

NAME _____ TA _____

7.013 Problem Set 7 FRIDAY April 16th 2004

Problem sets will NOT be accepted late.

Problem 1

a) What are the four features of the adaptive immune system discussed in *Purves et al.* that allow it to effectively fight a multitude of possible infections? Why is each necessary?

Specificity: It is important to activate a response against only the offending pathogen.

Diversity: The immune system can respond to pathogens that it has never encountered, allowing it to be ready for any eventuality.

Tolerance of Self: The immune system will do far more harm than good if it is always activated against the body's own tissues.

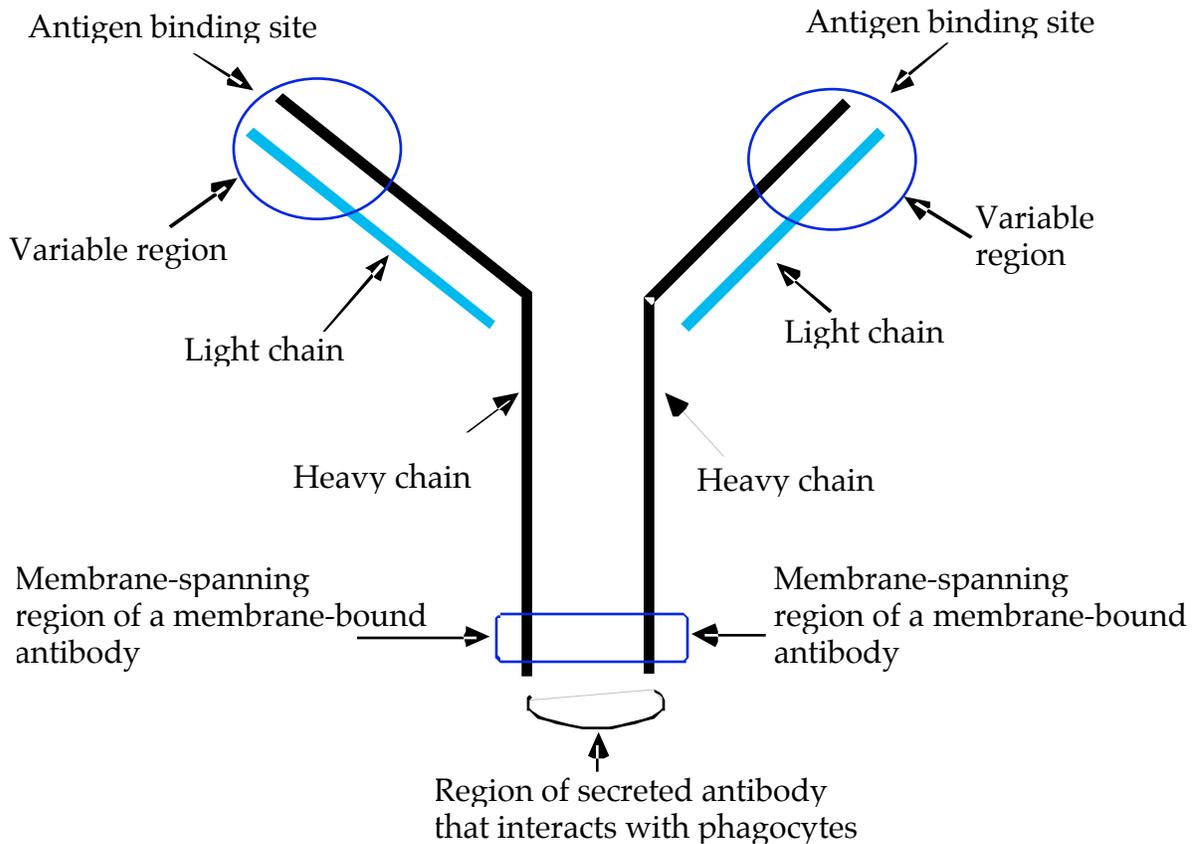
Memory: This allows the immune system to specialize in fighting the diseases the body is more likely to encounter, those which it already has encountered.

b) How do the jawless fishes and invertebrates survive without an adaptive immune system?

They have an innate immune system that protects them from many pathogens, but lacks the specificity and diversity of the adaptive immune system.

Problem 2

Shown below is a schematic representation of an antibody made in B cells.



a) i) On the diagram above label the following structures on the antibody diagram.

- the heavy chains
- the light chains
- the variable regions
- the antigen binding sites
- the constant regions

ii) If this were a secreted antibody, indicate on the diagram the region of the antibody that would interact with phagocytic cells.

iii) If this were a membrane-bound antibody, indicate on the diagram the membrane-spanning region of the antibody.

b) What are the interactions between the light and heavy chains that make them associate with each other?

Disulfide bridges = covalent bonds

c) What are four ways in which variation is introduced into T- and B-cell receptors during T- and B-cell development?

VDJ recombination among multiple regions, terminal transferase creates insertion mutations, unusually high mutation rate at the immunoglobulin loci, and imprecise recombination

d) How does the immune system increase receptor avidity after T- and B- cell development?

Somatic hypermutation

e) How are the various antibody classes different? What are the advantages of changing an antibody class?

The various antibody classes have specialized functions. Some act as specific signals, while other classes confer tissue type-specific advantages, such as when an infection must be fought in the mucus rather than the bloodstream.

f) How does the body select effective, non-self T cells?

First, there is a round of positive selection, where only cells with receptors that can bind MHC molecules survive.

Then, there is a second round of selection where T cells that bind self-peptide/MHC complexes specifically are either deactivated or eliminated.

g) Why do T- and B-cells recombine their DNA? Why not just use alternative splicing to create diversity? (Hint: Think about the impact on descendant cells and their ability to fight an infection.)

All clonal descendants of an activated immune cell must respond to the same antigen. In this way, the immune system can launch a specific and large response localized to the site of infection.

Problem 3

The Nasal-Spray Flu Vaccine (Live Attenuated Influenza Vaccine [LAIV]) was recently introduced under the name FluMist as an alternative to the traditional flu shot.

a) Besides the route of inoculation, how is FluMist fundamentally different from a flu shot?

FluMist uses a live, attenuated virus, where the traditional flu shot uses killed virus.

b) Why may FluMist be more effective than a flu shot?

The live virus will activate the cellular immune response, not just the humoral.

c) Why should people who are allergic to eggs not get a flu vaccine?

The virus is grown in fertilized eggs and may contain egg antigens.

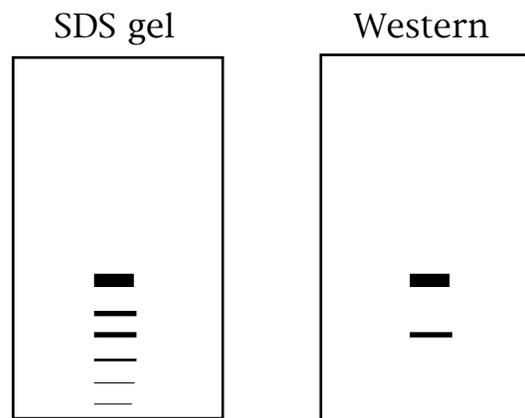
d) What is a possible drawback of using a live, attenuated virus vaccine not shared with using the traditional flu shot? How does FluMist reduce the possibility of such a drawback? (Hint: Go online to find more information about the vaccine. Extra Hint: Not at flumist.com)

It is possible, though less likely, to contract the disease from a live virus vaccine. FluMist has an extra level of protection in that the virus is cold adapted and temperature sensitive. It can survive in the upper respiratory tract, but not in the lungs, where the temperature is higher and a virus can cause respiratory disease.

Problem 4

A researcher is trying to purify a protein he is interested in studying. He performs SDS polyacrylamide electrophoresis, which separates proteins by size, on what he believes to be his purified sample. When he stains the gel with Coomassie blue (a dye that stains all proteins), he sees not only a band corresponding to the molecular weight of the protein he is interested in, but also a few other bands of lower molecular weight.

The researcher thinks these might be proteolytic fragments of the protein he has purified, perhaps caused by an undetectable contaminating protease (i.e., cannot be seen on the gel). To test this hypothesis, he decides to do a Western blot of his gel using a monoclonal antibody to the protein. The only bands that show up on the blot are the one corresponding to the protein of interest and one of the lower bands. See below.



Since the antibody only bound to one lower band, can the researcher conclude that the other bands correspond to different contaminating proteins? Why or why not? If not, what other reagent(s) could make this a more informative experiment?

*No, the researcher cannot conclude that the other bands on the gel correspond to different proteins. He performed his Western analysis using monoclonal antibodies; therefore, the bands of protein that did not show up on the Western blot might be proteolytic fragments of his protein **that do not contain the epitope (or antigenic determinant) that this particular antibody recognizes.***

Polyclonal antibodies would give more information about the identity of more of the unidentified proteins. In a polyclonal antiserum, there are antibodies to many different epitopes on the same protein (remember, epitopes are relatively small regions of proteins).

Different fragments of a protein are likely to contain epitopes for different antibodies.

Problem 5

a) When an organ is transplanted, the patient must take immunosuppressant drugs for the rest of his or her life. Why is that?

The immune system will recognize the transplanted organ as foreign, and mount a response against it. For the organ, and therefore the patient, to survive, that response must be limited.

b) The exception to this is bone marrow transplants. What makes bone marrow different from, say, a kidney that the patient does not require immunosuppressants to live?

The immune cells originate in the bone marrow. In most bone marrow transplants, the patient's immune system is already compromised, as in high-dose chemo and radiation therapy. As the bone marrow grows and takes hold in the body, the immune cells from it will be as self, while the patient's own immune cells will have long been dead.

c) What is a complication of bone marrow transplants that is generally not a concern in other transplants, and how is it obviated?

In some cases, where the match is not perfect, the immune cells of the marrow can mount a response against the body of the recipient. In anything less than an extremely close match, the immune cells of the bone marrow will launch an attack on the recipient's body, causing graft-versus-host disease. Patients are matched as closely as possible by HLA's. The closer the match, the less severe this problem becomes. In autologous bone marrow transplants, this is not a concern at all.

d) Explain why, after a bone marrow transplant, the patient must often get an entire complement of vaccinations.

The memory cells in the periphery, that held the immune system's memory against those diseases, were killed off. When the immune system is repopulated, there are no memory cells, and so the patient must get all new vaccinations