Written midterm exam: immunology (advanced topics)

Last Name :

First Name:

SIGNATURE :

IMPORTANT !!! **Include your name, the question number and page number at the bottom of each answer page**

- Total Time allowed = 1.5 hours
- The exam consists of questions worth a total of ? points
- Please respond directly on the exam for ALL Questions.
- For multiple choice questions simply circle the correct answer or indicate “t” for true or “f” for false. For short answers and essays you can use the extra sheets provided when more space is required. However please LABEL all sheets clearly with your name and the question number.

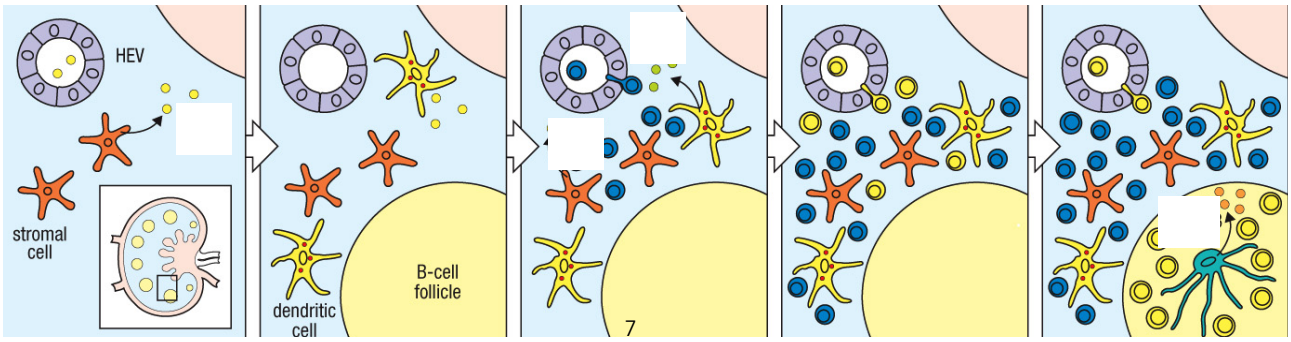
SECTION I_Open Questions

Question 1_(6 Points):
To mount immediate defense against pathogen, innate immune cells are equipped with so-called Pattern Recognition Receptors (PRRs). Give 3 examples of microbial substances recognized and name the receptors for these substances?

Question 2_(4 Points):
Phagocytosis is a critical mechanism through which pathogens are eliminated. Give examples of a phagocytic cell type and explain how this cell type ingests and kills microbes!

Question 3_(4.5 points):
Epithelial surfaces bear potent antimicrobial functions. Enlist three examples on mechanisms involved in this function of epithelial surfaces!

Question 4_(4 points):
Briefly explain based on the scheme below how T cells and B cells are guided to their specific location within lymphnodes at stead-state (that is in the absence of an infection)! What molecules play a role during this process?



Question 5_(3 points):
Dendritic cells are key in priming naive T cells. What key signals are necessary to prime T cells?(Short answer)

Question 6_(8 points):
Regulatory T (T_{regs}) cells are important to control and balance immune response. Explain two mechanisms on how T_{regs} can be induced! How do regulatory T cells dampen immune responses?

Question 7_(6 points):
Activation of B cells by T cells follows a concept referred to “linked” recognition. Briefly explain the basis for this concept! How is “linked” recognition applied in vaccine design?

Question 8_(6 points):
Draw a schematic of an IgG antibody and name the major parts. What regions of antibody molecules are involved in the functions of antibodies? Indicate in your drawing the localisation of the CDRs!

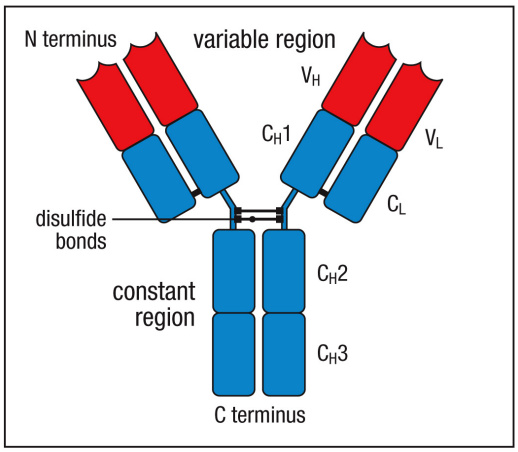


Figure 4.1c Janeway's Immunobiology, 9th ed. (© Garland Science 2017)

SECTION II_Multiple Choice Questions_(2 points per question)

Multiple Choice 1_ The Complement System
Indicate which of the following statement(s) is/are **TRUE**!
a) The complement system is a composition of several soluble proteins
b) An important effector function of the complement system is to trigger an inflammatory response
c) There are 2 major pathways of complement activation
d) Complement can enhance the phagocytosis of bacteria
e) Deficiency in factors of the complement system increases resistance to bacterial infection

Multiple Choice 2_Cytotoxic T cell-triggered apoptosis
What is **NOT** considered as a hallmark of apoptosis:
(a) Membrane blebbing
(b) Activation of caspase proteins
(c) Fragmentation of DNA
(d) Formation of membrane pores

Multiple Choice 3_Effector T cells
What of the following assignments is **NOT** correct?
a) T_H1 cells - IFN-ɣ
b) T_H2 cells - IL-4
c) T_H2 cells - IFN-α
d) T_H17 cells - IL-22
e) $T_{Reg}2$ cells - IL-10

Multiple Choice 4_ Antibodies (AB)
Indicate which of the following statement(s) is/are **TRUE**!
a) The affinity and avidity of an AB is always identical
b) AB can bind to pathogens and prevent them from infecting cells
c) AB can mark pathogens and enhance phagocytosis
d) IgM AB is the isotype most abundant in the serum of humans
e) AB are produced by plasma cells and plasmablasts

Multiple Choice 5_Initiation of humoral responses by B cells
What of the following statements is **NOT** correct?
a) Naive B cells do not require co-stimulatory signals
b) Protein AGs are considered to dependent on T cell help
c) Polysaccharide AGs can induce B cell activation in the absence of T cell help
d) An important co-stimulatory signals is CD40L expressed by T cells

Multiple Choice 6_AG presentation
What of the following statements is **NOT** correct?
a) MHC class II molecules present peptides that are generated by macophages and DCs
b) Cross-presentation is the presentation of endogenous AGs by MHC class I molecules
c) MHC class I molecules are found on almost all cell types
d) MHC class II molecules are blocked by Clip so to prevent binding of endogenous AGs in the endoplasmic reticulum

SECTION III_Analysis and interpretation of primary research findings

Type I interferons (IFNs) are crucial cytokines in host defense against viral infection. Multiple mechanisms have been identified through which type I IFNs promote host resistance and block viral replication. The following model and figure is extracted from a a preview and a paper, which described a new function on how type I IFNs promotes antiviral T cell immunity. Briefly, it is shown that type I IFNs act on T cells to trigger the expression of inhibitory NK-cell-receptor ligands. Consequently, T cells are more resistant to NK-cell mediated killing and, thus, it is concluded that type I IFNs protect T cells against regulatory NK cell function.

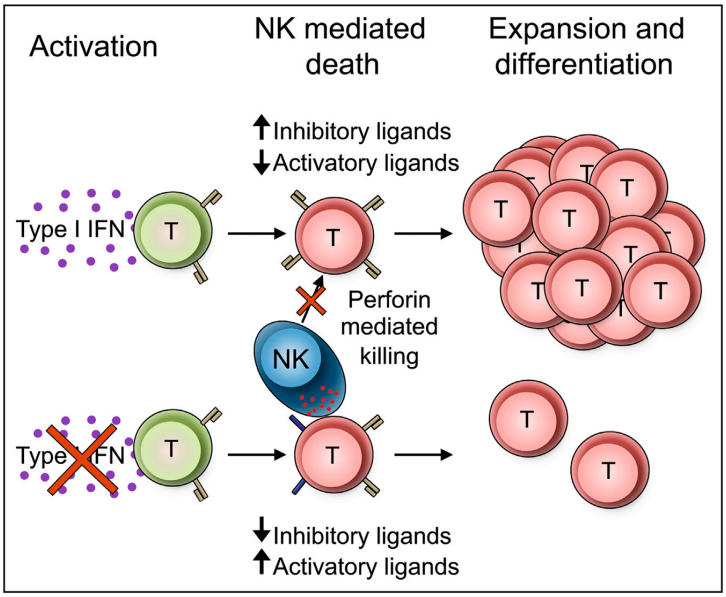
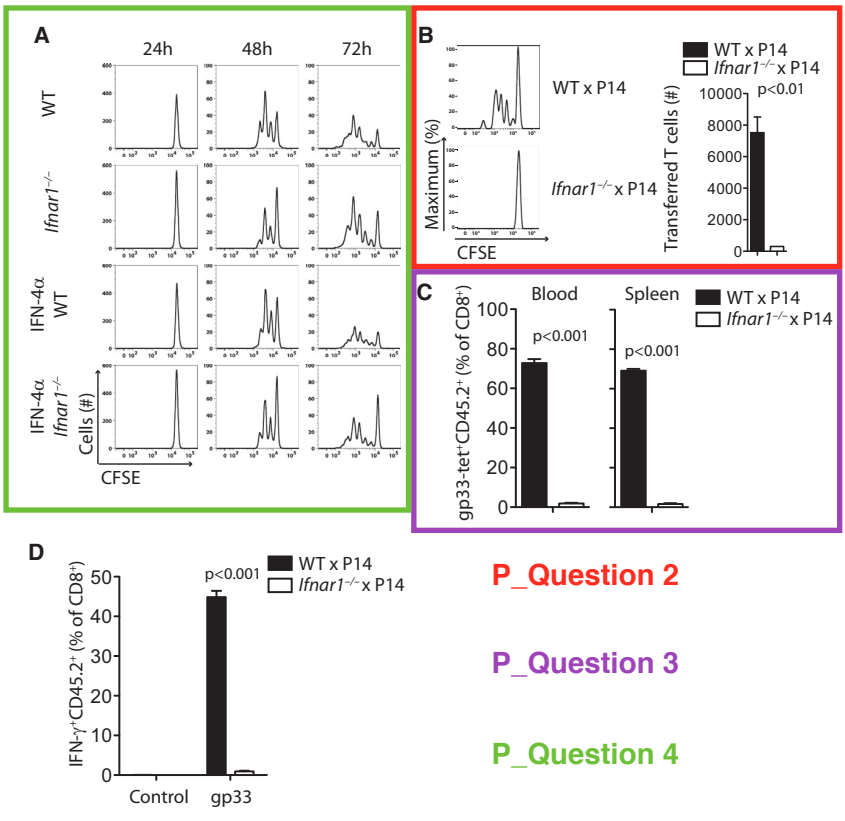


Figure 1. Type I IFN Signaling Protects Activated T Cells from NK-Cell-Mediated Death
Type I IFN signals to antigen-activated T cells reduce the expression of NK cell activatory ligands and elevates the levels of inhibitory ligands, rendering the responding T cell resistant to NK cell attack. Without type I IFN signals, activated T cells can be targeted by perforin-dependent NK cell killing.



P_Question 2

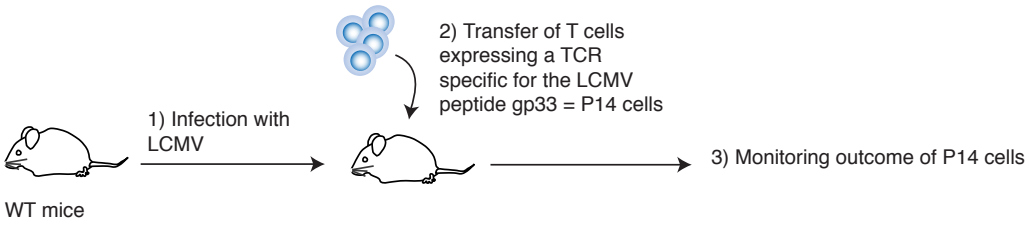
P_Question 3

P_Question 4

Figure 1. IFN-I Affects T Cell Immunity In Vivo
(A) Negatively sorted CFSE labeled CD8$^+$ T cells from WT and IFNAR1-deficient animals were stimulated for 24 hr (left panels), 48 hr (middle panels), and 72 hr (right panels) with anti-CD3 antibody in presence or absence of IFN-4α (50U/mL, one representative of n = 6 is shown).
(B) CD45.1$^+$ animals were infected with 200 pfu LCMV WE. 10^6 negatively sorted CFSE labeled T cells from P14$^+$ WT and *Ifnar1*$^{-/-}$ mice were transferred into infected CD45.1$^+$ mice 2 days postinfection (p.i.). At day 4 p.i., CFSE expression on T cells (left panel) and cell number of transferred cells was analyzed (right panel, error bars show SEM; n = 3, one of two independent experiments is shown).
(C and D) Prior to infection, 10^5 negatively sorted T cells from P14$^+$ or P14$^+$*Ifnar1*$^{-/-}$ animals were transferred into CD45.1$^+$ mice. (C) Gp33-tetramer$^+$CD8$^+$CD45.2$^+$ T cells were determined in the blood (left panel) and in spleen tissue (right panel) 8 days p.i. (percentage of CD8$^+$ cells, error bars show SEM; n = 5) (D) IFN-γ^+CD8$^+$CD45.2$^+$ cells were measured after restimulation with the LCMV epitope gp33 8 days p.i. (percentage of CD8$^+$ cells, error bars show SEM; n = 5).
(E) We stimulated 2 × 10^6 negatively sorted CD8$^+$ T cells from WT and *Ifnar1*$^{-/-}$ mice in vitro with anti-CD3 and anti-CD28 antibodies for 72 hr followed by injection into CD45.1$^+$ animals. Two days following infection with 200 pfu of LCMV WE, transferred T cells were measured in spleen tissue (error bars show SEM; n = 3–4, one of two independent experiments is shown).

P_Question 1_(6 points):
A critical role in antiviral immunity is taken over by type I IFNs. What cells produce type I IFNs upon viral infection? Give an example of a mechanism on how type I IFNs promote viral eradication!

P_Question 2_(3 points):
In Figure 1B the authors take advantage of T cells that recognize a specific viral LCMV peptide (P14 cells). They inject these antigen-specific T cells into mice after infection with LCMV (See illustration below). What happens to the T cells in case they do not express the type I IFN receptor?



P_Question 3_(6 points):
In Figure 1C the authors attempt to measure the proliferation of antigen-specific T cells (P14 cells). For this a tetramer-approach is used. Briefly, explain the concept of tetramer staining! How does the absence of type I IFNs influence the proliferation of AG-specific T cells?

P_Question 4_(2 points):
In Figure 1A it is shown that in vitro (!) there is no difference in the proliferation of T cells in the presence or absence of type I IFN signaling. However there is an observed difference in vivo. Generally, what could be a possible explanation for this discrepancy? Along these lines, what could be an important control experiment that should be done to conclude that absence of type I IFN on T cells blocks their proliferation upon AG encounter in vivo?

P_Question 5_(6 points):
The authors go on to show that type I IFNs up-regulate the expression of inhibitory NK-cell receptor ligands! What are inhibitory NK cells ligands? What is their mechanism of action? What is their biological significance?