

**HST 175 Final Examination, December 14th, 1999 1.30 - 3.30 P.M.**  
**Answer all questions.**

*Please use three separate "answerbooks" for questions 1&2, 3&4, and 5 &6 respectively, and write your name on each answerbook.*

An 11-year-old boy, AB, presented with a history of recurrent sinusitis and ear infections caused by *H. influenzae* and *S.pneumoniae*. His IgM levels were 1200 mg/100ml (normal 45-150mg/100 ml) but serum IgA, IgG, and IgE were barely detectable. He had been diagnosed with recurrent *Pneumocystis carinii* pneumonia (PCP). A brother who also had recurrent upper and lower respiratory tract infections died at age 14. A sister is now in college and is relatively well although she has occasional attacks of bronchial asthma. His mother is well but is also asthmatic. One of her brothers died of "pneumonia" when he was 11 years old. AB presents with a history and findings consistent with a diagnosis of X-linked hyper-IgM syndrome.

1. A critical cell surface protein, X, is not expressed on AB's activated T cells. What molecule does it trigger on B cells (1)? List three events in B cells that are induced by X (9).
2. When activated T cells from a normal individual encounter macrophages and quiescent dendritic cells, X also induces the "amplified" activation of APCs. This activation event does not readily occur in AB's lymph nodes, and this failure of APC activation could explain his predilection for PCP.
  - a). What are the costimulatory ligands that would normally be turned on in APCs by X (2)? What receptor or receptors on T cells may be triggered by these ligands expressed on activated APCs (2)? Explain how these particular costimulatory receptors regulate immune responses when naïve T cells encounter APCs which have internalized innocuous food proteins on the one hand, or APCs which have ingested intracellular pathogens on the other (16).
  - b). Macrophages activated by intracellular pathogens secrete a cytokine that leads to the polarized differentiation of a subset of helper T cells that in turn contribute to the ability of macrophages to destroy internalized pathogens. List the following:
    - i). A cytokine secreted by the above macrophages that induces T cell differentiation (3).
    - ii). Two of the cytokines secreted by these differentiated T cells (4).

iii). Two of the cytokines secreted in turn by macrophages that are further activated by the above T cells (3).

3. When AB visits his aunt Ida B (who has three cats), he does wheeze occasionally but does not need to use an inhaler. His sister and his mother suffer terribly in Aunt Ida's home and absolutely require using their inhalers during each of their visits. What subset of T cells is being provoked in AB, his sister, and his mother, when they are exposed to feline antigens (3)? Describe the events orchestrated by these T cells that may be relevant to allergen-induced symptoms (14). Why do you think AB might experience less severe symptoms in this situation than his sister (3)?
4. List the sequential molecular interactions that facilitate the entry of naïve T cells into lymph nodes (10).
5. In a different X-linked condition, B cell development is blocked at the pre-B stage. What does the pre-B receptor normally look like (5)? List three events mediated by the pre-B receptor (5)? What molecule is mutated in X-linked agammaglobulinemia (2)?
6. A subset of patients with Familial Hemophagocytic Lymphohistiocytosis has mutations in the perforin gene on chromosome 10. Which activated immune cells do you think are functionally compromised because of this mutation (2)? Explain how perforin may participate in target cell destruction (8). List the participants in the molecular pathway that is responsible for Activation Induced Cell Death (AICD) of helper T cells (8).

Happy holidays! Stay in touch during the next millennium!