Complement-mediated pathway and diseases

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The complement system makes up part of the innate immune system and contains over 30 different activating and inhibiting proteins, regulators and receptors. When functioning correctly, these work together to destroy foreign or damaged cells without causing damage to healthy cells and tissues.¹⁻³

Complement pathways

Complement can be activated by three distinct pathways:

- classical pathway (triggered by antibodies), lectin pathway (triggered by sugars on the
- surface of bacteria or viruses), and alternative pathway (which can be independently

activated, and also amplifies the effects of the other pathways).

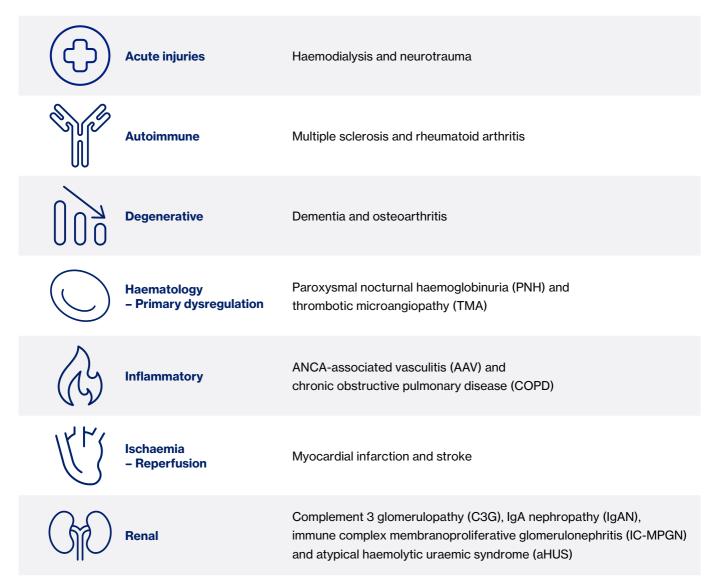
These occur via a cascade reaction, which converge into a common cell-killing pathway.1,2

Watch the animation here to learn more about the three pathways that make up the complement system.

Complement-mediated diseases

Different factors can disrupt the functions of the pathways, leading to a cascade of reactions that mistakenly attack healthy cells and tissues.^{1,2} Deficiencies in these systems can lead to a variety of diseases.3,4

Complement-mediated diseases most commonly fall into the following categories (please note this is not an exhaustive list):2,5,6



These types of complement-mediated diseases can occur throughout the complement pathway, along the classical, lectin and alternative pathways.

Examples of conditions that can occur from each pathway are:

Classical pathway Antigen-antibody complex activation In autoimmune conditions

like systemic lupus erythematosus (lupus), the over-activation of the classical pathway is a major influencing factor.1,2

The classical pathway can also malfunction after acute injuries such as neurotrauma or infection (post-infection haemolytic uremic syndrome [HUS]),7 or after ischaemic events such as a stroke.8

Lectin pathway

Mannose-driven immune response

Diabetic angiopathy, a serious consequence of diabetes mellitus, encompasses cardiovascular disease, retinopathy, nephropathy, and neuropathy.

Recent data suggests that dysregulation of the lectin pathway is associated with the exacerbation of inflammation.9



Amplification loop

Complement 3 glomerulopathy (C3G) is an autoimmune kidney disease where abnormal activation of the alternative pathway leads to a build-up of C3 protein fragments, damaging glomeruli and impairing kidney function.6,10

Paroxysmal nocturnal haemoglobinuria (PNH), a rare stem cell disorder, and age-related macular degeneration (AMD) both have genetic triggers leading to uncontrolled alternative pathway activity destroying healthy cells.1

Complement-mediated diseases can cause a downstream effect by disrupting the three major effector functions which are:1,2

- **Opsonisation** (pathogen recognition and immune signalling)
- **Cell activation** (immune cell stimulation)
- Cell lysis (pathogen destruction)

Treating complement-mediated disease

The aim of complement-specific targeted therapies in development, is to benefit patients across these disease areas.2



To find out more about the complement pathway, visit: www.pro.novartis.com/uk-en/therapy-areas/haematology/ complement-mediated-diseases

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