Spring 2003 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, except for typing. You are not allowed to use your notes, or any books, any electronic sources, nor are you allowed to discuss the test with anyone until all exams are turned in at noon on Friday February, 28. **EXAMS ARE DUE AT NOON ON FRIDAY FEBRUARY 28**. The **answers to the questions must be typed on a separate sheet of paper** unless the question specifically says to write the answer in the space provided. If you do not write your answers on the appropriate pages, I may not find them unless you have indicated where the answers are. There is one question where you will have to use the internet. For this question only, you may use a browser but you may only go to the one site indicated in this test.
There are 3 pages to this exam, including the cover sheet.

When you are ready to take the exam, send me an email with the subject line of **Immunology Test**. This will generate an automated email telling you how to download the exam.

-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:

Average = 79.7%
Range = 45-100%
Points added = 11

Write out the full pledge and sign:
"On my honor I have neither given nor received unauthorized information regarding this work, I have followed and will continue to observe all regulations regarding it, and I am unaware of any violation of the Honor Code by others."

10 pts.

I. Define these terms: 1 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. However, note that unlike the first test, I will not be grading these as harshly since they are worth fewer points.

AIRE – transcription factor found in thymic epithelial cells that drives ectopic expression of proteins normally not expressed in thymic cells. Ectopic expression helps with negative selection of T cells.

tapasin – protein binds TAP1/2 with MHCI to help ensure loading of peptide fragments.

HLA-B53 – a particular allele of MHC I, gene B. Extra points if you remembered this was the allele that gave West Africans immunity to malaria.

toxic shock syndrome – illness caused by bacterial (*S. aureus*) production of a superantigen that binds to about 10% of TCR (CD4+):MHC II (APC) partners. Unrelated to peptide specificity of TCR.

SH2 – protein domain that binds to phosphotyrosines. SH2 domains are found on adaptor proteins and kinases used in cell signaling.

CD3 – complex of four subunits that form the full TCR. They have ITAM domains to help with signaling.

double positive thymocyte – CD4+/CD8+ T cells prior to positive selection. After pre-TCR and full TCR formed.

pT□ □ surrogate alpha chain used to form pre-TCR.

isotype exclusion – B cells express only □ or □ light chains, and never both.

CAD – caspase activated DNase that cleaves nuclear DNA into 200 bp pieces during apoptosis.

Part II

These questions are intended to be very large ones. Your answers should summarize a lot of information. I decided to see how you can integrate this information rather than breaking it up into smaller unrelated questions.

12 pts.

1) Explain how the tetanus vaccine works. Begin with what is injected and follow it through to the adaptive immune response. Do not address the issue of being re-exposed to tetanus toxin due to exposure after immunization. For your answer, please use an outline and/or pictures to show all the significant steps in this process. Do not address lymphocyte development or selection in this answer. Do not address details of signal

transduction either.
Your answer should have included the following:
a. toxoid plus adjuvant
b. BCR binds to toxoid
c. toxoid internalized by B cell
d. toxoid processed into peptides that are displayed in MHC II on B cell plasma membrane.
e. adjuvant activates B cell to act as a full blown APC.
f. CD4+ T cell can bind to MHC:toxoid peptide via TCR.
g. CD4+ cell receives first and second signals from APC (B cell).
h. CD4+ cell divides and differentiates into effector and memory T cells.
i. Th cell bind to B cell displaying toxoid peptide in MHC II.
j. B cell gets two stimulating signals from CD4+ Th cell and becomes activated.
k. B cell divides, becomes plasma cells and memory cells. Plasma cells secrete IgM.

12 pts.
2) Explain how a small pox vaccine works. Begin with what is injected and follow it through to the adaptive immune response. Do not address the issue of being re-exposed to the virus due to exposure after immunization. For your answer, please use an outline and/or pictures to show all the significant steps in this process. Do not address lymphocyte development or selection in this answer. Do not address details of signal transduction either.
Your answer should have included the following:
a. Cow pox/vaccina virus injected along with adjuvant.
b. virus infects APC (dendritic or macrophage)
c. virus makes proteins and APC presents peptides in MHC I.
d. CD8+ cell binds to APC via TCR and recognizes viral peptide.
e. CD8+ cell gets two stimulatory signals from APC -> becomes activated, divides, forms effector and memory cells.
f. Tc cell binds to any virally infected cell that displays recognized peptide in MCHI.
g. Tc kills infected cell via toxins, holes and FAS-induced apoptosis.

12 pts.
3) Make two flow charts or outlines to show how information flows from ligand binding to a BCR to the production of secreted IgA. Your answer should be divided into two halves. The first half is information from the outside to the inside. The second half is how the B cell responds to produce secreted IgA. For this question, assume the antigen stimulates a thymus-independent response. Remember to stick to the significant steps of signal transduction and antibody production. Start with a mature B cell and make all of your flow charts/outlines legible.
#1 BCR cross-links
kinases activated
G proteins loaded with GTP -> MAPK -> AP-1 transcription factor activated
Phospholipase C activated -> PIP2 cleaved into DAG and IP3
DAG -> Protein kinase C -> NFkB activated
IP3 -> Calcium increases -> NFAT activated via calcineurin
#2 B cell expressing IgM/D on surface

APC activates B cell,
cytokines secreted to induce isotype switching to IgA
alternative splicing permits membrane-bound and secreted forms of IgA to be produced

5 pts.

4) One way to treat someone with allergies is to inject them with the soluble allergy-producing antigen over a long period of time. Explain how this might lead to the reduction of an immune response.

One possible mechanism would be that excess soluble antigen would bind to BCR but not lead to cross-linking. Furthermore, in the absence of adjuvant, B cells would not be induced to become APC. Finally, we might expect that antigen in the absence of co-stimulation would lead to anergy and eventually loss of all allergy producing B cells.

34 pts.

5) Each year, Project Life raises money to tissue type people on campus. Imagine a donor has this genotype

A1 B1 C1 DP□1□1 DQ□1□1 DR□1□1□2
A2 B2 C2 DP□2□2 DQ□2□2 DR□2□4□3

while the recipient has this genotype

A3 B3 C3 DP□3□3 DQ□3□3 DR□3□5□6
A4 B4 C4 DP□4□4 DQ□4□4 DR□4□8□7

First, none of these alleles are shared between the donor and the host.

Part a: Explain what would happen to develop immature B cells if the donor's bone marrow were transplanted into the host and the host was first treated to kill all of the host's bone marrow. Begin your answer with a B cell that has a fully formed BCR and stop your answer once the B cell leaves the bone marrow, if that is possible.

B cells undergo + selection and survive if they have full BCR.
B cells undergo – selection and die if they bind to any self antigens. Self means any proteins produced by either host or donor cells.
B cells leave bone marrow if they survive these two rounds of selection.

Part b: Explain what would happen to developing immature T cells if the donor's bone marrow were transplanted into the host and the host was first treated to kill all of the host's bone marrow. Begin your answer with a T cell that has a fully formed TCR and stop your answer once the T cell leaves the thymus, if that is possible.

T cells leaves marrow and enters thymus.
T cells undergo + selection by binding to thymic (host) epithelial cells and thus are restricted to MHC^{3x4} alleles.
T cells undergo – selection and are deleted if they bind too well to any APC of MHC^{1x2} alleles.
T cells that survive these two rounds exit thymus.

Part c: Explain what would happen to the bone marrow recipient if he/she were infected with a virus 1 year after the bone marrow transplant. Start you answer after the virus has infected a particular cell and stop your answer

after the adaptive immune response, if that is possible.
Because there are no MHC alleles in common, the MHC^{1x2} APC cells cannot be recognized by the MHC^{3x4}–restricted T cells. Therefore, the patient has no adaptive immune response and the virus will never be killed unless the NK cells and innate immunity can, though this is unlikely.

9 pts.
6) a. Where does an anergic B cell die?
T cells zone of secondary lymphoid organs.
b. How/why does it die?
It dies due to programmed cell death that all lymphocytes have unless they get a survival signal. Anergic cells cannot be stimulated to survive, so they die by apoptosis in T cell zones.
c. Does the death of an anergic B cell differ from the death of the other 5×10^5 newly made B cells? Explain your answer.
This number indicates the B cells that exit bone marrow. They all will die without survival signal in the T cell zone since they are not able to compete for access to follicular dendritic cells which are the source of survival signals. So they too die by apoptosis due to lack of survival signal.

6 pts.
7) How are recirculating T cells kept alive? In other words, describe the interactions that mature but naïve T cells use to avoid apoptosis.
T cells receive survival signals from APC cells displaying MHC:peptide similar to the ones used for positive selection in the thymus. This is due to partial agonist or other similar mechanism.

+2 Bonus Points: Would a surviving T cell have more or less Bcl-2 than a T cell that fails positive selection? Explain your answer.
We might expect surviving T cells to have more Bcl-2 than T cells that fail positive selection since Bcl-2 blocks apoptosis.