Spring 2006 Immunology Exam #2 - Chapters 5 - 7

There is no time limit on this test, though I have tried to design one that you should be able to complete within 4 hours. You are not allowed to use your notes, any books, any electronic sources, nor are you allowed to discuss the test with anyone until all exams are turned in at 9:30 am on Friday February 24. **EXAMS ARE DUE AT CLASS TIME ON FRIDAY FEBRUARY 24**. Turning in an exam late will cost you a letter grade for each 24 hours. The **answers to the questions must be typed** unless the question specifically says to write/draw the answer in the space provided. If you do not type your answers on the appropriate pages, I may not find them unless you have indicated where the answers are. You will need *black, blue, and red* ink pens, as well as a regular pencil to answer at least one question on this exam.

There are 3 pages to this exam, including the cover sheet.

-3 pts if you do not follow this direction.
Please do not write or type your name on any page other than this cover page. Staple all your pages (INCLUDING THE TEST PAGES) together when finished with the exam.
Name (please print here):

Write out the full pledge and sign:

How long did this exam take you to complete this exam?

Avg. = 82.7 Range = 60 – 100 13 pts added.

20 pts.

I. Define these terms: 2 pts each. Define the terms and demonstrate your knowledge. These terms can be define succinctly so using a lot of words is not the best way to demonstrate your fluency with these terms. You may combine words with pictures if this helps, but don't hand write the words unless you print VERY neatly.

Ii

Invariant chain, trimerizes with an alpha/beta MHC II and this threesome forms a ninemer (3 trimers). Ii blocks self peptides from binding to MHC II while is it being made in the endoplasmic reticulum.

Haplotype

Collection of linked alleles that are inherited as an block that resists recombination. MHC complex is an example of such a sight in our genomes.

AP1

Transcription factor activated by GEF/small G proteins in the MAP kinase pathway. Composed of Fos and Jun.

JAKs

Intracellular part of a receptor that is a kinase; usually occur in paired receptor halves. JAKs bind to STATS and JAKs phosphorylate the STATS.

pro-B cell

immature B cell prior to the pre-B cell receptor appearing on the surface of the developing B cell. Pro-B cells are undergoing heavy chain gene somatic recombination.

nude mice

A genetically mutated mouse that has no hair (thus the name) but more importantly to us, has no functional thymus. Thus, the mouse has practically zero functional T cells (or adaptive immunity) since they require a thymus for maturation.

NK T cells

A double negative T cell whose TCR binds to CD1 which presents glycolipids as antigen.

receptor editing

A process of modifying the light chain on a BCR that has been productive during B cell development but it binds to a surface antigen inside the bone marrow. The light chain gene tries more V → J recombinations to make a new BCR that no longer recognizes self. If this fails, the B cell will undergo clonal deletion.

anergy

If a B cell binds to a soluble antigen during development and it is not activated, then the B cell will probably enter a state of anergy – unable to be activated but not entering apoptosis either.

qualitative signaling hypothesis
An attempt to explain positive selection of a T cell; the affinity of the TCR → MHC:peptide is not the key but the nature of the peptide binding is. The best we can say at this time is perhaps an antagonistic peptide allows for partial activation which leads to MHC restriction and thus survival and entry to negative selection.

Part II

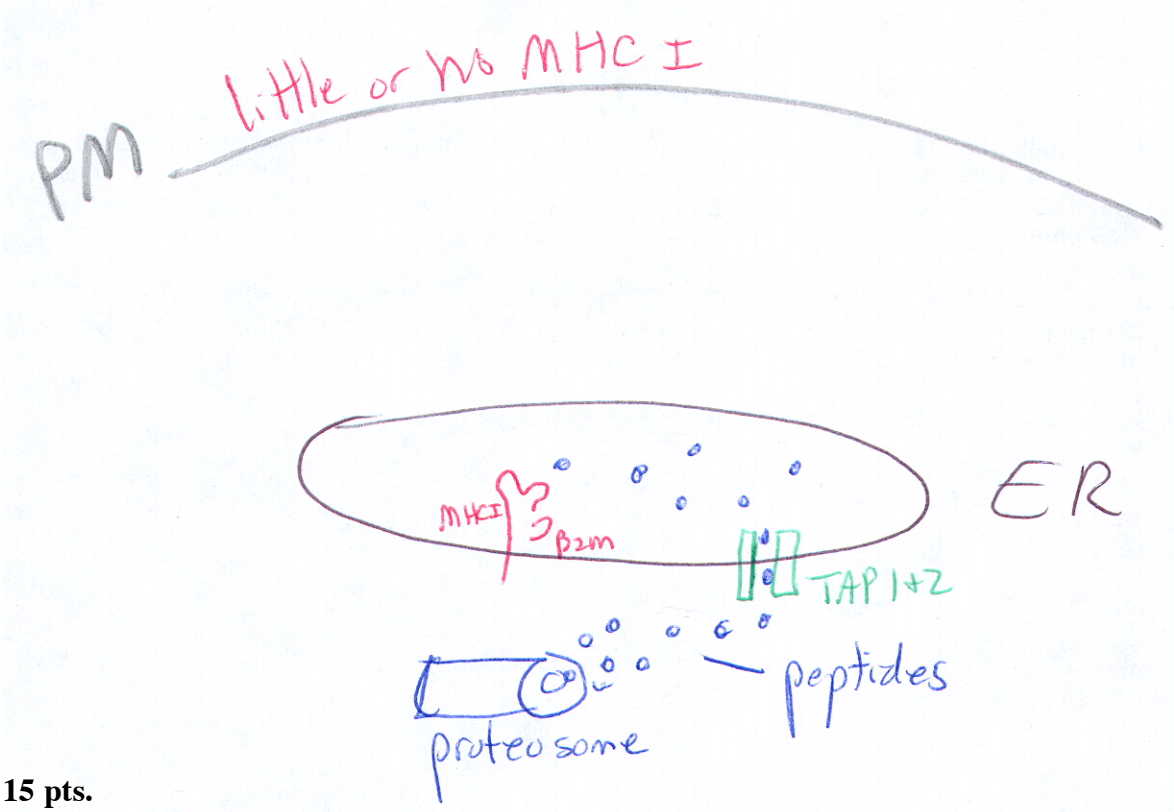
Many of these questions require you to synthesize a lot of information and put what you know into a single answer. Volume of words is not the best response. If you say something wrong, it will cost you points. Be concise and answer the question I have asked.

15 pts.

1) Draw a cross-sectional picture of a non-leukocyte cell that has no functional tapasin. Your picture should show:

a. MHC I in red
b. peptides in blue
c. ER in black
d. Plasma membrane in pencil

You may show any other IMPORTANT molecules/structures you want.



15 pts.

2) OUTLINE the steps of vaccination beginning with what you put in the syringe to the production of secreted antibodies. Include the major steps of our immune systems response. To make it easier for me to grade, everyone should generate a vaccine against the bacterium that causes plague (black death).

Bacterial protein + adjuvant injected

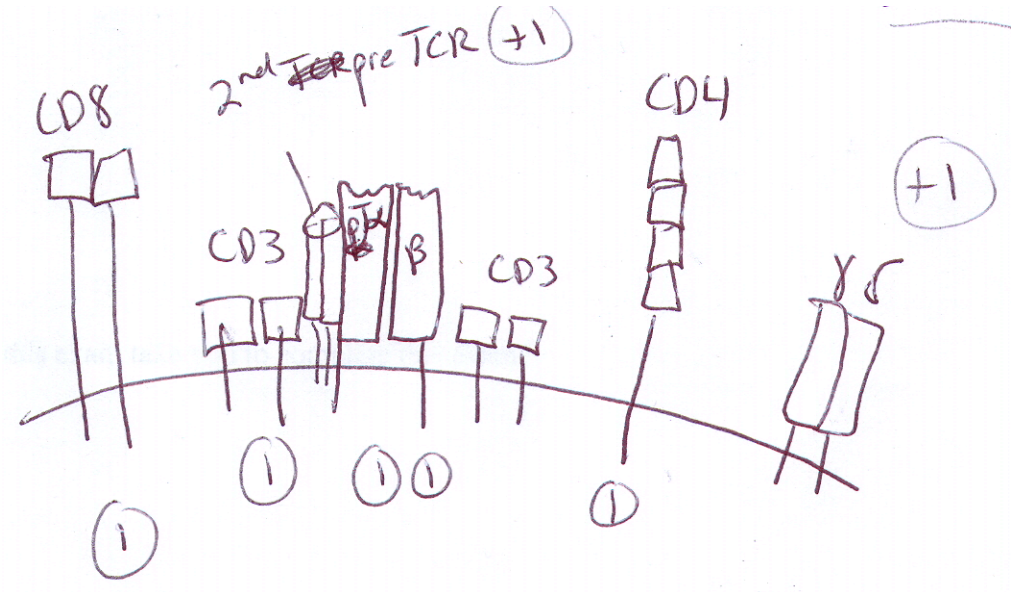
Protein engulfed by specific B cell or non-specific macrophage (I accepted either one and slight variation of answers depending on which you chose)
APC is activated by adjuvant/ innate immune response and produces costimulatory molecules.
MHC II presents peptides from the bacterial protein.
Th cell is activated if its TCR recognizes this peptide.
Th cell activates B cell that bound and presented the bacterial protein in MHC II; B cell divides.
B cell differentiates into effecter plasma cells and memory cells.
Antibodies are secreted (IgM and later IgG if isotype switching is induced).

15 pts.
3) Many anesthetics work because they block calcium channels. OUTLINE the signaling steps involved in T cell activation when the T cell is exposed to an anesthetic that blocks all calcium fluctuations, and where any of these pathways would be blocked.
TCRs are clustered and this leads to activation
Lck/Fyn kinases become activated and phosphorylate the many ITAMs on the TCR complex.
ZAP70 becomes activated; it is a kinase.
PLC-γ and GEFs become activated:
a. PLC cleaves PIP2 into IP3 and DAG.
i. IP3 leads to an increase of cytoplasmic calcium BUT THIS IS BLOCKED BY THE ANESTHETIC (therefore transcription factor NFAT is not activated)

ii. DAG plus calcium activates PKC which leads to the activation of NFκB; BUT THIS IS BLOCKED BY LACK OF ELEVATED CALCIUM.

b. GEF leads to the activation of small G proteins that lead to the activation of AP1, another transcription factor.

5 pts.
4) Draw a picture of a T cell surface when it first becomes double positive. Use colors as you see fit. Label all the proteins you want me to grade.



15 pts.

5) Explain the final T cell outcome for these experimental conditions:

a. Thymectomized mouse with MHC^{bxc} given donor thymus of genotype MHC^{c}.

Thy = MHC^{c}: APC = MHC^{bxc}

+ve selection on MHC^{c} and –ve selection on MCHbc

Immune system function because T cells restricted to MHC^{c} but also tolerant of MHC^{bxc}.

CD4+ and CD8+ T cells are present.

b. Male MHC^{d} mouse bone marrow injected into irradiated female MHC^{c} mouse.

Thy = MHC^{c}: APC = MHC^{d}

+ve selection on MHC^{c} and –ve selection on MCH^{d}

Immune system cannot function because thymus and APC have no MHC alleles in common. Furthermore, the T cells may reject the mouse (graft vs. host) because the –ve selection on MCH^{d} did not prevent anti-MHC^{c} alloreaction.

CD4+ and CD8+ T cells are present.

c. Transgenic mouse with mutated MHC I such that CD8 cannot bind to MHC I.

CD4+ T cells are present and working fine, but few if any CD8+ T cells would survive +ve selection.

d. MHC^{a} mouse has its HLA-DM mutated (mouse ortholog = H-2M).

CD4+ and CD8+ T cells are present. CD8+ Tc cells work normally. CD4+ cells are of limited variety in their TCR and reduced in number. There would be no abnormal self-reaction since all cells would present CLIP and anti-CLIP TCR would have been deleted during –ve selection.

Now, describe whether this organ transplants will work or not and explain your answer:

e. A mouse called Mickey is MHC^{b} has no bone marrow.

A mouse called Daffy is MHC^{a} and donates some bone marrow to Mickey.

A mouse called Tweety is MCH^{axb} and donates a kidney. Will the kidney transplant work?

No, the transplanted organ would be rejected, because

Thy = MHC^{b}: APC = MHC^{a}

+ve selection on MHC^{b} and –ve selection on MCH^{a}

Kidney is MCH^{axb} and the T cells would reject any cells that carried MCH^{b}

15 pts.

6) Explain what you would have to do to produce a vaccine that could cure the common cold virus but does NOT use antibodies to work. Include in your answer how a normal immune system would respond in order to produce an adaptive immune response.

Isolate DNA from a cold virus (ideally at least one conserved gene).

Insert DNA into any cells of the body (skin, fat, etc.)

MHC I would present the viral protein fragments

Perhaps inject IFN-γ at the same time to increase anti-viral responses, including MHC I presentation.
Tc cells would be activated to kill the vaccinated cells but would produce memory Tc as well.

3 pts. Bonus

Sometimes a bone marrow transplant leads to a graft vs. host rejection where the new lymphocytes attack the new body. Explain how this can happen based on what we have learned so far.

See the answer to question 5b above. –ve selection by an APC does not deplete alloreactivity from Tc that could bind to the rest of the body's MHCs.