Case 6

J. D. is a 27-year-old medical resident who reported to the outpatient department on January 10th complaining of headache, myalgias, and fever, consistent with a diagnosis of influenza. The patient reported receiving influenza vaccine (composed of killed influenza virus) two months previously. On physical examination she had a T 102°F, pulse of 90, respirations of 16 and a BP of 120/80 mm Hg. She had an injected (erythematous) pharynx, enlarged cervical lymph nodes, and a clear chest (no abnormal breath sounds). The patient was sent home with a presumptive diagnosis of influenza and told to rest, drink fluids, and take Tylenol. Her symptoms resolved over 72 hours. Viral cultures taken at the time of visit grew an H4N2* strain of influenza. The influenza vaccine that year consisted of the H1N1, H2N2, and H3N3 strains.

*The "H4N2" designation refers to the polymorphic viral hemagglutinin and neuraminidase molecules that characterize various viral strains. These proteins, located on the viral surface, are the major antigenic determinants that account for specific viral immunity.

Questions for Case 6

(1) Based on what you know about antigen processing and presentation, how might the immune responses to the killed virus vaccines differ from the response to the viral infection? How can a cytotoxic T cell response result from a viral infection if the APCs are not themselves directly infected?

(2) Using the information provided above regarding the influenza antigens present in the vaccine and the influenza strain isolated from the patient, which immune responses occurring in the setting of the infection are primary and which are secondary?

(3) The patient was recruited into a study of anti-influenza cytotoxic lymphocytes (CTL). In this study, a $CD8^+$ CTL clone was derived from the patient and shown to respond to hemagglutinin peptide 11-19. This clone was tested for the ability to kill influenza infected cells derived from the patient or from other volunteers (X, Y, Z). The results of the study show that the patient's CTL clone killed the patient's cells and killed cells from individual X when infected with the influenza virus. However, the CTL clone did not kill influenza-infected cells from individuals Y or Z:

Source of APC	HLA-A	HLA-B	HLA-C	Killed?
Patient	A*0201 A*2414	B*2702 B*3701	C*0601 C*0801	Yes
Subject X	A*0201 A*0304	B*4401 B*3701	C*0301	Yes
Subject Y	A*1101 A*0304	B*3701 B*1516	C*0802	No
Subject Z	A*1101 A*2414	B*2702 B*1516	C*0601 C*0801	No

3a- To which HLA molecule is this particular $CD8^+$ CTL line restricted? If other $CD8^+$ T-cell lines were generated from this individual, to which HLA molecules might they be restricted?

Case 6, cont'd

3b. A different CTL line from this patient was restricted by the same HLA molecule as the first line but responded to amino acids 109-117 of the viral nucleoprotein. Other than being the same length, in what ways would you predict the sequence of the NP109-117 and HA11-19 peptides to be similar? How would they differ?

4. Using mouse models of influenza, the following cells have been shown to be important in immunity against influenza: APCs, CD4+ T cells, CD8+ T cells, B cells. Explain how each of these might contribute to immunity against influenza.