Problem Set #1 Molecular Immunology Spring 2006

1) Compare natural (innate) and acquired immunity with regards to

a) speed of response—*innate is much faster*

b) how "foreignness" is recognized- *innate uses mediators released by damaged tissues as well as receptors for common features of microbes. Acquired uses antigen specific receptors, Ig and TCR*

c) how tolerance of self is mediated—*innate avoids self-reactivity since normal tissue lacks microbial features; also, self tissues express inhibitors of innate immunity. As you will learn shortly, acquired immunity either inactivates or deletes cells with self-specificity.*

d) how they interact with one another—*antibody targets phagocytosis (opsonization) and complement; phagocytes present antigen to T cells; T cells and phagocytes release interferons.*

2) What would be the effect on T cell activation of a drug which interfered with phagocytosis of bacteria?
Phagocytosis is essential for the proper exposure of antigen to T cells. Hence, T cell immunity would be profoundly diminished.

3) What are defensins? Which cells make them? How do they work?
Low molecular weight polypeptides secreted by epithelial cells and fibroblasts which bind to microbial membranes and create pores leading to osmotic lysis.

4) Name three autoimmune diseases and describe their immunological characteristics.
myasthenia gravis—antoantibody specific for acetylcholine receptor.
juvenile diabetes—immune response which kills islet cells in pancreas which secrete insulin
SLE (lupus)—auto-antibodies against normal cellular components such as DNA and various RNPs. Leads to vascular inflammation.

5) What is vaccination? How does it help prevent infection?
exposure of an individual to an infectious agent or toxin in a form which doesn't produce significant disease but generates immunity to subsequent infection by the same organism.

6) Why would it be useful for infected cells to commit suicide (undergo apoptosis)?
to prevent viral replication and spread.

7) Describe the four classic features of inflammation? What causes them?

reddnes (due to increased local blood flow), swelling, (due to capillary leakiness and accumulation of phagocytes), pain (due to swelling), and heat (again due to increased local blood flow).

8) Based on the Toll/ NF-κB pathway described in lecture, how might you devise a drug to block inflammation? Under what circumstances might it be useful? What side effects might you expect?

Find a drug which interferes with IkB kinase for example. Useful when excessive inflammation is causing disease (arthritis or lupus, for example). Side effects might include susceptibility to infections.

9) A bacterium (for example, E. coli) divides every 10 to 15 minutes in a rich growth medium (such as blood).

a) If the lethal dose of this bacteria in the bloodstream is one billion, how long would it take for a single bacterium introduced into the bloodstream to kill you if there were NO immune response? *About 5 hours*

b)Which aspects of the immune system normally prevent this from happening?
natural immunity—phagocytes, complement

c) Which diseases block these defense mechanisms?
although we didn't mention them in class, there are genetic deficiencies of complement components and of phagocyte killing pathways.

10) What is passive immunity? How can it be used to treat an infection? What limits it's utility?

Immunity due to the transfer of immunoglobulin or T cells from one individual to another. It is limited by the half-life of the transferred Ig or cells. In addition, the host's immune system might mount a response against the transferred Ig or cells depending upon the circumstances.

11) You are using gel electrophoresis to analyze the structure of a novel protein you just purified from serum. When you simply boil the protein prior to electrophoresis, you see a single band on the protein gel, but when you boil the protein in the presence of β-mercaptoethanol, you see two bands on the protein gel. What can you deduce about the structure of your novel protein from this data?

The protein consists of at least two polypeptide chains held together by one or several disulfide bonds.

12) How were myeloma cells critical to the elucidation of immunoglobulin structure? Why couldn't serum be used as a source of immunoglobulin for structural studies?

Myeloma provided a source of homogeneous Ig for structural studies. Serum contains a mixture of enormous numbers of different Ig molecules. This heterogeneity makes structural studies problematic.

13) You are analyzing the properties of an antibody specific for protein X and find that the antibody can no longer recognize protein X after the protein has been boiled. What does this tell you about the nature of the epitope recognized by the antibody?

it must be dependent on the three dimensional structure of the antigen—it is a conformational epitope.

14) What is the most significant difference between the isotypes of antibodies found in serum as compared with those found in saliva?

IgA is highly enriched in body secretions whereas IgG predominates in blood

15) What is meant by the terms primary, secondary, and tertiary structure of a protein?

Primary structure is amino acid sequence. Secondary structure consists of alpha helices and β pleated sheets. Tertiary structure is the three dimensional folding of the entire polypeptide chain.

16) What are the chemical forces that hold proteins into a precise three dimensional shape? Which of these forces are also involved in the binding of antigen to antibody?

Peptide bonds, disulfide bonds, ionic interactions, hydrophobic interactions, hydrogen bonding, and van der Waals interactions. All but the first two are involved in antigen-antibody interaction.