HST.176 – Sample Final Exam

Please answer all questions. Be brief and to the point.

Question 1

a) In mice that lack CD40L, as well as in boys with the X-linked hyper-IgM syndrome, a deficiency in cell mediated immunity is observed. Pneumocystis carinii pneumonia is a common presentation in patients. Why does the absence of the CD40L lead to a defect in CMI (5 points)?

b) Explain with the aid of a diagram (showing what you know of the pathway involved) why a homozygous hypomorphic mutation in IKK- (I B kinase, also known as NEMO) might contribute to a hyper-IgM like syndrome (10 points).

c) Children born with mutant AID develop a hyper-IgM like syndrome and fail to generate high affinity antibodies. What is the mechanistic basis for AID's presumed role in somatic mutation (10 points)?

Question 2

Superantigens can bind to a large number of V regions on TCRs and simultaneously also associate with MHC class II molecules on APCs (see figure). A typical superantigen may crosslink MHC class II molecules to TCRs on as many as 5-20% of all CD4 T cells (which all share a subset of V domains). Superantigens are distinct from "normal" antigens and they do not bind to the class II groove. They bind to structural determinants on class II molecules and framework determinants on specific V proteins, and can bypass the need for costimulation.

a) In the Toxic shock syndrome caused by the TSST1 toxin from S.aureus, TSST1 has been demonstrated to be a superantigen that causes high fever, shock, and a diffuse erythematous rash. It can be life-threatening. Given the above information, what do you think (in one or two sentences) is the pathogenic basis of this syndrome? (5 points)

b) A superantigen that binds to V 4 and V 11 containing murine TCRs was expressed transgenically in mice. Transgenic mice are viable. You are given monoclonal antibodies to all 20 murine V family proteins (V 1 to V 20). Do you expect to see any differences in the immune system between transgenic and non-transgenic mice? Explain in no more than one sentence (5 points).

c) Explain briefly the function of HLA-DM (5 points).

Question 3

What is granzyme B's substrate specificity (5 points)? What exactly are caspases? (5 points). The cation-independent mannose-6-phosphate receptor (CI-M6PR) is a protein that can function as a cell surface endocytic receptor and the gene for this protein is frequently deleted in tumors. It is a tumor suppressor - loss of both alleles favors tumor progression. Why do you think loss of CI-M6PR favors tumorigenesis? (No more than two sentences please) (5 points).

Question 4

Describe in a point-by-point manner three ways in which certain proteins in tumors might be recognized as tumor antigens by host T cells (10 points).

Question 5

Describe how cyclosporin A interferes with cytokine gene transcription (10 points).

Question 6

a) Direct immunization with plasmid DNA of bacterial origin induces immune responses. Assuming that the plasmid DNA is endotoxin-free, mention how you think "danger" is signaled by DNA of bacterial or plasmid origin (5 points).

b) How do signal one and signal two cooperate in the cytosol and nucleus to induce IL-2 transcription during T cell activation? Please be brief (5 points).

Question 7

Where is AIRE expressed and what is it's presumed function? (5 points)? Why do you think patients with AIRE mutations develop recurrent mucocutaneous candidiasis (5 points)?