ImmunoBiology, July 1, 2011 Naam: Collegekaartnummer:

Question 1 (45 pnts):

Make sure that your answers are as short as possible.

a) What is the function of KIR molecules? Explain two different selection pressures playing a role in the evolution of human KIR genes.

b) Name four main antibody isotypes and their functions. Shortly explain what isotype switching is, where it takes place, and how it is regulated.

c) Explain the main mechanisms responsible for T cell tolerance to self. What is the role of regulatory $CD4^+$ T cells in self tolerance?

d) Name three reasons why a memory B cell response clear antigens faster than a primary B cell response.

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Question 2 (30 pnts):

Write a short essay (at least half a page, max. one page) on diversity in the immune system. Make sure that you cover the following list of concepts: MHC molecules, KIR molecules, V-D-J recombination, B cell receptors, T cell receptors, specificity, RAG, and evolution.

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Question 3 (25pnts):

The below figure is taken from the article by Nakanishi, et al. *Nature* **462**, 510-514 (Figure S2, November 2009).



Supplementary Figure 2 (modified from the original).

gBT-I T cells are CD8⁺ T cells with a transgenic T cell receptor (i.e. all cells are expressing the same T cell receptor) specific for one epitope of the herpes simplex virus (HSV). 100,000 naïve gBT-I cells were transferred into either WT (wild type) mice or mice deficient in CD4 T cells (CD4^{-/-} mice). One group of WT recipient mice was injected with anti-CD4 depletion antibody at days -4, -2 and 2 post infection. Recipient mice (n=5 per group) were infected intravaginally with HSV. The number of gBT-I cells within each tissue at 7 days after infection were determined by FACS (error bars indicate the standard deviation, and the height of the bars give the mean values). These experiments were repeated four times, where similar results were obtained (results not shown). Statistics were determined by unpaired two-tailed t-test; *: p<0.05; **: p<0.01.

a) Which conclusions would you draw from these results?

b) An important cytokine procuded by CD4⁺ T cells is IFN- γ . How would you proceed in the experimental system of Nakanishi, et al., to study the role of IFN- γ in the results shown above?