Problem Set #3 Molecular Immunology Fall 2006

1) Estimate how many potential Ig molecules could be encoded by a heavy-chain locus with 100 VH, 13 DH, 4 JH gene segments, and a light chain locus with 100 Vκ and 4 Jκ gene segments? Is this an underestimate or an overestimate? Why?

2) Why don't V_H gene segments rearrange with other V_H gene segments?

3) What is a non-productive V(D)J rearrangement?

4) Why does the Leukemia Society of America fund research into the mechanism of the V(D)J recombinase?

5) Sketch the pathway of the V(D)J recombination reaction. Indicate where the pathway would be affected by homozygous null mutations in the following proteins:

a) terminal transferase (TdT)
b) RAG-2
c) DNA-PK
d) DNA polymerase α
e) Ku70

6) Under what circumstances does V(D)J recombination result in a chromosomal inversion? (extra credit)

7) What is allelic exclusion? Why is it important for the regulation of antibody-mediated (humoral) immunity?

8) How would you distinguish a pro-B cell from a pre-B cell from a mature B cell?

9) What is the difference between transgenesis and "gene targeting.?"

10) Mice with a null mutation in the surrogate light chain gene λ5 show a block in development at the pro-B cell stage. Sketch what you think the FACS analysis of bone marrow from this mouse would look like when stained with anti-B220 and anti-CD43? What do you expect would happen to this pattern if you bred a productively rearranged Igκ transgene into the λ5-mutant genetic background?

11) What is receptor editing? Why is receptor editing more likely in the Igκ locus than in the IgHCμ locus?

12) What is clonal deletion? How does it differ from clonal anergy?