

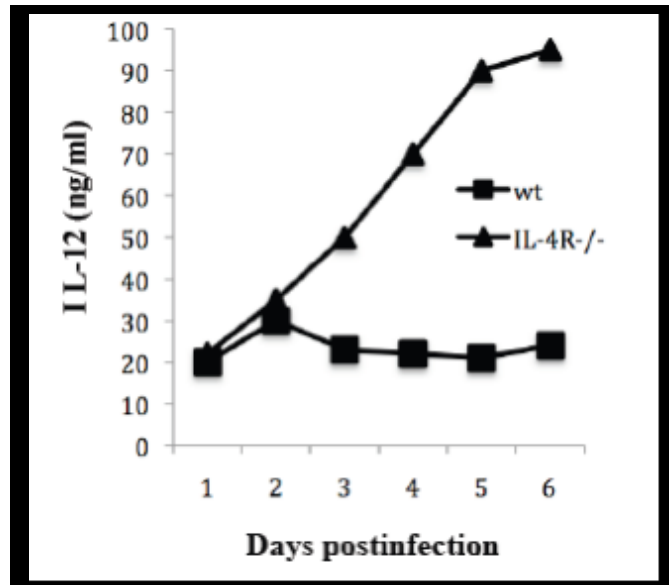
Student-written practice questions: Midterm 2

One of these questions will appear on the midterm. For the most part I have tried to stick with minimal editing for clarity, but note that your question may have an adjustment or addition that could affect the interpretation of the question. If you need to make assumptions to answer any question, make sure that you describe your assumptions!

1. In 2020, a group of scientists discovers a new virus called palinivirus. It is first isolated from a patient who suffers from a severe respiratory disease. One interesting feature of this virus is that a segment of its genome can encode an IL-4-like molecule, but the scientists are unsure whether the protein is expressed in host cells. To find the answer, the scientists infect a lethal dose of palinivirus into wild-type (wt) mice and mice deficient for IL-4 receptor (IL-4R^{-/-} mice). They monitor these mice daily for survival.

a. If this virus is able to express an IL-4-like molecule, which type of mice should be more resistant to the palinivirus infection? Explain your reasoning.

The scientists take lung fluids from wt mice and IL-4R^{-/-} mice daily after infection to determine levels of IL-12 over the course of 6 days. The result is shown below.



b. Does the result support the expression of viral IL-4 in mice? Explain.

2. Mouse ear thickness is sometimes used as a measure for immunological response to antigenic challenge. An increase in the thickness of the mouse ear is correlated to a T-cell response to an antigen. Deficiency of T cell response is correlated to little to no change in ear thickness. You have bred two mouse lines, the first with a defect in the gene for CD45RA, and the second is defective for CD45RO. CD45RA is found mainly on naïve T cells while CD45RO is found mainly on memory T cells.

a. What is the role of CD45 in T-cell activation?

b. What will be the difference in ear thickness as a measure of T-cell response between the CD45RA and CD45RO knockout mice upon primary exposure to an antigen? Upon secondary exposure?

3. Type 1 diabetes (juvenile diabetes) is an autoimmune disorder, in which the immune system attacks insulin-secreting pancreatic cells (beta cells). This attack damages and induces apoptosis of beta cells, obliterating insulin production. Researchers believe that enterovirus infections, like Coxsackie B4 virus (which causes German Measles) can lead to type 1 diabetes. You wish to study the link between Coxsackie B4, natural killer (NK) cells, and beta cell apoptosis. You use RAG-1 knockout mice (which do not produce B or T cells, but can still fight infection because they have NK cells).

a. Given that type 1 diabetes is a pancreatic disease, how would you test for beta cell apoptosis? If you were to use antibodies to test, what molecules would you link the antibodies to? What are your expected results?

Suppose you mix up your mice cages and accidentally infect both RAG-1 KO mice and regular mice with Coxsackie B4.

b. Propose an experiment to identify which mice are which (besides observing which one gets more sick). Make sure to describe both how you perform your experiment and what your expected results would be.

4. A group of Bolivian researchers have discovered a new disease (named "Blastastic" disease after the primary researcher) that causes excessive B-cell proliferation in infected Amazonian Howler Monkeys. The scientists interested in the disease immediately investigated infected monkey's production levels of IL-750, a cytokine known to be a principle player in Howler monkey B-cell proliferation.

a. Based on what we have learned about the human system, what role do you think IL-750 might play in Howler monkey B-cell proliferation?

After completing their experiments and looking at the levels of IL-750 in the diseased monkey populations, the researchers were dismayed to find that diseased individuals actual showed negligible levels of the cytokine.

b. Explain two possible ways how, in the absence of IL-750, B-cell proliferation could still occur at all.

c. Briefly outline an experiment to determine which of these two possibilities is actually occurring in Blastastic monkeys and describe your expected results for each possibility.

5. Grave's disease is an autoimmune disorder that results in over-activity of the thyroid gland. People with Grave's disease commonly suffer from severely enlarged thymus glands and [exophthalmos](#), or bulging of the eyes. Recent research has discovered a genetic link between Grave's disease and the CTLA-4 molecule, which is expressed on the surface of activated T cells. Studies have shown that an allele that codes for alanine at codon 17 of CTLA-4 results in susceptibility for Grave's disease.

a. Based on your knowledge of T-cell activation and costimulatory signals, why do you think CTLA-4 could play a role in Grave's disease?

b. Explain why CTLA-4 might be even more important in the presence of superantigens that are often secreted by many types of bacteria.

6. An 2-month old infant has been hospitalized with high fever, rapid heart rate and shallow breathing. The infant is diagnosed with acute bacterial sepsis. After prompt treatment with antibiotics, the infant's condition stabilizes. This individual has a history of recurrent infections. Hematological analysis also indicates severe hypogammaglobulinemia (low levels of serum Ig) as well as very low levels of T and B lymphocytes. Subsequent genetic analysis determines that the infant is heterozygous for a point mutation in one of the JAK genes in which a tyrosine is substituted with a valine.

Explain, biochemically, how the mutant JAK might lead to the observed immunodeficient phenotype.

7. You are in between grant proposals and are sitting around your lab with nothing to do. You put some old cheese in your mouse cage and leave. A little while later, you return to find that one of your mice is vomiting (you didn't even know mice could vomit, so this is surprising in itself). You realize the cheese was rotten, and you have given your mouse food poisoning. You believe that exotoxins secreted by *Staphylococcus* have made your mouse ill.

a. What is this staphylococcal toxin and others like it called?

b. Explain how this bacterial toxin inhibits your mouse's immune system.

c. If this toxin were a normal antigen, how could your mouse's adaptive immune system respond? Include one example of an adaptive immune response, from antigen binding or presentation to communication with other lymphocytes.

Another mouse in the cage took a bite out of the cheese as well, not learning from his friend's mistake. However, this mouse had been used in a previous experiment that knocked out his MHC class II expression.

d. Will this mouse fall ill as well? Explain why or why not.

8. You are studying an autoimmune disease characterized by severe inflammation caused by excessive and abnormal recruitment of T cells in the epithelia of the stomach. You are specifically interested in abnormal expression of ICAM molecules on the epithelial membranes.

a. Why are you interested in ICAM expression? How can it be related to T-cell recruitment?

b. Describe an experiment to determine whether the epithelia cells from an autoimmune patient express more ICAM cell surface proteins than a healthy person. You have cell cultures from autoimmune and normal person as well as a well equipped biochem lab and ICAM antibodies against conserved regions of the protein.

After much research you find that ICAM-1 is indeed upregulated in the cells from the autoimmune patient. Happy that you discovered the cause of the disease you share the good news with your research advisor, but she is skeptical. She says that you do not have enough information to know if the over-expression of ICAM 1 is the cause of the inflammation or the result of it.

c. How can T-cells change gene expression in nearby cells during inflammation?

d. How would you test if T-cell activity upregulates ICAM1 expression? Describe an experiment with appropriate controls. You have intestinal cell cultures from healthy and sick patients, ICAM1 antibodies, a modern Biochem lab and a choice of purified Th1 and Th2 specific cytokines. **Which ones would you choose for your experiment? Why?**