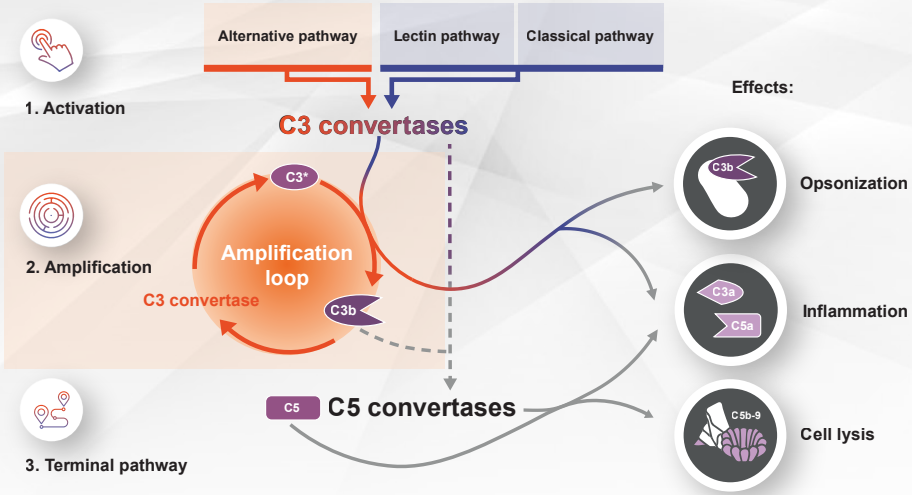
AT A GLANCE

THE COMPLEMENT SYSTEM

The complement system plays a key role in the immune system and comprises **three pathways**, which converge at the formation of the **C3 convertase**. The **amplification loop**, which resides in the alternative pathway, intensifies the activation signal from all three pathways[1,2]



C, complement component; C5b-9, membrane attack complex.

*C3 may also be cleaved to C3a and C3b in the absence of the amplification loop.

1. Zipfel PF et al. *Cell Tissue Res*. 2021;385(2):355-370. doi:10.1007/s00441-021-03485-w 2. Thurman JM, Nester CM. *Clin J Am Soc Nephrol*. 2016;11(10):1856-1866. doi:10.2215/CJN.01710216.

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AT A GLANCE

THE COMPLEMENT SYSTEM

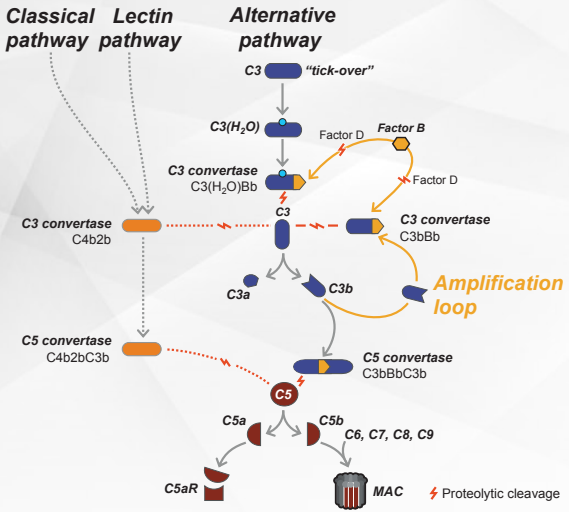
The complement system can be activated through the **classical pathway**, **lectin pathway**, or **alternative pathway**[1]

Activation of the complement system via any one of the three pathways results in the generation of the enzymes **C3 convertase** and **C5 convertase**, which cleave complement proteins **C3** and **C5**, respectively[1]

The **C3b** generated by the activation of any of the three pathways can enter into the **amplification loop** of the alternative pathway, leading to formation of additional **C3 convertase** and further breakdown of **C3**, thus amplifying the initial activation signal[2]

This sequential cascade and amplification generates effector molecules that mediate inflammatory response (anaphylatoxins **C3a** and **C5a**), opsonize (opsonin **C3b**), and promote phagocytosis of pathogens[3]

All three pathways culminate in the activation of the terminal pathway, resulting in the association of C6, C7, C8, and multiple copies of C9 to form **C5b-9 or membrane attack complex (MAC)**, which forms pores in the membranes of pathogens and damaged cells, causing cell lysis[2]



Adapted with permission from Rizk DV et al.[4]

C, complement component; C5aR, complement component 5a receptor; C5b-9, membrane attack complex; MAC, membrane attack complex.

1. Rizk DV et al. *Front Immunol*. 2019;10:504. doi:10.3389/fimmu.2019.00504 2. Thurman JM, Nester CM. *Clin J Am Soc Nephrol*. 2016;11(10):1856-1866. doi:10.2215/CJN.01710216 3. Merle NS et al. *Front Immunol*. 2015;6:262. doi:10.3389/fimmu.2015.00262. 4. Rizk DV et al. *Kidney Int Rep*. 2023;8(5):968-979. doi:10.3389/fimmu.2015/00262.

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