

Immunology and Virology (Bio 440) #3: Innate Immunity: NK Cells and Complement

Terms you should know:

natural killer (NK) cells	complement	inflammation
activating, inhibitory receptors	classical pathway	mannose-binding lectin (MBL)
MHC class I	alternative pathway	C-reactive protein (CRP)
IL-12	lectin pathway	second signal
degranulation	C3b	adjuvant
apoptosis	opsonization	costimulator
IFN- γ		

Guide questions to help you prepare for lecture:

1. How are NK cells similar to the cytotoxic T lymphocytes that function in adaptive immunity? How are they different?
2. NK cells have activating receptors for molecules commonly found on host cell surfaces. Why don't they kill uninfected host cells?
3. What important cell-surface protein binds NK cells' inhibitory receptors? Why does this interaction change when a cell is infected by a virus?
4. How do NK cells kill infected cells?
5. NK cells and macrophages communicate with each other. What signal is passed from NK cell to macrophage, and what is its effect? What signal is passed from macrophage to NK cell, and what is its effect?
6. What is meant by opsonization? What are three different proteins discussed in this chapter that can opsonize?
7. In addition to opsonization, what are two more general functions of complement?
8. What are the two kinds of signals that are needed in order for adaptive immunity to be activated? Why isn't one signal sufficient? How is the innate immune response important in this activation process?

Problem Solving: Innate Immunity 2

A vaccine is an agent that cannot cause disease but that will produce an effective adaptive immune response that will protect the recipient from an actual pathogen. Suppose you are concerned about bioterrorism and you want to produce a new anthrax vaccine that might work better than our current one. Anthrax is caused by a Gram-positive bacterium, *Bacillus anthracis*. You have two possible vaccines you would like to test:

- (A) A culture of bacterial cells that have been killed using chemicals that won't lyse cells or greatly disrupt protein structure ("whole cell vaccine").
- (B) A purified preparation of one surface protein from the bacteria, made by genetic engineering ("subunit vaccine"). It is known that people who are immune to anthrax produce antibodies that bind this particular protein.

In order to test the effectiveness of your vaccines, you administer them to mice and test for the production of an antibody response. In some cases, you also administer purified lipopolysaccharide as an adjuvant. The results are shown in the table below; more (+) symbols represent a better antibody response.

trial	vaccine	LPS	antibody production
trial #1	whole cell	no	+++
trial #2	whole cell	yes	+++
trial #3	subunit	no	+
trial #4	subunit	yes	+++

- a. Why was it necessary to add the LPS to get a good antibody response for the subunit vaccine, when LPS had no effect on antibody production with the whole cell vaccine?
- b. Describe the sequence of events that would allow LPS to activate a stronger adaptive immune response.
- c. LPS is not used as an adjuvant in humans because it produces inflammation even when injected alone, with no antigen at all. Explain why this would be the case.
- d. In humans, alum (aluminum hydroxide)—a completely non-biological molecule that just happens to work—is commonly used as an adjuvant. It doesn't produce significant inflammation. Given your answers to (b) and (c) above, what do you think this molecule might be able to do, and what do you think it would not do?