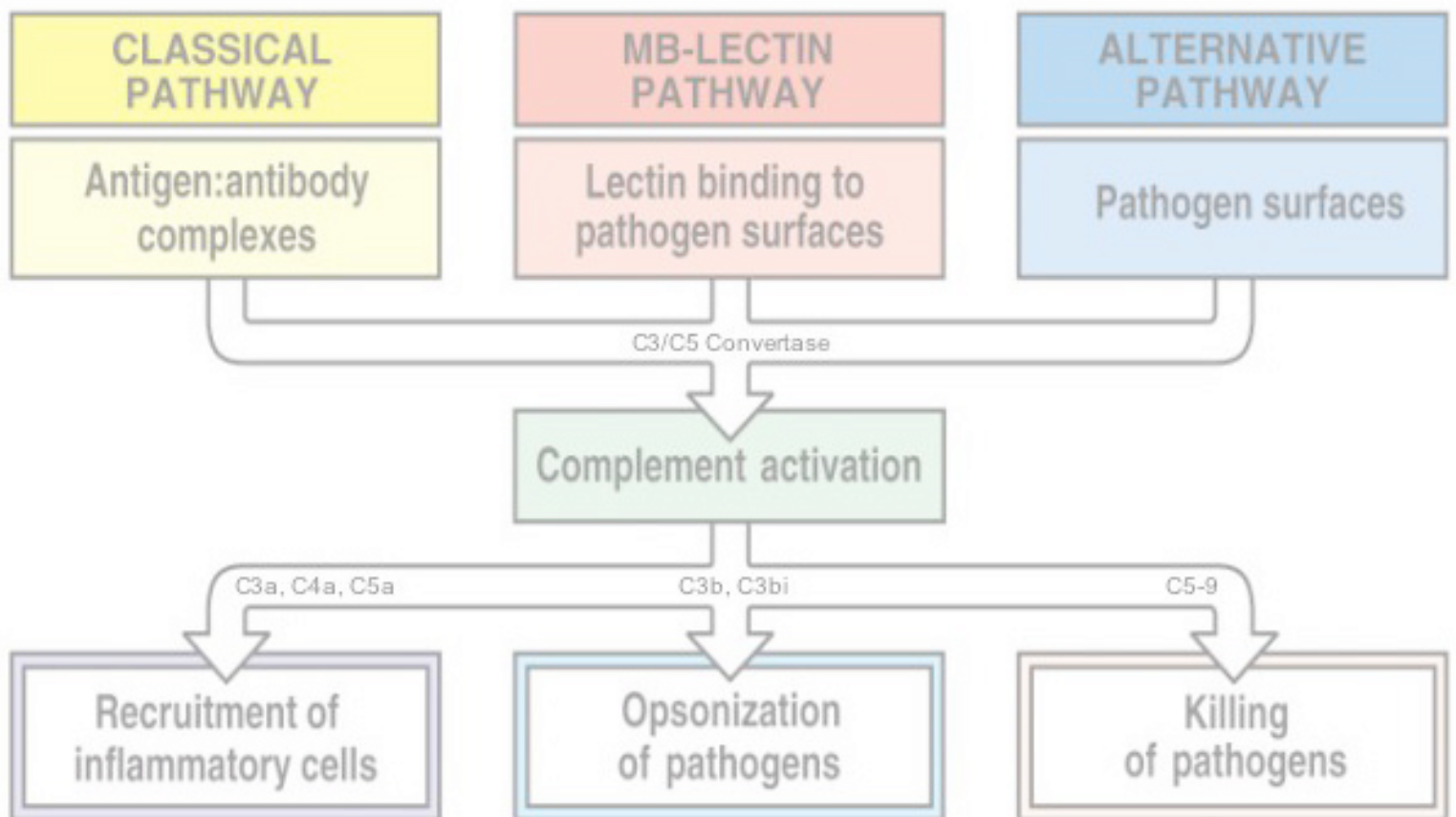


Lecture 8. B cell effector mechanisms: Fc_γ receptors and complement

Learning Objectives and Summary



8. B cell effector mechanisms: Fc_γ receptors and complement

Learning objectives:

1. Understand the structure and various immune functions of IgG
2. Distinguish between “activating” and “inhibitory” Fc_γ receptors, both in terms of how they signal (ITAMs vs ITIMs) and what their roles are in the immune system.
3. Understand the role that tyrosine kinases play in signal transduction mechanisms used by Fc_γ receptors and appreciate that they are similar to those of the TCR and BCR.
4. Appreciate how unregulated activation of Fc_γ receptors can lead to immune complex disease.
5. Learn how complement is activated by pathogens and understand the major functions of complement in the host response to bacteria and fungi.
6. Learn how the complement system is regulated and how inherited defects in complement lead to disease in humans. Be able to identify the major complement receptors in the immune system.

SUMMARY

1. Ig has multiple isotypes each with unique functions.
2. Receptors for the Fc portion of IgG (Fc_γ receptors) come in two basic types: ITAM-containing activating receptors that bind PTKs and an ITIM-containing inhibitory receptor that antagonizes the PI 3-kinase pathway. Their relative expression determines the outcome of a given engagement of IgG ligand.
3. Fc_γ receptors mediate a variety of immune functions: phagocytosis, secretion of pro-inflammatory mediators, and ADCC.
4. Unregulated activation of Fc_γ receptors can lead to immune complex disease. Complement is an ancient system of host defense that has well-defined functions in host defense: it opsonizes microbes (C3b, C3bi), stimulates inflammation (C3a, C4a, C5a), and mediates lysis of pathogens by the membrane attack complex (C5-9).
5. Additional functions of complement include clearance of immune complexes and apoptotic debris. These functions have major implications for the emergence of autoimmunity.
6. Among the known inherited complement deficiencies include Leukocyte Adhesion Deficiency (LAD) and complement component deficiencies; these are associated with frequent infections and, in the latter case, autoimmunity.