Request for Notetaker

Please Contact Dr. Klingbeil ASAP if you are willing to contribute your notes to students who have been sick since EXAM 2.

You only need to provide the notes and they will be returned same day.

Your cooperation is greatly appreciated!

Review Concepts of Complement

Complement was addressed in Lecture 3

Major first line of defense (innate immunity)

Major functions:
- Opsonization
- Cell Lysis
- Activation of phagocytic cells
Overview of Complement

Complement as an Important Bridge

Complement Evasion - General
Recognition of Conserved Cell wall Features

Loose unstructured network of polysaccharides
Protects against phagocytosis
Aids in adherence
Inhibits complement activation through binding of factor H

Evasion of Toll-like Receptors (TLR)

Pathogens can modify targets of innate immunity
The gram-negative bacteria Salmonella and Yersinia can change their LPS structure, making it less stimulatory for TLR4.
Many pathogens down-regulate their flagellin genes upon entry into the host. This prevents recognition by TLR5.

LPS - lipopolysaccharide, abundant molecules in most Gram-

Streptococcus pneumoniae produces >100 types of capsular polysaccharide

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Complement: Added Features - Lambris, 2008

Complement Regulation

Regulators of Complement Activation (RCA)
Proteins that regulate complement
Structurally similar proteins
Complement receptor 1 (CR1)
Factor H (fH)
C4-binding protein (C4BP)
Decay accelerating factor (DAF)

Complement Regulation - Complexity

Normal conditions
Addition of lipids
Addition of ions
Addition of complex
Complement: Added Features - Lambris, 2008

Mechanisms of Complement Evasion

Three main strategies addressed in review

Making use of the host’s arsenal - acquiring regulators
adaptations by binding RCA that circulate
RCA are the natural regulators
Recruitment and mimicry

Cutting through complement - pathogen proteases

Direct interventions - microbial complement inhibitors
Factor H as a Complement Regulator

What is Factor H?
- 150 kDa glycoprotein
- Circulates in plasma (0.5 - 0.8 mM concentration)
- Central role in regulating Alternative Pathway

How does Factor H regulate complement?
- Binds to complement factor-3b, making inactivated complement factor-3b (iC3b) susceptible to cleavage by complement factor I, and by interfering with the binding of properdin factor B (complement factor B) to complement factor C3b

Factor H in Complement Regulation

A. Activation
- Amplification of complement activation

B. Inactivation
- CCP 16-20
- Factor H
- Cell surface
Role of Factor H

Pathogen proteins that bind complement

Evading Complement Regulation