormalities are seen in some autoimmune disorders.

The Complement Family

Complement refers to a family of approximately 30 immune system proteins that interact in a sequence of steps known as a cascade. Here, one chemical activates the next chemical in the series. Complement protein particles remain inactive until they are activated by protease enzymes released during initiation of the cascade. Once activated, complement proteins become protease enzymes. Errors in sustained complement activation or deficiencies of specific complement components contribute to and are associated with specific autoimmune disorders. For instance, a C2 deficiency is highly associated with systemic lupus erythematosus (SLE).

Complement Pathways

The classical complement pathway becomes activated when the immune system encounters complexes of antigens and antibodies or antibodies and cells. These complexes form as the immune system orders antibodies to attack the specific infectious organism that they’re intended to target. For instance, antibodies to polio resulting from polio vaccines specifically react with polio’s viral particles when the body is exposed to them.

Normally, this binding of antigen and antibody coats the infectious agent, preventing it from infecting or invading a host cell. Antibodies can also bind to toxin molecules, for instance the toxins in diphtheria or tetanus, destroying the toxin. The antigen-antibody complex represents the targeting of infectious agents, whereas complement destroys the infectious agent.

The alternative pathway is initiated when previously activated complement components bind to the surface of a pathogen (a viral, bacterial, or parasitic protein particle). In this case the activated complement component is protected.

Complement Activation

Activation of complement is an immune system function designed to protect us from infection. Activation of complement results in the recruitment of inflammatory white blood cells, the tagging of pathogens, and the killing of pathogens.
**Complement Components**

In the classical complement pathway, the components are termed C1, followed by C4, and then C2, C3, and C5 through C9. In the alternate pathway C1, C4 and C2 are bypassed and C3 is activated by an initiating factor (IF), and two substances called Properdin Factors D and B. Complement components have specific functions. For instance, C3 and C5 can cause certain cells, particularly basophils and mast cells, to release their histamine-rich granules, causing anaphylaxis. Total levels of complement are measured as CH50 levels.

C3 is considered to be the key complement component. C3 is an abundant protein found in the blood that has the ability to activate itself. C3 contains an unusual internal thiolester (sulfur-containing) bond that’s stable in native C3. However, this bond can become highly reactive as a result of conformational changes in the C3 protein structure during activation. When activated, C3 is split or cleaved into two biologically active fragments known as C3a and C3b.

C3a is the smaller fragment. It causes vascular permeability and recruitment and activation of phagocytic white blood cells capable of trapping and engulfing infected cells and infectious particles. C3b is larger and contains the highly reactive thiolester. It acts by tagging infectious particles and enhancing the destruction of these particles and infected cells by white blood cells.

**Alternative Pathway of Complement**

The alternative pathway is an innate mechanism which exploits the properties of C3. The alternative pathway does not require antigen-antibody complexes to trigger it. The presence of activated C3 can cause the spontaneous conversion of C3 into C3b, which, in turn, causes the production of more C3.

**Regulation of Complement Activity**

Because of its explosive potential, the complement system is kept under tight control by at least 12 different proteins. These include Factor H, which removes Bb from the alternative pathway and breaks the loop leading to sustained C3 production; Factor I which inactivates C3b; and C1 inhibitor (C1 INH), which binds to sites on activated C1 fragments (C1r and C1s) causing them to shut down their enzyme activity.

**Resources:**

