

Immunology and Virology (Bio 440) #2:

Innate Immunity: Barriers and Phagocytosis

Terms you should know:

innate immunity	cytokines	lipopolysaccharide (LPS)
adaptive immunity	chemokines	mannose
dendritic cells	TNF, IL-1	unmethylated CpG nucleotides
epithelial barriers	selectins	flagellin
phagocytosis	integrins	lipoglycans
inflammation	affinity	<i>N</i> -formylmethionine
monocytes, macrophages	Toll-like receptors	NF- κ B
neutrophils		

Guide questions to help you prepare for lecture:

1. How are adaptive and innate immunity different?
2. Why is “innate immunity” a better name for this first line of defense than the older term, “non-specific defenses?”
3. What are the major portals of entry for invading microorganisms?
4. What are some examples of barriers, and how do the barriers function to exclude invading microbes from the body?
5. How does a phagocytic cell (neutrophil or macrophage) recognize a microbe?
6. What are some molecules that can be used by phagocytes to distinguish an invading microbe from a host cell or some non-infectious debris?
7. What key transcription factor is activated when these cells encounter invading microbes? What products are made by the cell when this transcription factor is activated?
8. What two important cytokines cause blood-vessel cells to express selectins? What change in the behavior of neutrophils results?
9. How are integrins on the surface of neutrophils switched from a low-affinity to a high-affinity state? (And what exactly does that mean?) What change in the behavior of neutrophils results?
10. What bacterial product can affect phagocytic cells in a manner similar to chemokines?
11. How do phagocytes actually ingest microbes? Once ingested, how do they kill them?

Problem Solving: Innate Immunity 1

1. *Helicobacter pylori*, a bacterium uniquely well-adapted to growing in the stomach, is the major cause of gastric ulcers—which are really just sores caused by inflammation of the stomach epithelium. In patients who take strong stomach acid blockers for a long period, however, other bacteria such as *Lactobacillus* can grow in the stomach and sometimes become very numerous. These patients may develop ulcers even though no *Helicobacter* is present.
 - a. *Lactobacillus* is a Gram-positive bacterium. What receptors might be involved in recognizing it as an invader, and what bacterial components might they recognize?
 - b. Review the sequence of events that would occur as the innate immune system responds to this bacterium.
 - c. *Lactobacillus* is a harmless bacterium: it produces no toxins and has no direct means of damaging cells. Explain how its presence in high numbers in the stomach could lead to an ulcer.

2. Immunodeficiency refers to a disease in which the ability of the immune system to respond to invading microbes is reduced. Immunodeficiency can be caused by an infectious agent (the most famous example being AIDS caused by HIV), or it can be a genetic condition. Below are some different kinds of mutation that can cause some level of immunodeficiency. For each, discuss (1) how severe you think the resulting immunodeficiency would be; (2) whether you think the affected individual would have a defect in the inflammatory response, (3) whether the affected individual will have more trouble responding to bacterial or viral infections (or whether both responses will be affected equally, and (4) whether you think the affected individual would have a serious defect in the adaptive immune response.
 - a. A mutation preventing macrophages from synthesizing TNF
 - b. A mutation preventing endothelial cells from expressing selectins
 - c. A mutation preventing macrophages and dendritic cells from producing TLR-4