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**Multiple choice questions (each question is 2 points). Choose the most correct answer.**

1. A person is stung by a bee and experiences serious respiratory problems within minutes. This process is most likely mediated by:
  - a. IgG antibodies
  - b. IgE antibodies
  - c. IgM antibodies
  - d. NK cells
  
2. Which statement is most correct?
  - a. The MHC is polygenic and evolved 250.000 years ago.
  - b. The MHC regulates innate immune responses and is polymorphic
  - c. The MHC is present in Fruit flies and regulates antibody responses
  - d. The MHC is polymorphic and evolved about 450 million years ago
  
3. Most chimpanzees are naturally resistant to AIDS because
  - a. they have a skewed MHC class I repertoire
  - b. CD4 molecules on chimpanzee T cells evolved resistance to SIV infection
  - c. they have autoantibodies that provide resistance to SIV
  - d. they are homozygous in CCR5 deletions that also in humans provide resistance to HIV infection.
  
4. Which statement is most correct?
  - a. The thymus is involved in regulating central tolerance
  - b. The spleen is a primary lymphoid organ
  - c. T cells rearrange their receptors in the bone marrow
  - d. MHC class II molecules preferentially bind peptides from intracellular pathogens.
  
5. Which of the following characteristics is common to both T-cell receptors and immunoglobulins?
  - a. Somatic hypermutation changes the affinity of antigen-binding sites and contributes to further diversification.
  - b. Class switching enables a change in effector function.
  - c. The antigen receptor is composed of two identical heavy chains and two identical light chains.
  - d. Somatic recombination of V, D and J segments forms the basis for the diversity of antigen-binding sites.

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6. Which is the most likely reason that HIV-infected people with heterozygous HLA loci have a delayed progression to AIDS compared with patients who are homozygous at one or more HLA loci?
- The greater number of HLA alleles provides a wider variety of HIV-derived peptides presented to CD8 T cells even if HIV mutates during the course of infection.
  - Heterozygotes have more opportunity for interallelic conversion and can therefore express novel MHC alleles.
  - Being heterozygous in HLA helps selecting a partner that is not HIV infected.
  - As heterozygosity increases, so does the concentration of alloantibodies in the serum, some of which cross-react with and neutralize HIV.
7. Why are lymphocytes so specific?
- to recognize many different pathogens
  - to avoid apoptosis during self tolerance
  - they are not specific, they are crossreactive
  - to increase the affinity of each immune response.
8. What is the best explanation for the immunodominance ranking within a host?
- some clones proliferate faster than others
  - some clones die less than others
  - some clones start with more naive cells than others
  - none of the above.
9. What is the advantage of having a low diversity of MHC molecules per individual?
- too many MHC molecules would delete too many T cells by negative selection
  - too many MHC molecules would select for an autoreactive repertoire by positive selection
  - too few MHC molecules would select a too narrow repertoire.
  - the diversity in a host is not low because of the MHC polymorphism.
10. IgM and IgD are co-expressed on naive B cells by a process called:
- isotype switching
  - somatic recombination
  - somatic hypermutation
  - alternative mRNA splicing
11. What would happen if the cell surface IgM on an immature B cell binds a multivalent self antigen in the bone marrow?
- B cell reduces the amount of IgG on its surface.
  - B cell undergoes somatic hypermutation.
  - B cell rearranges its light-chain genes.
  - B cell dies immediately.

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**12.** Which one of the following cells is not crucial for making a germinal center reaction?

- a. naive B cells
- b. T cells
- c. Macrophages
- d. Follicular dendritic cells

**13.** Which of the following is not used by the herpes simplex virus to subvert host immune responses?

- a. a virus-encoded complement receptor
- b. inhibition of MHC class I expression
- c. inhibition of peptide transport by the transporter associated with antigen processing (TAP)
- d. inducing apoptosis of activated T cells

**14.** In order to be able to use tumor infiltrating lymphocytes as a possible cure for cancer, we need to identify:

- a. An antigen that is I) derived from a tumor specific mutations, II) also expressed on normal tissue, III) recognized by the B cells of the cancer patient;
- b. An antigen that is I) derived from a protein that is overexpressed within the tumor, II) exclusively expressed on tumor tissue, III) is not recognized by the T cells of the cancer patient;
- c. An antigen that is I) derived from a tumor specific mutations, II) exclusively expressed on tumor tissue, III) recognized by the T cells of the cancer patient.

**15.** Which of the following statements is wrong?

- a. Naive T cells in human live longer than memory T cells.
- b. Naive T-cell production in mice is almost completely due to thymic output.
- c. Naive T cell production in humans is almost completely due to thymic output.
- d. Memory T cell production in humans is almost completely dependent on the thymic output.

**16.** The primary function of the transcription factor AIRE is to:

- a. facilitate apoptosis of self-reactive B lymphocytes in the bone marrow
- b. activate the expression of tissue-specific proteins in the thymus
- c. activate regulatory T cells
- d. regulate antigen presentation in DCs

**17.** Which of the following describe the characteristics of KIRs?

- a. They are expressed in all vertebrates as functional genes.
- b. They are inhibitory receptors of NK cells.
- c. They bind to complexes of leader sequences of HLA-A, -B, and C heavy chains bound to HLA-E.
- d. They are polygenic and polymorphic.

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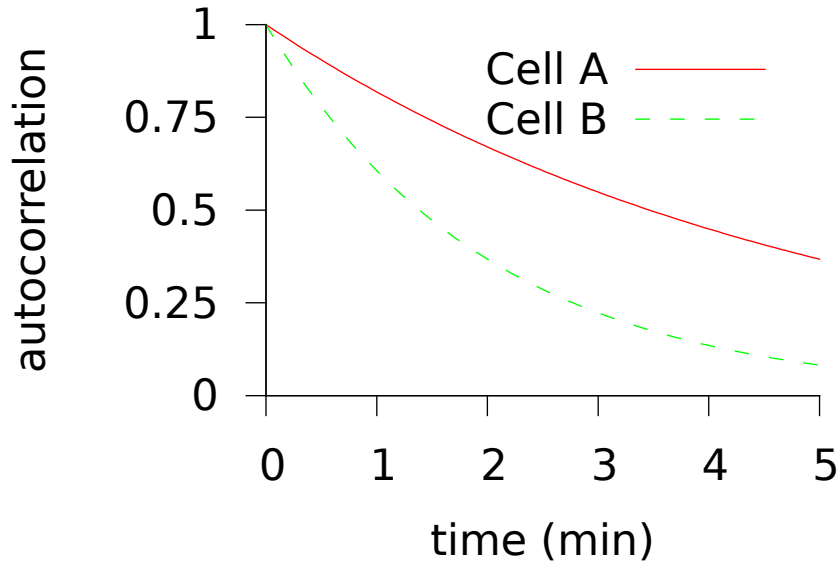
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18. The average number of T-cell receptor excision circles (TRECs) per  $CD4^+$  T cell in HIV patients is typically lower than in healthy age-matched controls. What is the most likely explanation for this finding?

- a. HIV reduces thymic output.
- b. HIV increases T-cell proliferation rates.
- c. HIV increases T-cell death rates.
- d. HIV infection induces naive T cells to become memory T cells.

19. What can you conclude from the plot below? Reminder: In the lecture, we defined the autocorrelation function  $a(t)$  as the average correlation between cell directions time  $\Delta t$  apart.

- a. Cell A turns more often than cell B.
- b. Cell A moves faster than cell B.
- c. Cells A and B move in different directions.
- d. Cell A has a straighter track than cell B.



20. Which of the following properties is common to macrophages and neutrophils?

- a. life span
- b. anatomical location
- c. ability to phagocytose
- d. morphology

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**Short questions:**

**1.** (7 points) Make your own multiple choice question on dendritic cells and answer the question. The question should have four (might also be five) possible answers, and the quality of the question and the multiple choice answers matter.

**2.** (7 points) What are the different immunoglobulin isotypes (name at least three)? For every subtype mention one physical property (structure, size, function, serum level, half life etc) that is unique to this subtype.

**3.** (7 points) Do female mice reject male skin grafts? Why? or Why not? Answer in max. 3 sentences.

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4. Indicate whether the following statements are true (T) or false (F). Each question is 2 points:

- NK cells can show memory like behaviour.
- Plasma cells generated in a secondary immune response have longer life-spans than those made during a primary immune response.
- Peptide-MHC complexes serve as ligands to T cells only.
- Gene rearrangement can, theoretically, generate upto  $10^8$  different TCRs.

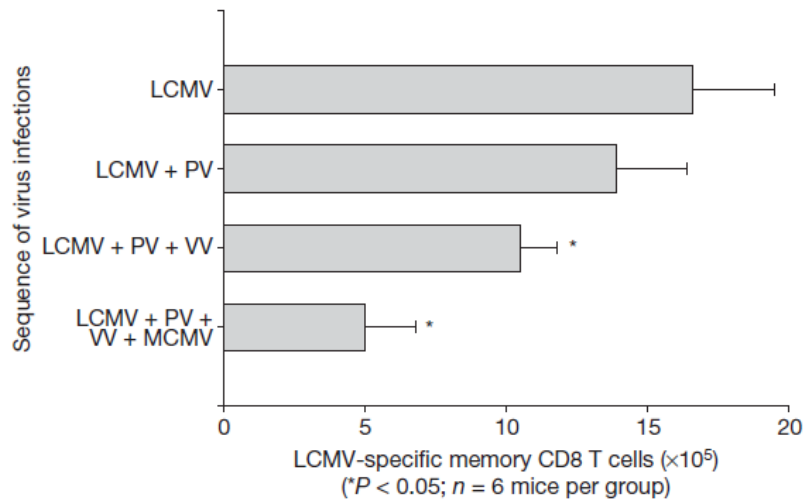
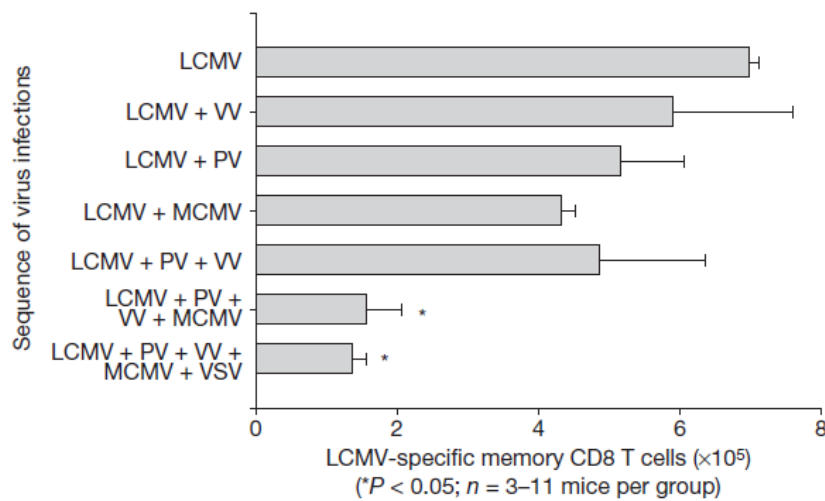
5. (7 points) Explain why a genetic deficiency of C3 leads to severe immunodeficiencies.

6. (7 points) Give one reason (at most three sentences) why naive T cells move between different lymph nodes.

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7. (17 points) The below figure is taken from the short discussion article "Attrition of memory CD8 T cells" by Raymond M. Welsh & Liisa K. Selin, Nature 459, E3-E4 (4 June 2009). Attrition means here "loss". Which conclusions would you draw from these results? What could be the mechanism causing this effect? Explain in max. 5 sentences.



Total numbers of lymphocytic choriomeningitis virus (LCMV)-epitope-specific CD8 T cells per spleen in mice immune to LCMV and subsequently infected with Pichinde virus (PV), vaccinia virus (VV), murine cytomegalovirus (MCMV) or vesicular stomatitis virus (VSV). Data are reworked from refs 3 and 4. These are controlled experiments in which all measurements were taken at the same time after LCMV infection. **a**, Attrition of LCMV-specific memory cells as measured by limiting dilution assays after sequential virus infections. **b**, Attrition of LCMV-specific memory cells as measured by MHC-dimer or intracellular IFN- $\gamma$  assays after sequential virus infections. Combined frequencies of T cells specific to LCMV-encoded epitopes NP396, GP33/34 and GP276 (GP, glycoprotein; NP, nucleoprotein).