HST 176 Problem Set

1. This is a schematic view of a rearranged $\mu$ chain.

   ![Diagram of rearranged $\mu$ chain]

a. What is coded by the unfilled box at the left? What does the second box from the left in light gray code for? What regions are at the locations of the two question marks?
b. In which box will the first amino acid of the mature protein be located?
c. What function is mediated by the protein sequences in the unfilled box on the left? Describe how these sequences are critical and what they might bind to in the cell.
d. How does the above protein contribute to opsonization? Describe what structural region of the protein may contribute to this process.
e. What is the functional role of the second unfilled box on the right?
f. Which portions of the above protein are associated with light chains?
g. Name the proteins that are physically associated with this protein in pre-B cells.
h. In one of the forms of the $\mu$ protein, some portion of the protein must be involved in stopping the transfer process across the ER membrane. Where in the protein is this sequence? What does it look like?
i. Put together the required boxes from the above figure to recreate what a cDNA for the secretory form of the $\mu$ heavy chain may look like. Where will the untranslated regions be? Where do you think the transcriptional and translational start sites will be located on your figure?
2. The affinity of CTLA-4 is much higher than that of CD28 for B7. Signal One induces CTLA-4 in T cells, but not to high enough levels to sequester all the B7 on an activated APC.
   a. How does CD28 cooperate with Signal One?
   b. What is the role played by CTLA-4 in the induction of an immune response?
   c. As a consequence of the cooperation between Signal One and Signal Two, a cytokine is produced that signals for the proliferation of T cells. Name an immunosuppressive drug that interferes specifically with this cytokine signaling event. Which other drug binds to the same protein as this inhibitor of cytokine signaling? Which pathway does this other drug inhibit?

3. Describe the term transcytosis and explain two important examples of this in the immune system.
4. Fc receptors come in many flavors and have many different functions. List three different Fc receptors with different functional roles in the immune system.

5. Describe the process of making monoclonal antibodies in the lab.
Clinical Correlates

6. A family undergoes pedigree analysis for a disease in which affected individuals lack the Ig peak in serum electrophoresis tests (usually < 100 mg/dL). Also, affected family members have experienced recurrent infections with pneumococcus and streptococcus. Only males are affected with the disease. Identify a likely candidate gene for the mutation and explain the mechanism of the disease. What other gene mutations could cause the same phenotype?

7. A 56-year-old male patient presents to you with recurrent bacterial infections of *Staph. aureus*. Laboratory analysis reveals to you that he is anemic, is hypercalcemic, and has large amounts of proteinuria. Creatinine and BUN levels are also elevated. Within the past few months, the patient has noted back pain. X-ray examination reveals a punched-out osteolytic lesion of the spine.
   a. What diagnosis are you suspicious of? How would you confirm the diagnosis?
   b. Describe the mechanisms for the recurrent bacterial infections, the proteinuria, elevated creatinine/BUN, and the osteolytic lesions. What important cytokines are thought to be involved in the pathogenesis?
   c. How would you treat this patient? What are the major concerns for cause of death?
8. Describe the clinical symptoms one would see in a patient with deficient expression of β2 integrins (i.e., which includes LFA-1). How would you treat such a disease?

9. A 24-year-old female patient complains of a red rash on her cheeks that she has had for a few months that becomes worse if she has too much sun exposure. Lately she has been feeling pain in her joints and some shortness of breath upon exertion. Lab analysis reveals that she has hemolytic anemia and proteinuria.
   a. What is your diagnosis and how would you confirm this diagnosis? Explain the mechanisms by which the joint pain, anemia, and proteinuria develop.
   b. Compare and contrast the mechanisms of pathogenesis for this disease with that of rheumatoid arthritis.

10. Describe the process by which HIV enters into a T cell. Give the names of the important viral proteins as well as the host receptor proteins.
11. Severe Combined Immunodeficiency (SCID) represents a group of disorders in which both B and T cell populations are affected. In X-linked SCID, patients are observed to have a marked decrease in T cells and impaired function of B cells (although the numbers of B cells may be normal).

   a. Describe the mutation causing X-linked SCID and how this results in T cell deficiency. What is a salient feature of lymphocytes in females carrying this mutation?
   
   b. What is the status of natural killer cells in these patients?
   
   c. What is another mutation in humans that has been shown to cause the same disease phenotype as X-linked SCID, but is found in both males and females?
   
   d. What mutations can cause a lack of both T cells and B cells, but do not affect other cell types?