

Complement Pathways ❹ The Classical Pathway C1, which binds to the Fc region of an immunoglobulin, is composed of three proteins: C1q, C1r, and C1s. C1q is an aggregate of polypeptides that bind to the Fc portion of IgG and IgM. The antibody–antigen immune complex bound to C1 activates C1s, which cleaves C4 and C2 to form C4b2b. The latter protein (C4b2b) is an active C3 convertase, which splits C3 molecules into two fragments: C3a and C3b (C3a is a potent anaphylatoxin). C3b forms a complex with C4b2b, producing a new enzyme, C5 convertase, which cleaves C5 to form C5a and C5b. C5b is now available to bind to C6 and C7 and form the C5b/C6/C7 complex. Finally, C9 binds to this newly formed complex to produce the formation of the MAC. Once the MAC is formed, cell lysis ensues shortly thereafter. Only IgM and IgG fix complement via the classic pathway.