Bonus Problem set – Due Friday February 26 @ 4:30 PM

1. Correct the mistake(s) in the following diagram. Does this represent a light chain or heavy chain? Germ line, or mature/naive B-cell?

2. Sketch all of the DNA products that would occur after recombination at D1 and J3.

3. How many different chains can be made from the above DNA, after the corrections (Q1) have been applied to the DNA. If the organism can make 100 of the other chain type, how many different specificities can this organism develop?

4. Case Study: Sally has a genetic immunodeficiency that presents as a history of lung, gastrointestinal and urinary tract infections that began after about 6 months of birth, when Sally’s mother stopped breast-feeding.

   i) Based on the above information, what is the most likely source of Sally’s medical problems? Which antibody type is she likely missing? Why?

   ii) Assume that Sally was able to produce B-cells, but they lack the immunoglobulin component of the B-cell Receptor. What genetic deficiencies might Sally have?

   iii) Lets now assume that Sally had B-cells that have IgM/IgD as part of the BCR, but she cannot make any soluble antibodies. What additional genetic deficiencies might Sally have?
5. How would deletion/mutation of the enhancer sequence affect the production of antibodies?

6. The structure of a rearranged heavy chain is shown below. There are four polyA addition sites where the mRNA would be cleaved and A residues would be added to the 3' end of the mRNA transcript. Briefly describe how deletion/mutation of the following polyA sites would affect the immune response:

   polyA site #1:

   polyA site #2:

   polyA site #3:

7. An outbred organism contains the following organization of genes that code for its MHC proteins:

   --P---Q---IAα--IAβ--IBα1--IBα2--IBβ--

   a) How many different class I MHC molecules would you find on macrophages?
   b) How many different class II MHC molecules would you find on macrophages?
   c) How many different class II MHC molecules would you find on liver cells?

8. i) An H-2^k and an H-2^d mouse are injected with flu virus. The H-2^k mouse is capable of killing the virus, but the H-2^d mouse cannot. Provide a possible explanation.
   ii) A strain that is congenic to H-2^k, but has IAα^d instead of IAα^k also cannot make antibodies, how does this data refine your answer to part i?

9. In humans, skin transplants between unrelated individuals are typically rejected, however it is possible to have successful skin transplants between most Cheetahs, explain this result.

10. An individual produces normal levels of B-cells in the bone marrow, but there is a severe reduction in the number of circulating naïve B-cells. In addition, single plasma cells will produce antibodies with many different specificities. What process in non-functional in this individual?