Q1. Immunotherapy for cancer treatment is being experimentally developed. Tumors are most effectively eliminated through T cell mediated immune responses. Researchers have recently identified many different tumor antigens.  
A. What types of tumor antigens would make good vaccine candidates? Why?  

B. For many cancers there are still no identified tumor antigens. Describe either an immune based or mechanism based therapy that could be used on these tumors (that is not slash/burn/poison)?  

C. Researchers have developed mechanisms to manipulate the costimulation signal required for T cell activation. Why would this be beneficial for anti-tumor immunotherapy and how would you attempt to alter costimulation to boost anti-tumor immune response?  

Q2. Specific MHC alleles are often linked to specific autoimmune diseases. The risk of developing a specific disease such as Type I Diabetes Mellitus may be 5 to 10 fold higher than “average” in the presence of such an allele,  
A. What does the association of a disease with a particular MHC allele tell you about potential mechanisms underlying such a disease?  

B. Even in the presence of the disease-associated MHC allele, only a fraction of individuals develop the diabetes. What does this fact tell you about the cause of the disease?  

Q3. Hepatitis A virus (HAV) is an RNA virus, Hepatitis B virus (HBV) is a DNA virus, and Hepatitis C virus (HCV) is a RNA virus. All three viruses are from different families and have little or no genetic homology yet all three can replicate in hepatocytes and cause liver disease.  
A. Both HBV and HCV can result in chronic infections and liver cancer (hepatocellular carcinoma). How could these viral infections cause cancer?  

B. The primary HBV vaccine is a recombinant protein vaccine consisting of the HBV surface antigen. Normally this vaccine results in the production of antibodies but occasionally is able to elicit CTLs. Why is this unusual? Explain how this vaccine could elicit CTLs.  

Q4. Liver transplants in humans are much more readily rejected than liver tumors (hepatomas) which are often unnoticed by the immune system.  
A. What types of immune responses are elicited by both transplanted liver tissue and sometimes against hepatomas (what is common between them)?  

B. Hepatomas often do not elicit a strong immune response whereas liver transplants are rejected without chemical immunosuppression. Why is the immune rejection response so vigorous to transplanted solid organs and less vigorous to tumors (what is different between the immune response to transplants and tumors)?
**Q5.** Multiple sclerosis (MS) is a human autoimmune disease that involves destruction of the myelin sheath and results in neurological symptoms. The animal model of this disease is called Experimental allergic encephalomyelitis (EAE). The primary autoantigen in both MS and EAE is myelin basic protein.

**A.** In the EAE animal model mouse myelin basic protein (MBP) is injected with oil and bacterial cell components. The immune responses to MBP in EAE have been well characterized and they found that T cell mediated immune responses were clearly involved.

How would you experimentally test whether it was CD4$^+$ or CD8$^+$ T cells that are responsible for the actual autoimmune effects of the EAE?

**B.** If you determined that it was CD4 T cells that were primarily responsible for the immunopathology of EAE, how could you try to experimentally test in vivo (in the mice) that it was a Th1 or Th2 mediated immune response? (Northern blots do not count as in vivo experiments).

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**Q6.** Joe needs a kidney transplant. Joe is one of 12 children and the other 11 were tissue typed by flow cytometry and 3 were found to be identical at all MHC loci.

**A.** How would you determine which of these 3 siblings would be the best match as a living related donor?

**B.** Joe receives kidney from his MHC matched sister and 1 year after surgery even with immunosuppression treatment he rejects and kills the organ. What is most likely to be the cause of this rejection?

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**Q7.** What is the potential rationale behind clinical trials using monoclonal antibodies against LFA-1 to prevent organ graft rejection?