**MCIM 321 Assignment #4 for December 2, 2020**

Please formulate your answer in the space provided, and employing about the same size font. This assignment is open-book and should be delivered by email to me by noon, Nov Dec 2. The assignment covers sessions 1-26, with emphasis on sessions 20-26. The purpose of these assignments is to help you study and understand the material in a focused way. All questions have equal weight. The small space for answering questions is to help you formulate your own answers in your own words in a concise fashion, rather than pasting from the notes!! Actually, expressing the correct ideas succinctly is a very good sign of your understanding of what is important. I will try to assess, in the marking, whether I think you understand what you write in your answers.

These questions are a bit more challenging than in previous assignments. I am open to receiving questions pertinent to this assignment. If I decide to “help” anyone, I will give the same help to all by including the question and the “help” in a Q & A posting. Each question is worth 10 points, and there are 20 potential bonus points to encourage you to be imaginative and brave!

1. In session 20, an experiment is described (Figure 2) in which mice were generated by giving irradiated A strain mice bone-marrow stem cells from AxB mice, where A and B MHC antigens are different. The immune systems of these mice were allowed to regenerate over a period of 2 months. These mice were now grafted with skin from B strain mice, which was rejected in about 45 days. The researchers concluded that the skin of B mice was regarded as foreign and therefore the skin has antigens unique to it, not encountered by the AxB lymphocytes that developed in the irradiated A mice. Some immunologists are discussing this classic experiment over morning coffee. Some claim that to get this rejection the alleles coding for the “skin antigen” must be different in strain A and B strain mice, whereas other maintain this is not the case. Who is correct and why?
2. Why is it that most T cells can only “recognize” protein but not carbohydrate antigens? It has been discovered that antibody responses to carbohydrate are often very poor or non-existent, but can be considerably improved if the carbohydrate antigens are coupled to a protein carrier. Explain why.
3. We have discussed how the interaction of an anti-hapten B cell (anti-h) with a T helper cell specific for a protein carrier C, requires the presence of the hapten linked to the carrier, ie of h-C, but this interaction does not take place in the presence of h-Q and C, where Q and C are not cross-reactive. In others words, the cellular interaction requires not only the presence of h and C but that they are linked. However, we know that the antigen-specific receptors of T helper cells do not recognize the intact protein, but peptides of the protein bound to class II MHC molecules. Assume, as is most often the case, that the peptide of the peptide/MHC complex recognized by the T cell receptor is not haptenated. How can we explain the finding that the interaction of the anti-h B cell and C-specific Th cell only occurs when the hapten is linked to C, when C must be processed into small peptides “c”, unconjugated with h, before the receptor of the Th cell can recognize its ligand? It would appear the linkage must be destroyed before the peptide MHC complex can be formed that the Th cell recognizes.

1. It turns out that mice, given a prolonged and substantial exposure to a protein antigen through their drinking water, produce IgA antibody to the antigen. Such mice are unable to produce IgG2a antibody to a subcutaneous challenge of the antigen that results in the production of such antibody in age-matched but naïve mice. Design an experiment to test the idea that this unresponsiveness is due to the generation of suppressor T cells that inhibit the induction of such Ig2a antibody. You may assume such suppressor cells, if the exist, are present in the spleen of the “suppressed” animal.

Questions 5 & 6:

We have seen in class the central role T helper cells play in initiating immune responses and the class of immunity induced. We discussed two main models for how antigen interacts differently with naïve CD4 T cells to activate or inactivate them: the DAMP/PAMP model, according to which a PAMP-dependent signal, or a danger (danger associated molecular pattern-DAMP)-dependent signal is required for activation, and where, in the absence of such a signal, antigen inactivates the CD4 T cell. The alternative model is the CD4 T cell cooperation model, according to which the activation of the CD4 T cell requires antigen-mediated CD4 T cell cooperation and where, in its absence, the CD4 T cell is inactivated. Q 5 is: what are the most compelling arguments for the DAMP/PAMP model? There will be 10 bonus points for reasonable considerations NOT discussed in class. Q 6 is: what are the most compelling arguments for the CD4 T cell cooperation model? There will be 10 bonus points for reasonable considerations NOT discussed in class.