FABHALTA - Complement-mediated diseases - Therapy Area

Image

Image

Complement-mediated diseases

The complement system

The complement system is part of the immune system, consisting of over 30 different activating and inhibiting proteins, regulators and receptors, working sequentially and collaboratively to clear toxic materials and defend against infection.[1,2]

When functioning correctly, the complement system leads to the destruction of foreign or damaged cells, while ensuring the destruction stops once the threat is removed, before causing damage to healthy cells and tissue.[3]

The complement system works as a sequence, running in three separate activation pathways that ultimately converge into a common cell-killing pathway.[2] Depending on the activators involved, the system follows either the:[1,2]

- Classical pathway (antibody-triggered)
- Lectin pathway (bacterial sugar-triggered)
- Alternative pathway (antibody-independent activation)

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

Introduction to the Complement System

This video is created and funded by Novartis Pharmaceuticals Ltd.

For UK healthcare professionals only
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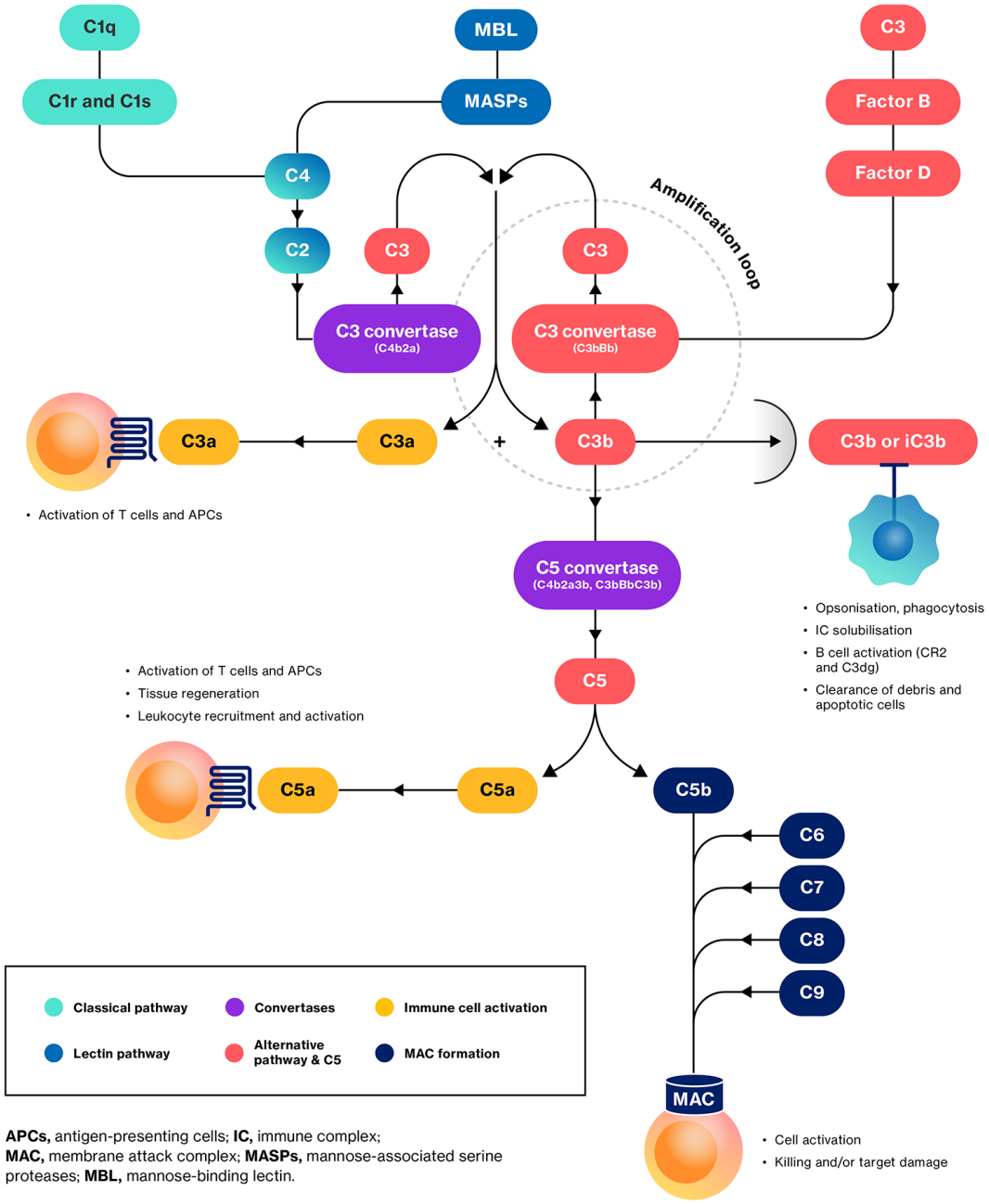
VIDEO

- Overview of the complement system
- Pathophysiology

The diagram below shows the proteins involved in the complement pathways and illustrates their convergence into one:[1,2]

Image



Adapted from Morgan BP & Harris CL, 2015.[2]

Activation of the complement system is tightly regulated by a series of soluble and membrane-bound proteins. Internal or external factors can disrupt the function of these proteins, causing dysregulation. Dysregulation can lead to the complement system mistakenly destroying healthy cells and tissue, causing a variety of complement-mediated diseases.[3,4]

Complement-mediated diseases

Defects at different stages of the complement system lead to various clinical outcomes. For example, defects in the early components of the classical pathway increase the risk of

autoimmune disease, and problems in the terminal pathways are associated with susceptibility to infections.[1,2]

Complement-mediated diseases can fall into several categories. An incomplete list is shown below.[2,5–10] For more information on the specific diseases, please follow the links where given .

Process	Disease examples
Acute injuries	Haemodialysis Neurotrauma Polytrauma Post-infection haemolytic uremic syndrome (HUS)
Autoimmune	Antiphospholipid syndrome Autoimmune haemolytic anaemia Crohn’s disease and ulcerative colitis Guillain–Barré syndrome IgA nephropathy Lupus nephritis Multiple sclerosis Myasthenia gravis Neuromyelitis optica Rheumatoid arthritis
Degenerative	Dementia Diabetic angiopathy Glaucoma Osteoarthritis
Haematological	Hereditary angioedema Paroxysmal nocturnal haemoglobinuria (PNH) Thrombotic microangiopathy Thrombotic thrombocytopenic purpura (TTP)
Inflammatory	Anaphylaxis ANCA-associated vasculitis (AAV) Asthma Atherosclerosis Cerebral malaria Chronic obstructive pulmonary disease (COPD) Dermatomyositis Macular degeneration Mood disorders Psoriatic arthropathy Sepsis and acute respiratory distress syndrome (ARDS) Uveitis
Ischaemia-reperfusion	Myocardial infarction Post-bypass Stroke
Renal	Atypical haemolytic uremic syndrome (aHUS) C3 glomerulopathy IgA nephropathy Membranoproliferative glomerulonephritis (MPGN) and immune complex-MPGN

Complement dysfunction has also been linked to other conditions, including cancer, allergic asthma, transplant rejection, and periodontitis.[5]

Download our infographic that outlines the conditions caused by dysfunctions of different proteins within the complement system.

Download

References

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www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Novartis online through the pharmacovigilance intake (PVI) tool at www.novartis.com/report, or alternatively email medinfo.uk@novartis.com or call 01276 698370.
