

Immunology and Virology (Bio 440) #5: Antigen Processing

Terms you should know:

antigen processing	CLIP peptide	proteasome
endosome (phagosome)	DM	TAP transporter
proteolysis	immunodominant epitopes	intracellular
invariant chain	ubiquitin	extracellular

Guide questions to help you prepare for lecture:

1. What are some ways that extracellular microbes (those that don't invade cells) or their components can be brought into APCs?
2. Where are MHC class II molecules synthesized?
3. Besides the α and β chains, what additional protein is attached to a newly synthesized MHC II molecule, and what is the function of that protein?
4. How does the MHC II molecule become available to bind Ag only in an endosome?
5. What is required in order for an MHC II molecule to become stable (resistant to proteolysis)?
6. What two steps are needed in order to break down a cytoplasmic protein?
7. How are MHC class I molecules in the ER exposed to peptides from cytoplasmic proteins?
8. What is required in order for an MHC I molecule to become stable?
9. After binding antigen peptides, how do MHC I and MHC II molecules reach the cell surface?
10. An MHC I-containing vesicle might fuse with an endosome; why wouldn't the MHC I then bind antigen peptides from the endosome?
11. How might a virus block the display of antigens bound to MHC I on the surface of the cell?
12. What are some advantages of requiring presentation on an MHC molecule in order for a T cell to "see" an antigen?

Problem Solving: Antigen Processing

1. Describe at least five ways that a virus could block display of antigens on MHC I. You don't need to know specifics; based on your knowledge of the pathway, just suggest possible points at which the virus could interfere.
2. Suppose a mutation in the α -chain gene alters the peptide-binding cleft of MHC I so that it can't bind peptides. Now, suppose (although this is extremely unlikely), that all six MHC I alleles of a particular individual had this mutation. Will this individual's cells carry: (a) MHC I bound to Ag; (b) "empty" MHC I, or (c) no MHC I at all? Justify your answer.
3. Phagocytes don't just ingest pathogens; they also ingest fragments of dead cells, for example. And, the proteasome isn't just for breaking down viral proteins but will also break down unfolded, non-functional cellular proteins. So, would MHC I and MHC II also display host antigens on the surface of cells? If your answer is yes, then explain why the immune system doesn't react to the host proteins. If your answer is no, explain how the MHC proteins are prevented from binding host antigens.