# Immunology and Virology (Bio 440) #4:
# Antigen Presentation and MHC

***Terms you should know:***

| | | |
|---|---|---|
| antigen (Ag) | MHC class I | polymorphic |
| antigen-presenting cell (APC) | MHC class II | peptide |
| dendritic cell | α chain, β chain | peptide-binding cleft |
| lymph node | $\beta_2$-microglobulin | MHC restriction |
| cross-presentation | CD4, CD8 | |

***Guide questions to help you prepare for lecture:***

1. Review the overview of the adaptive immune response in Chapter 1 so that you understand, in outline, the roles of B and T cells.

2. How would you define an antigen?

3. What types of cells need to come into contact with antigens?

4. What are the two major types of professional antigen-presenting cells?

5. How does a dendritic cell "capture" an antigen? Once it has done this, what signal tells it to leave the epithelium? How does it find its way to a lymph node?

6. What are the basic structures of the two classes of MHC molecule? What part of the molecule binds antigen, and what kinds of antigen molecules can it bind? What part of the molecule binds CD4 or CD8, and where are these co-receptors found?

7. Why is it important that one individual be able to express many different MHC proteins?

8. What types of cells express MHC class I? MHC class II?

9. Where do MHC I molecules encounter antigens? Where do MHC II molecules encounter antigens?

10. What prevents MHC molecules from binding and displaying peptides from host proteins?

# Problem Solving: Antigen Presentation & MHC

1. You are interested in studying human genetic diversity at the MHC (HLA) locus. You recruit 100 volunteers, swab their cheek to obtain some epithelial cells and use PCR to amplify their genes for the MHC class II α-chain. You then determine the DNA sequence of the PCR products and compare the genes.

   a. Epithelial cells are not professional APCs. Explain why you can use these cells as the source of your DNA in this experiment.

   b. In the α1 domain, would you expect to find many differences among different individuals' alleles, or would this domain be relatively conserved? Explain why high or low diversity is important in this region.

   c. In the α2 domain, would you expect to find many differences among different individuals' alleles, or would this domain be relatively concerved? Explain why high or low diversity is important in this region.

2. In the 1980s, Morrison and Braciale did a key experiment that demonstrated that there were two distinct pathways of antigen processing and MHC presentation.

   Cultured cells similar to macrophages that expressed <u>both</u> MHC I and MHC II were incubated with influenza virus. These cells were then exposed to either (A) cultured T cells that can recognize the influenza HA antigen bound to MHC I, or (B) cultured T cells that can recognize the same antigen when bound to MHC II. Activation of the T cells was measured, and it was found that the cells incubated with virus could activate <u>both</u> types of T cells.

   Morrison and Braciale didn't know the answer to these two questions when they started the experiment, but you already know enough about MHC to answer them:

   a. How is the HA antigen being presented to the "A" T cells? (On MHC I, of course, but how does it get there?)

   b. How is the HA antigen being presented to the "B" T cells?

   To learn more about antigen presentation by these cells, Morrison and Braciale tested T-cell activation under the following conditions:

   (i) Incubated with influenza virus that had been inactivated with UV light (virus particles are intact but can't replicate in cells)

   (ii) Incubated with live influenza virus plus chloroquine, a drug that inhibits breakdown of phagocytized materials in the endosome (phagosome)

   Fill in the table below with the results you would expect for this experiment:

| | **Activation of T cells** | |
|---|---|---|
| **Cells incubated with:** | **A** | **B** |
| Untreated influenza virus | + | + |
| UV treated virus | | |
| Live virus + chloroquine | | |