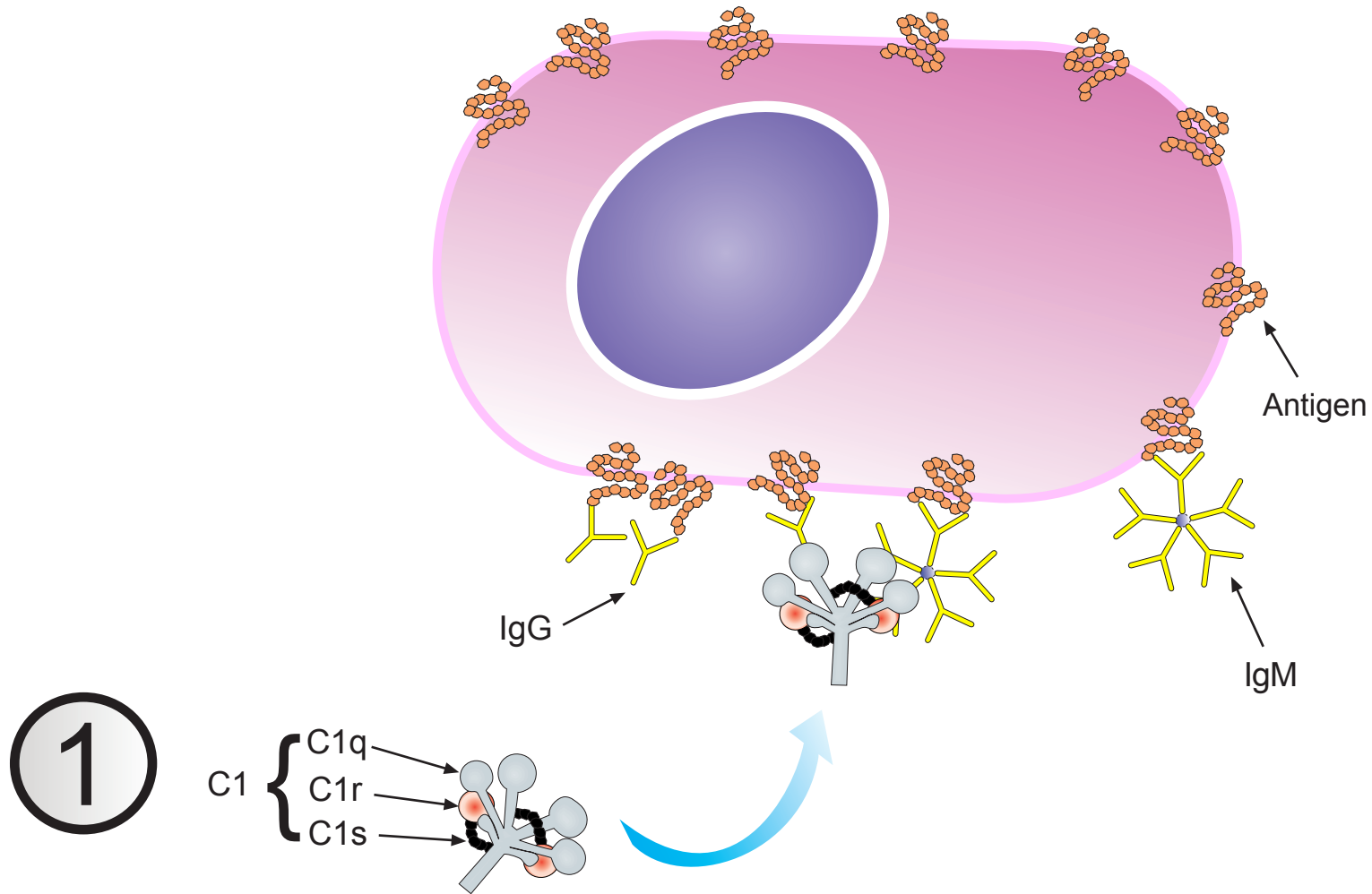


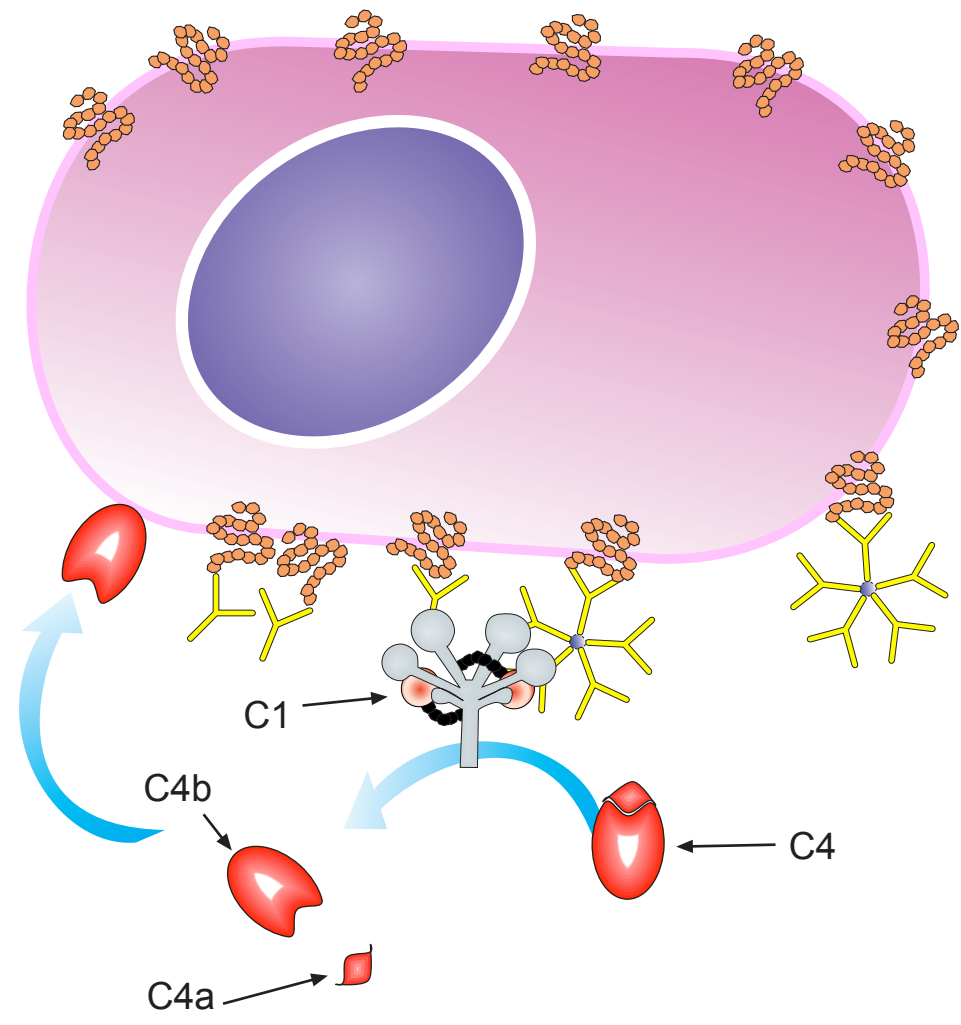
# Classical complement pathway

NEXT 



The classical complement pathway is initiated by the recruitment of C1 complement proteins to antibody-bound cell surface antigens. C1 specifically binds to the Fc domain of antigen-bound IgG and IgM. The C1 complement protein complex is composed of C1q, C1r and C1s protein subunits. The C1r subunit has protease activity that becomes active following C1 binding.

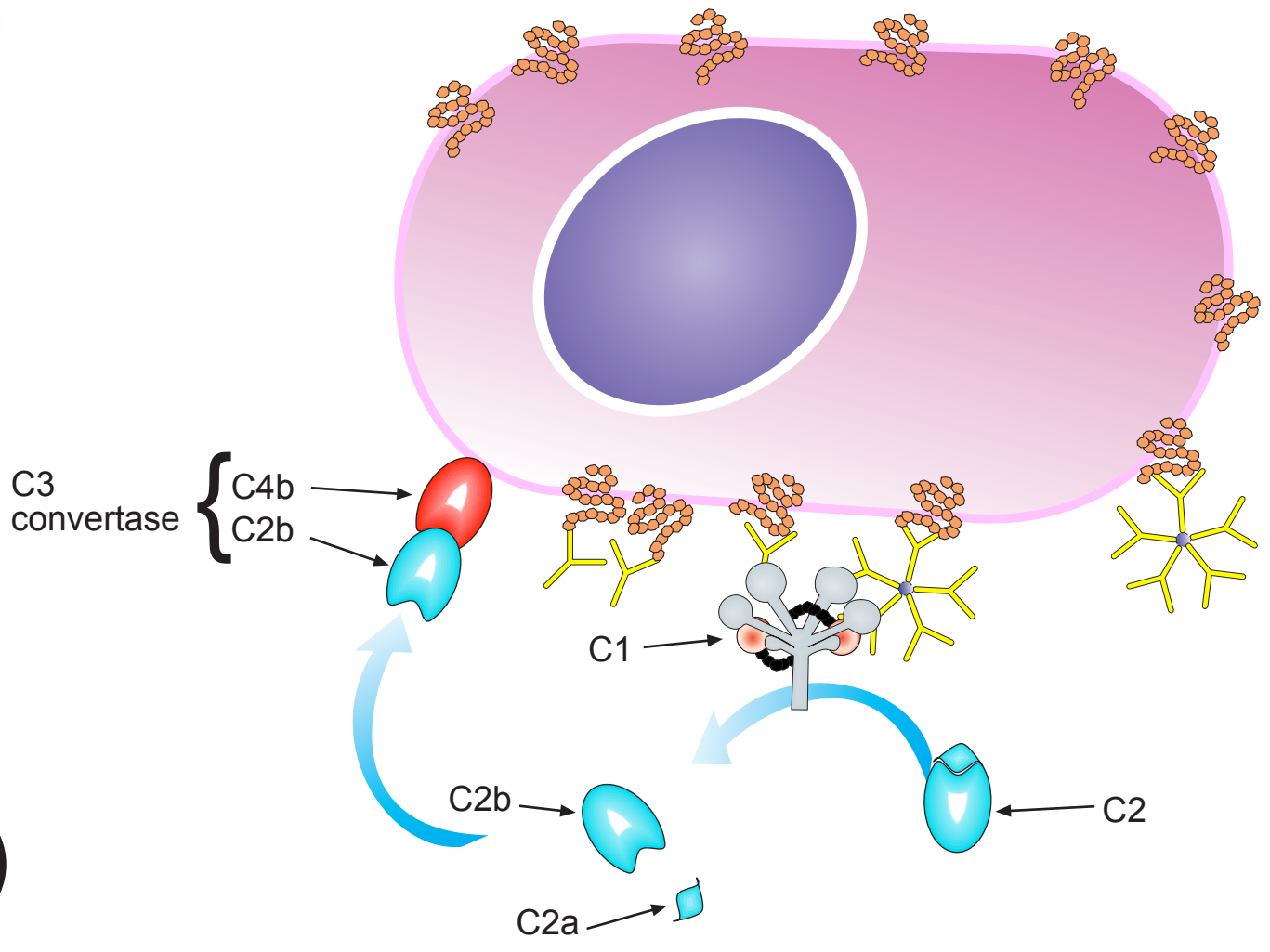




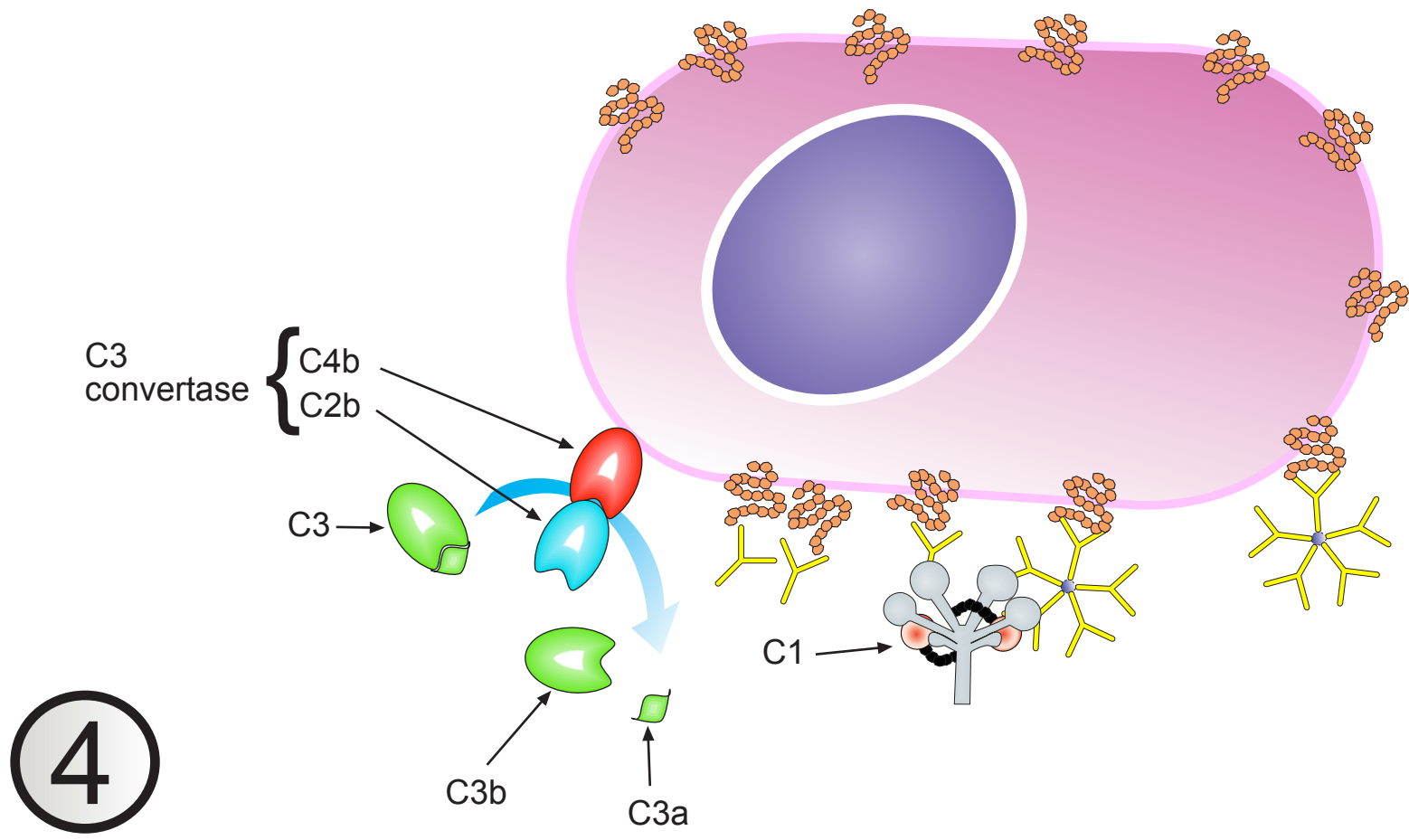
2

Binding of C1 to the Fc domains of antibodies activates C1 protease activity. Activated C1 cleaves C4 complement protein into C4a that is released and C4b that binds to the cell surface. C4a functions as an anaphylatoxin that stimulates inflammation.

3

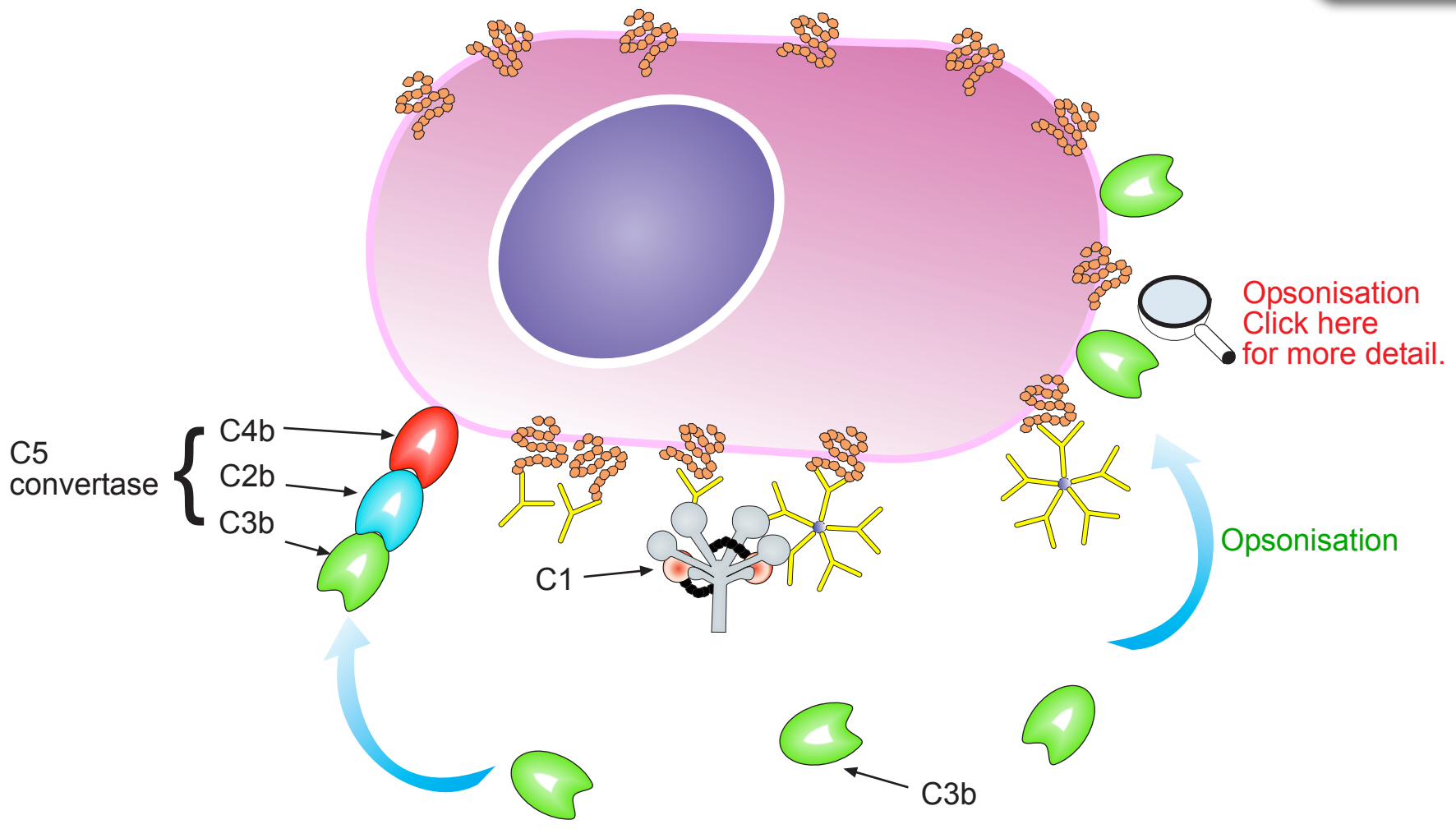


Activated C1 cleaves C2 complement protein into C2a that is released and C2b that binds to C4b on the cell surface. The C4b and C2b protein complex constitutes the C3 convertase enzyme system.



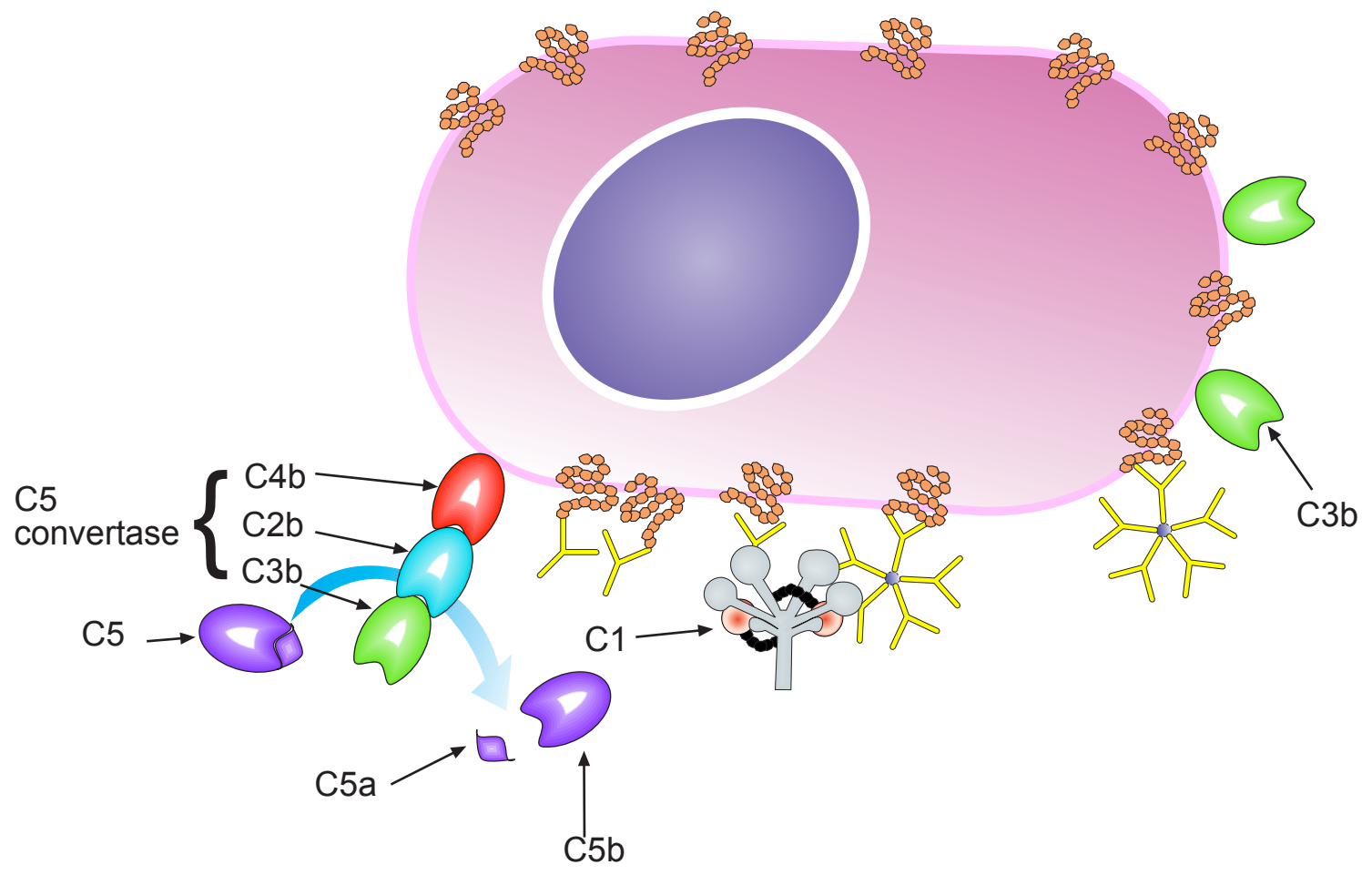
The C3 convertase cleaves C3 complement protein into C3a that is released and C3b that is required to constitute the C5 convertase enzyme system and also functions as an opsonin.

5

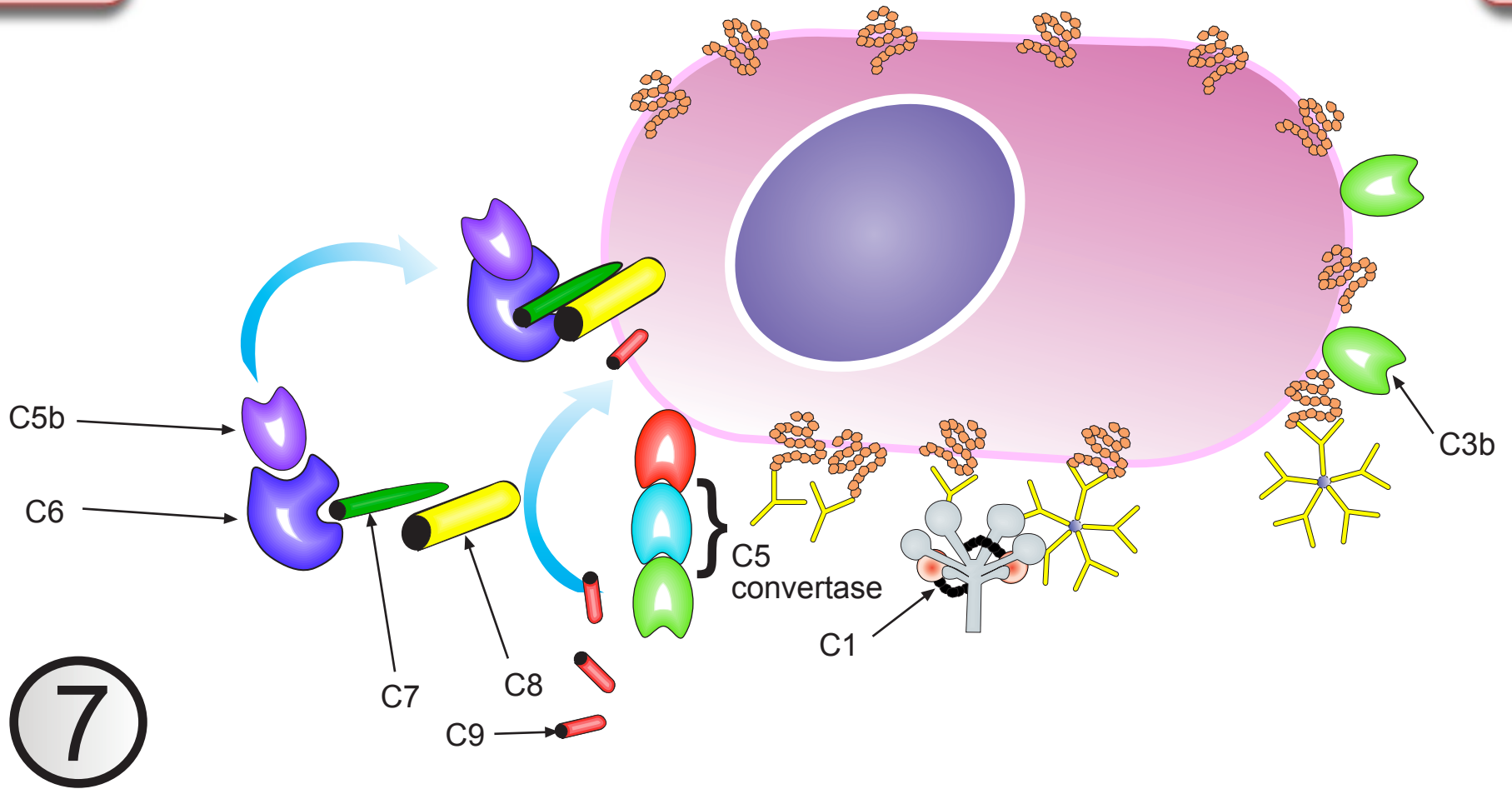


C3b associates with the C3 convertase and constitutes the C5 convertase enzyme system. C3b also binds to the cell surface as an opsonin for enhanced detection by phagocytes expressing complement receptors. Follicular dendritic cells in germinal centres also express complement receptors which enhances capture of immune complexes for presentation to B lymphocytes.

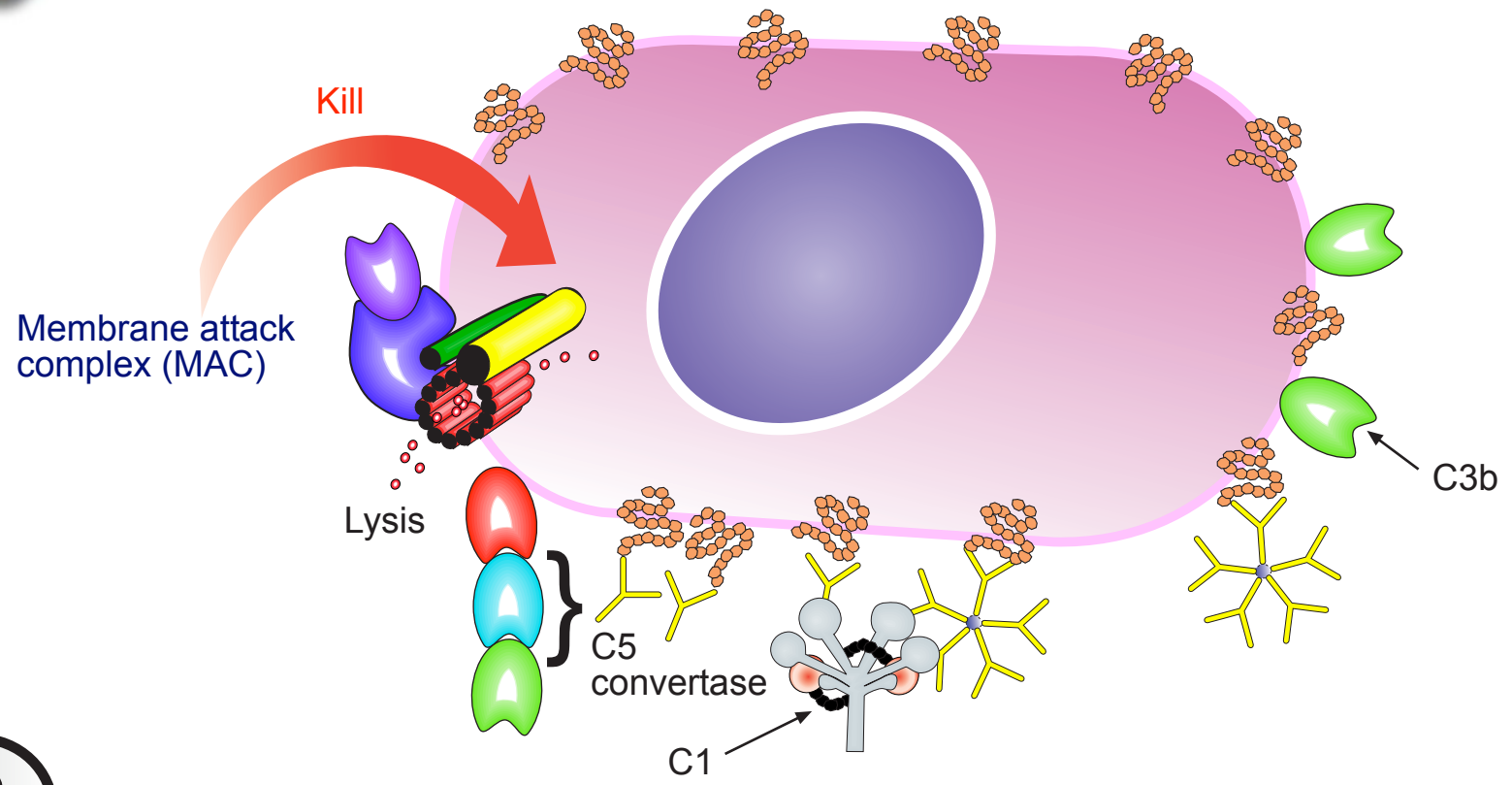
6



The C5 convertase cleaves C5 complement protein into C5a that is released and C5b that recruits additional complement proteins involved in the formation of the membrane attack complex (MAC). C5a functions as anaphylatoxin that stimulates inflammation.



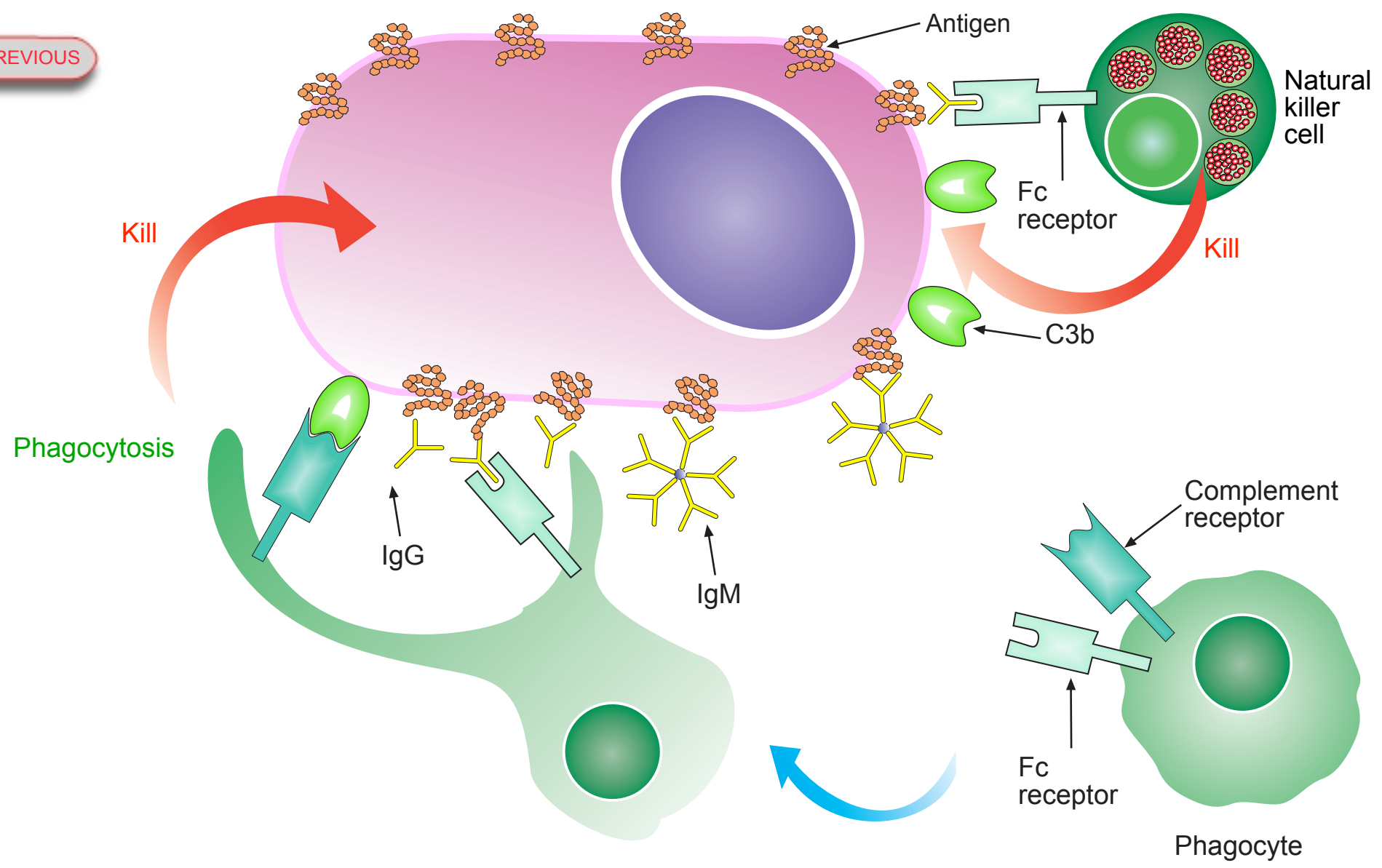
C5b recruits C6 and C7 complement proteins and the protein complex inserts into the cell membrane. Further recruitment of C8 and C9 complement proteins then follows.



8

C8 and C9 complement proteins constitute a membrane-bound pore that mediates cell lysis. The group of complement proteins C5b-C9 is known as the membrane attack complex (MAC). In addition, the Fc domain of bound antibody and cell surface bound C3b enhance detection by phagocytes expressing Fc and complement receptors.





Enhanced phagocytosis of the target cell is mediated by surface-bound C3b complement protein that functions as an opsonin and is detected by complement receptors expressed by phagocytes. Opsonisation of the target cell by IgG is also detectable by phagocytes and Natural killer cells expressing Fc receptors. Phagocytes primarily include macrophages, neutrophils and dendritic cells and to a lesser extent basophils and eosinophils. Follicular dendritic cells in germinal centres also express complement and Fc receptors which enhances capture of immune complexes for presentation to B lymphocytes.