Abbas: Basic Immunology, 4th Edition

Chapter 03: Antigen Capture and Presentation to Lymphocytes

Test Bank

MULTIPLE CHOICE

1. Antigen-presenting cells (APCs) perform which of the following functions in adaptive immune responses?
   A. Display major histocompatibility complex (MHC)-associated peptides on their cell surfaces for surveillance by B lymphocytes
   B. Initiate T cell responses by specifically recognizing and responding to foreign protein antigens
   C. Display MHC-associated peptides on their cell surfaces for surveillance by T lymphocytes
   D. Display polysaccharide antigens on their cell surfaces for surveillance by B lymphocytes
   E. Secrete peptides derived from protein antigens for binding to T cell antigen receptors

ANS: C
Antigen-presenting cells (APCs) degrade proteins derived from either the extracellular environment or the cytoplasm. They form complexes of peptide fragments of these proteins with major histocompatability complex (MHC) molecules and display these complexes on their cell surfaces, where T cells can "see" them. Neither processing nor MHC association of protein or polysaccharide antigens by B cells is required for recognition. APCs do not distinguish between self and foreign proteins and will display peptides derived from a sampling of all cytoplasmic and extracellular proteins. APCs do not secrete peptide antigens, and T cell antigen receptors do not bind free peptides.

2. A child who suffers from a persistent viral infection is found to have a deficiency in lymphocyte production and very few T and B cells. Other bone marrow–derived cells are produced in normal numbers, and MHC molecule expression on cells appears normal. Transfusion of mature T cells from an unrelated donor who had recovered from a previous infection by the same virus would not be expected to help the child clear his infection. Which one of the following is a reasonable explanation for why this therapeutic approach would fail?
   A. Viral infections are cleared by antibodies, not T cells.
   B. The patient's own immune system would destroy the transfused T cells before they could respond to the viral infection.
   C. T cells recognize peptides, not viral particles.
   D. Donor T cell viral antigen recognition is restricted by MHC molecules not expressed in the patient.
   E. In responding to the previous infection, the donor would have used up all his T cells specific for that virus.

ANS: D
T cells are "self MHC restricted," meaning they specifically recognize infected cells that display microbial peptides displayed by self MHC molecules. There may be no MHC molecules shared by donor and patient, and therefore the transfused T cells would not recognize virus-infected cells in the patient. Because the patient has very few B cells and T cells, his immune system is unlikely to be able to recognize and destroy (i.e., "reject") the transfused T cells. T cells do not recognize structures on intact viral particles but rather peptides derived from viral proteins bound to MHC molecules. Prior viral infection in the donor would be expected to generate memory T cells specific for the virus.

3. Many vaccines now in development will include highly purified, recombinant, or synthetic peptide antigens. These vaccine antigens are expected to stimulate highly specific immune responses, but they are less immunogenic than vaccines containing intact killed or live microbes. Adjuvants are substances added to such vaccines to enhance their ability to elicit T cell immune responses. Which of the following statements about adjuvants is NOT correct?

A. Adjuvants induce local inflammation, thereby increasing the number of antigen-presenting cells (APCs) at the site of immunization.
B. Adjuvants stimulate the expression of costimulators on local APCs.
C. Adjuvants enhance local production of cytokines that promote T cell activation.
D. Adjuvants prolong the expression of peptide-MHC complexes on the surface of APCs.
E. Adjuvants bind to T cell antigen receptors and promote their proliferation.

ANS: E
Adjuvants are not necessarily T cell antigens. Some adjuvants may be T cell antigens, but their adjuvant activity is unrelated to their ability to be recognized, in peptide form, by T cells. Adjuvants are surrogates of the innate immune response to a microbe, required along with antigen component of a vaccine for naive T cell activation. Adjuvants stimulate local inflammation, influx of antigen-presenting cells (APCs), and activation of APCs to secrete cytokines and express costimulatory molecules, and they prolong peptide-MHC expression on the APC membrane.

4. A helper T cell response to a protein antigen requires the participation of antigen-presenting cells that express which of the following types of molecules?

A. Class II MHC and costimulators
B. Class I MHC and CD4
C. Class II MHC and CD8
D. CD4 and costimulators
E. Class II MHC and CD4

ANS: A
Helper T cells are almost always $CD4^+$. The activation of naive $CD4^+$ T cells requires T cell receptor recognition of class II MHC-peptide complexes and the binding of costimulators, both on the antigen-presenting cell (APC) surface. $CD4^+$ helper T cells

bind to class II MHC molecules on the APC, not to class I MHC molecules. CD4 or CD8 expression on the APC surface is of no known relevance to T cell activation.

5. Which type of antigen-presenting cell is most important for activating naive T cells?
   A. Macrophage
   B. Dendritic cell
   C. Endothelial cell
   D. B lymphocyte
   E. Epithelial cell

ANS: B
Dendritic cells are the key type of antigen-presenting cell (APC) for activation of naive T cells and initiation of T cell immune responses. Macrophages and B lymphocytes function as APCs for already differentiated effector T cells in cell-mediated and humoral immune responses, respectively. Epithelial cells usually do not function as APCs.

6. Which of the following statements about the antigen-presenting function of macrophages is NOT correct?
   A. Macrophages are particularly important at presenting peptides derived from particulate or opsonized antigens that are internalized by phagocytosis.
   B. Macrophages become activated by the helper T cells to which they present microbial peptides, and as a result of this activation they become efficient at killing the microbes.
   C. Resting macrophages express low levels of class II MHC molecules, but higher class II MHC expression is induced on activation by the T cells to which they present antigen.
   D. Macrophages express highly variable, high-affinity receptors for many different antigens, and these receptors facilitate the internalization of the antigens for processing and presentation.
   E. Macrophages present antigen to T cells in lymphoid organs and many nonlymphoid organs.

ANS: D
The description of high-affinity and highly variable receptors for antigen applies to B cells, which can present antigen to helper T cells, but does not apply to macrophages. Macrophages express receptors for the Fc region of Ig molecules, and these receptors do facilitate internalization of antibody-opsonized antigens. These Fc receptors are not highly variable and do not recognize the antigen. Macrophages are also highly competent at internalizing intact microbes and other large particulate antigens through phagocytosis. Macrophage class II MHC expression and microbicidal activity are enhanced by signals from the T cells to which they present antigen, including cytokines and CD40 ligand. Macrophages are abundant in spleen, lymph nodes, and most nonlymphoid tissues. They may perform antigen-presenting functions in all these locations.

7. Which one of the following statements about dendritic cells is true?
   A. Immature dendritic cells are ubiquitously present in skin and mucosal tissues.

B. Dendritic cell maturation occurs after migration to lymph nodes in response to signals derived from activated T cells.
C. Class II MHC and T cell costimulators are highly expressed on immature dendritic cells and are down-regulated during maturation.
D. Dendritic cells that enter lymph nodes through draining lymphatics migrate to the B cell–rich follicles in response to chemokines.
E. The principal function of mature dendritic cells is antigen capture.

ANS: A
Tissues that are barriers between the external environment and the inside of the body, such as skin and mucosa, are rich in resting dendritic cells. In this location, the dendritic cells are well positioned to internalize samples of the environment and respond to innate immune system signals, which will drive their maturation into competent antigen-presenting cells. Dendritic cell maturation occurs during migration from infected tissues via lymphatics to the T cell zones of draining lymph nodes. Maturation must occur before, and is required for, activation of T cells, not vice versa. Class II MHC molecule up-regulation occurs during dendritic cell maturation and is one of the changes that make mature dendritic cells better able to present antigen to $CD4^+$ T.

8. Maturing dendritic cells that migrate to a lymph node from peripheral tissues end up mainly in:
A. Follicles
B. High endothelial venules
C. The medullary sinus
D. T cell zones
E. Efferent arterioles

ANS: D
Migrating dendritic cells express the chemokine receptor CCR7 and move into the T cell zones, where SLC and ELC, the chemokines that bind CCR7, are expressed. In this location, the dendritic cells they are most likely to interact with are naive T cells that also migrate to the same area.

9. A young adult is exposed to a virus that infects and replicates in mucosal epithelial cells of the upper respiratory tract. One component of the protective immune response to this viral infection is mediated by $CD8^+$ cytolytic T lymphocytes (CTLs), which recognize and kill virus-infected cells. The CTLs can recognize and kill the infected cells because:
A. In response to interferon-γ secreted during the innate immune response to the virus, the mucosal epithelial cells express class II MHC, with bound viral peptides, on their cell surfaces.
B. Mucosal epithelial cells, like all nucleated cells, express class I MHC molecules and are able to process cytoplasmic viral proteins and display complexes of class I MHC and bound viral peptides on their cell surfaces.

C. Antibodies specific for viral antigens bind to these antigens on infected cell surfaces and engage Ig Fc receptors on the CTL, thereby targeting the CTL to the infected cells.
D. Virus-infected mucosal epithelial cells migrate to draining lymphoid tissues, where they present viral peptide antigens to naive $CD8^+$ T cells.
E. Viral infection of the mucosal epithelial cells stimulates them to express E-selectin, which promotes $CD8^+$ T cell adhesion.

ANS: B
Differentiated $CD8^+$ cytolytic T lymphocytes (CTLs) can recognize class I–associated viral peptides on epithelial cells, as well as most other cell types, and become activated to kill those cells. Interferon-γ may be secreted during the innate immune response to a virus, and this cytokine can up-regulate both class I and class II MHC expression of various cell types, but $CD8^+$ T cells do not recognize class II–associated peptides. Antibodies may form a bridge between Fc receptor-bearing natural killer cells and infected cells expressing viral antigens on their surface, but this phenomenon does not apply to $CD8^+$ CTLs. Mucosal epithelial cells do not migrate to draining lymph nodes in response to viral infection, nor do they express E-selectin, which is an endothelium-specific adhesion molecule.

10. Naive $CD8^+$ T cells require signals in addition to T cell receptor recognition of peptide-MHC to become activated and differentiate into cytolytic T cells. These signals are called costimulatory signals and are provided by professional antigen-presenting cells (APCs), such as dendritic cells. If a virus infects epithelial cells in the respiratory tract but does not infect professional APCs, what process ensures that naive T cells specific for viral antigens will become activated?

A. Cross-reactivity, whereby the naive $CD8^+$ T cell recognizes a self antigen that is structurally similar to a viral antigen presented by dendritic cells
B. Crossover, whereby part of the viral genome is exchanged with part of one chromosome of the host
C. Crosstalk, whereby signals generated by the virus binding to class I MHC molecules intersect with T cell receptor signaling pathways
D. Cross-presentation, whereby infected epithelial cells are captured by dendritic cells, and the viral proteins originally synthesized in the epithelial cells are processed and presented in association with class I MHC molecules on the dendritic cell
E. Cross-dressing, whereby viral infection of the epithelial cell stimulates the expression of surface molecules that are typically found only on dendritic cells

ANS: D
Cross-presentation (or cross-priming) is the phenomenon by which a protein antigen made within one cell is processed and presented by the class I MHC pathway of a separate professional antigen-presenting cell (APC). Cross-presentation requires that the protein antigen from one cell be internalized from the extracellular milieu into the APC to gain access to the cytoplasm of the APC. *Crossover* and *crosstalk* are terms referring to

genetic and signaling phenomena, which are not accurately described in the question. *Cross-dressing* is not a term used in immunology.

11. Which of the following is the main criterion that determines whether a protein is processed and presented via the class I MHC pathway in an antigen-presenting cell (APC)?

A. Encoded by a viral gene
B. Present in an acidic vesicular compartment of the APC
C. Present in the cytosol of the APC
D. Internalized into the cell from the extracellular space
E. Small in size

ANS: C
Regardless of the source of the protein, its presence in the cytosol makes it accessible to the tagging and proteolytic processing mechanisms that initiate the class I MHC antigen presentation pathway. Microbial proteins and self proteins have equal access to this pathway if they are present in the cytosol. Presence in acidic vesicles is the comparable major criterion for inclusion in the class II MHC pathway; such proteins are usually, but not always, internalized from the extracellular space. The size of an intact protein is not relevant to which processing and presentation pathway it will enter.

12. Which one of the following molecules does NOT play an important role in the class II MHC pathway of antigen presentation?

A. β_2-Microglobulin
B. Cathepsin
C. Invariant chain
D. HLA-DM
E. Calnexin

ANS: A
β_2-Microglobulin is one of the polypeptide chains of a class I MHC molecule and is required for assembly of the peptide-class I MHC complex. All the other molecules listed are involved in the class II MHC of antigen presentation. Cathepsins are acid proteases that degrade proteins in acidic vesicles in the class II MHC pathway. The invariant chain directs appropriate sorting of new class II MHC molecules from the Golgi to endosomes, and it protects the class II MHC peptide binding groove from occupancy by peptides until the class II MHC molecules are delivered to the endosome. Calnexin is an endoplasmic reticulum chaperone involved in the assembly of both class I and class II molecules.

13. In the class I MHC pathway of antigen presentation, peptides generated in the cytosol are translocated into the endoplasmic reticulum in which of the following ways?

A. By ATP-dependent transport via the transporter associated with antigen-processing (TAP) 1/2 pump
B. By passive diffusion
C. By receptor-mediated endocytosis
D. Through membrane pores

E. Via the proteasome

ANS: A
The TAP1/TAP2 heterodimer is an ATP-dependent pump that delivers peptides generated by the proteasome into the endoplasmic reticulum.

14. In the class I MHC pathway of antigen presentation, cytoplasmic proteins are tagged for proteolytic degradation by covalent linkage with which of the following molecules?
A. Calreticulin
B. Nuclear factor (NF)-κB
C. Tapasin
D. Ubiquitin
E. Calnexin

ANS: D
In the class I pathway, proteins are tagged for proteasomal degradation by covalent addition of several copies of the polypeptide ubiquitin. Ubiquitin-dependent proteasomal degradation is also important in many other cellular processes besides antigen presentation. For example, NF-κB is a transcription factor whose activation is dependent on ubiquitination and proteasomal degradation of an inhibitor (called IκB). Calreticulin, tapasin, and calnexin regulate the assembly of class I MHC proteins within the endoplasmic reticulum.

15. Which one of the following statements about T cell tolerance to self proteins is accurate?
A. Self proteins are not presented by the class I pathway because only microbial proteins, and not self proteins, are ubiquinated in the cytosol.
B. Peptides derived from self proteins are not presented by the class I or class II pathways because MHC molecules are expressed only in response to infections.
C. Self proteins are not presented by the class II pathway because endosomal acidic proteases digest microbial proteins but not eukaryotic proteins.
D. Self peptide/self MHC complexes are formed and displayed by antigen-presenting cells in both class I and class II MHC pathways, but T cells that recognize these complexes usually are not present or are functionally inactive.
E. Peptides derived from self proteins are not displayed by MHC molecules because they usually are displaced by the more abundant microbial peptides.

ANS: D
T cell tolerance is a result of deletion or inactivation of self-reactive T cells. The various steps in both the class I and the class II MHC antigen-presenting pathways do not discriminate between self and microbial proteins. Although expression of MHC molecules is up-regulated as a result of the innate immune responses to infections, there is some degree of constitutive expression of class II MHC on professional antigen-presenting cells, and class I MHC is constitutively expressed on most cells in the body.

Only a small fraction of the surface MHC molecules of an infected cell will express peptides derived from microbial peptides.

16. In a clinical trial of a new antiviral vaccine composed of a recombinant viral peptide and adjuvant, 4% of the healthy recipients did not show evidence of response to the immunization. Further investigation revealed that all the nonresponders expressed the same, single allelic variant of HLA-DR but all the responders were heterozygous for HLA-DR alleles. Which of the following is the most likely explanation for this finding?

A. Response to the vaccine requires T cell recognition of complexes of the viral peptide with HLA-DR, but the peptide cannot bind to the allelic variant of HLA-DR found in the nonresponders.
B. The nonresponders could not express class II MHC proteins.
C. The viral peptide is not an immunodominant epitope.
D. The nonresponders underwent determinant selection of another viral epitope.
E. Because of technical errors, the nonresponders had not received adequate doses of the vaccine.

ANS: A
The response to a viral protein (or peptide) requires T cell recognition of the peptide bound to an MHC molecule. Although the viral peptide in the vaccine may bind to many different MHC alleles, it likely will not bind to all. The nonresponders express an allelic variant of HLA-DR, which is a class II MHC molecule. Because the peptide evoked a response in 96% of the people in the trial, it can be considered a dominant epitope. Formally, this can be concluded only when the whole protein is the immunogen and the specificities of the responses for different epitopes are compared. *Determinant selection* is an older term that predates our knowledge of peptide-MHC binding, but it does not mean active selection for one versus another epitope. It is highly unlikely that the only people in the trial who were not adequately immunized for technical reasons happen to be the only ones homozygous for a particular MHC allele.

17. The required number of complexes of a microbial peptide and a particular class II MHC allele on the surface of an antigen-presenting cell to initiate a T cell response specific for the viral peptide is:

A. At least equal to the number of complexes of self peptides with class II MHC on the cell surface
B. Greater than 10^3
C. Less than or equal to 0.1% of the total number of class II MHC molecules on the cell surface
D. Greater than 10^6
E. Zero

ANS: C
As few as 100 complexes of a particular peptide and a particular class II MHC molecule are needed to activate naive T cells specific for that complex and thereby initiate a detectable T cell response. This represents less than 0.1% of the total class II MHC molecules on a typical antigen-presenting cell surface.