

Abbas: Cellular and Molecular Immunology, 7th Edition

Activation of T Lymphocytes

Test Bank

Multiple Choice

1. All of the following protein-protein interactions are involved in activation of naive helper T cells by antigen-presenting cells (APCs) EXCEPT binding of:
 - A. Peptide-MHC complexes on the APC to the TCR on the T cell
 - B. CD4 on the T cell to nonpolymorphic regions of class II MHC molecules on the APC
 - C. Integrins on the T cell with adhesion ligands on the APC
 - D. B7-2 on the APC with CD28 on the T cell
 - E. CD40L on the T cell with CD40 on the APC

ANS: E. CD40L is not expressed on naive T cells and is only up-regulated subsequent to activation by an antigen-presenting cell (APC). In the naive helper T cell, the TCR binds to the MHC-peptide complex whereas the CD4 coreceptor engages a conserved region on the MHC II molecule. Integrins on the T cell interact with adhesion ligands on the APC. This region of binding between the T cell and the APC is known as the immunologic synapse and also includes costimulatory interactions, such as CD28 on the T cell binding to B7 on the APC.

2. Which one of the following statements about MHC-TCR interactions is NOT true?
 - A. Antigen receptors on T cells bind to MHC molecules for only brief periods of time.
 - B. The affinity of most TCRs for peptide-MHC complexes is similar to the affinity of antibodies for their antigens.
 - C. Only 1% or less of the MHC molecules on any antigen-presenting cell (APC) display a peptide recognized by a particular T cell.
 - D. T cells usually require multiple engagements with an APC before a threshold of activation is reached.
 - E. A subthreshold number of MHC-TCR interactions can lead to T cell inactivation.

ANS: B. In general, the TCR binds to peptide-MHC complexes with lower affinity than antigen-antibody interactions. This relatively low-affinity interaction occurs briefly; thus, a T cell may need multiple engagements with the antigen-presenting cell (APC) before a threshold of activation occurs. If this threshold is not reached, the T cell may enter into an inactive state known as anergy. On any given APC, less than 1% of the MHC molecules display the same peptide.

Matching

Questions 3-10

For each of the descriptions in questions 3-10, choose the T cell signaling molecule that best matches it from the list below (A-O).

- A. CD3
- B. Lck
- C. Zap-70
- D. LAT
- E. Ras
- F. PLC γ
- G. PIP2
- H. PIP3
- I. IP3
- J. DAG
- K. Calcineurin
- L. NFAT
- M. Jun
- N. Fos
- O. NF- κ B

3. This molecule becomes an active transcription factor on dephosphorylation.

ANS: L. NFAT is a transcription factor required by T cells for the expression of interleukin (IL)-2, IL-4, tumor necrosis factor (TNF), and other cytokine genes. NFAT is present in an inactive, phosphorylated form in the cytosol of resting T cells. On dephosphorylation by calcineurin, a nuclear localization sequence is uncovered that permits NFAT to translocate to the nucleus. Once in the nucleus, NFAT induces transcription of these genes.

4. This protein is a well-characterized proto-oncogene product that on mutation to a constitutively active form has been associated with multiple neoplasms.

ANS: E. *Ras* was one of the first proto-oncogenes characterized. Normal *ras* is involved in TCR signaling pathways. On mutation to a constitutively active state, *ras* promotes the survival and proliferation of malignant cells.

5. Binding of this molecule to Jun is needed for transcriptional activation of the IL-2 gene.

ANS: N. Fos combines with phosphorylated Jun to form activation protein-1 (AP-1). AP-1 is the name for a family of DNA-binding factors composed of dimers of two different proteins. Transcription of *fos* is enhanced by the Erk pathway, whereas phosphorylation of preexisting Jun is induced through the Vav/Rac pathway. AP-1 physically associates with other transcription factors in the nucleus, and together they activate transcription of cytokine genes essential for T cell activation.

6. This is a transcription factor that exists in the phosphorylated form within the nucleus.

ANS: M. On phosphorylation, c-Jun translocates to the nucleus and binds to Fos to form AP-1.

7. Immunosuppressive therapy with the drugs cyclosporine and FK506 inhibits T cell activation by blocking the protein phosphatase activity of this molecule.

ANS: K. Calcineurin is responsible for the dephosphorylation of NFAT, which is an essential transcription factor for the activation of T and B cells. The immunosuppressive drugs cyclosporine and FK506 function by inhibiting calcineurin. These drugs are commonly used to prevent transplant rejection.

8. This molecule binds to a receptor on the endoplasmic reticulum and stimulates release of calcium into the cytosol.

ANS: I. IP3 is generated from the cleavage of PIP2 in the membrane to DAG and IP3 by the enzyme PLC γ , and it stimulates release of calcium into the cytosol.

9. This molecule has the same downstream effect as addition of the drug phorbol myristate acetate (PMA) to T cells.

ANS: J. Both DAG and pharmacologic agents such as phorbol myristate acetate (PMA) activate protein kinase C (PKC). PKC has many substrates and is a potent activator of many transcription factors in T cells.

10. This molecule is a transcription factor involved in the expression of several T cell activation genes activated when its bound inhibitor is phosphorylated.

ANS: O. NF- κ B is present in the cytoplasm and is bound to an inhibitor called I- κ B. On stimulation with antigen, I- κ B becomes phosphorylated, dissociates from NF- κ B, and is degraded by the ubiquitin-proteosomal pathway. NF- κ B then translocates to the nucleus, where it participates in transcriptional activation of several genes.