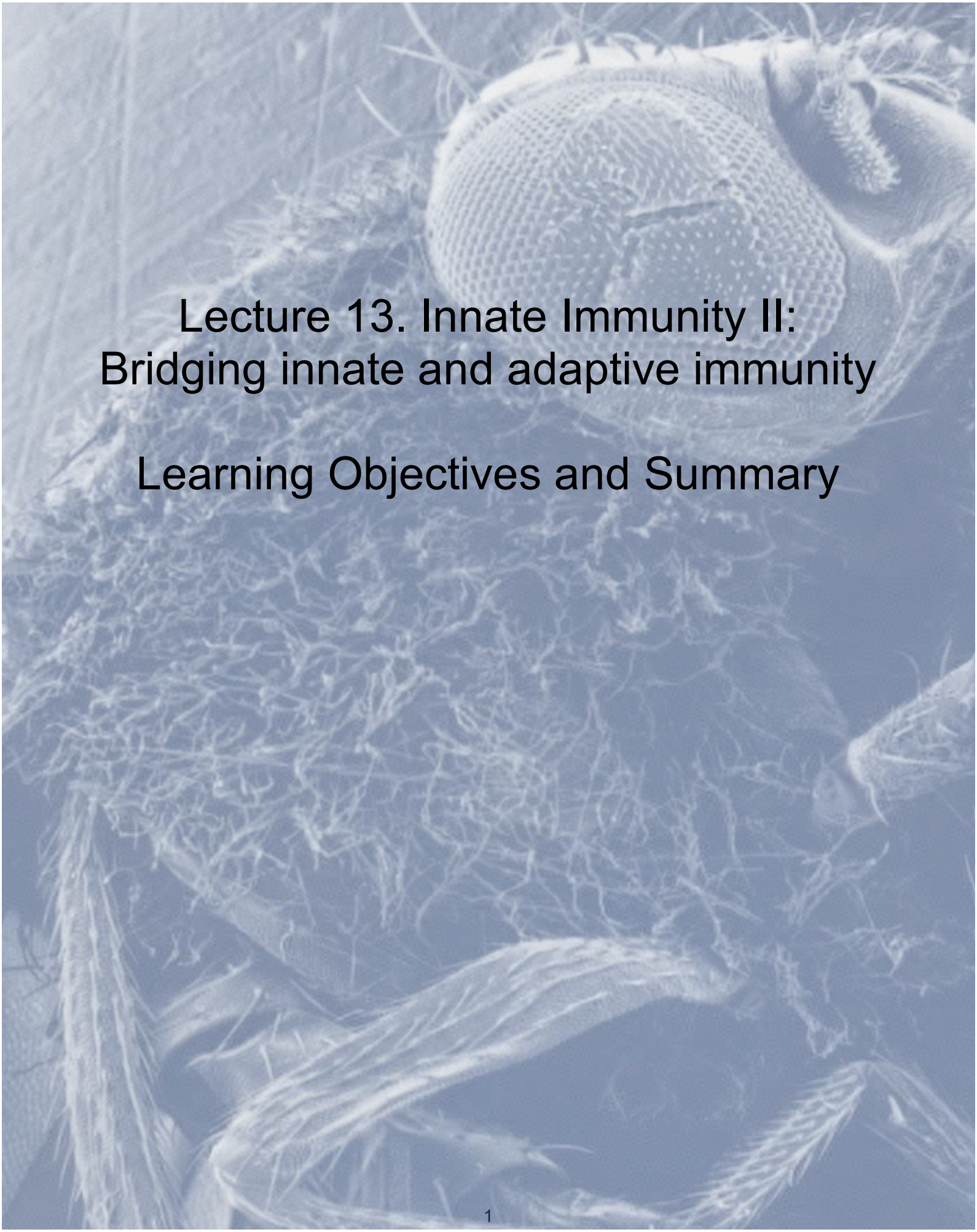

Lecture 13. Innate Immunity II: Bridging innate and adaptive immunity

Learning Objectives and Summary

13. Innate Immunity II: Bridging innate and adaptive immunity

Learning objectives:

1. Be able to describe the mechanisms used by the immune system to recognize non-peptide antigens, such as LPS and carbohydrates.
2. Appreciate the role that "pattern recognizing receptors," such as TLRs and members of the scavenger receptor superfamily, play in immunity.
3. Be able to explain in general terms how TLRs signal to activate a dual program of gene expression: pro-inflammatory genes via activation of NF-κB and a separate program that results in production of Type I interferons.
4. Appreciate that other bacterial recognition systems exist in specific subcellular compartments, such as the cytosol.
5. Be able to explain functional differences between immature and mature DCs.
6. Be prepared to explain the statement: "The acquired immune response is initiated by activation of the innate immune system."
7. Describe the innate immune response to viral infections.

SUMMARY

1. Innate immunity is conserved throughout evolution and is triggered by recognition of "pathogen-associated molecular patterns" (e.g., LPS) by "pattern recognition receptors."

2. Collectins (e.g., SP-A, C1q, MBP) recognize carbohydrates on pathogen surfaces and perform multiple anti-microbial functions (e.g., opsonization). Collectins are essential for innate immunity, but also help clear apoptotic debris.

3. Members of the Scavenger Receptor superfamily recognize bacteria as well as glucose-modified proteins and oxidized lipoproteins. They are implicated in the response to infection as well as atherosclerosis and other degenerative diseases.

4. TLR4 is the major LPS receptor in mammalian cells. TLR4 triggers activation of NF-kB (leading to production of TNF-α, for example). Other TLRs recognize additional microbial products. Nod-like receptors (NLRs) are intracellular sensors of bacterial products that activate the "inflammasome," triggering caspase-dependent maturation of IL-1.

5. Dendritic cells undergo a maturation program: immature DCs, which traffic to the periphery, capture antigen, and mature DCs, which traffic to the lymph node, present antigen. Innate immune stimuli trigger DC maturation, which upregulates co-stimulatory molecules and facilitates antigen presentation. Thus, the innate immune response ushers in the acquired immune response.

6. NK cells, a component of innate immunity, especially to viruses, represent an early source of IFN-γ and serve to stimulate macrophages and DCs in inflammatory sites. Additional components of the antiviral response include intracellular dsRNA sensors (RIG-like proteins) that activate the IRF pathway to signal antiviral gene expression.