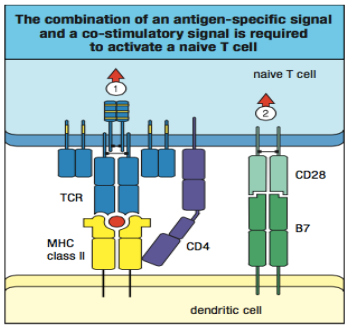
The dendritic cells in the skin and other peripheral tissues are called **immature dendritic cells**, whereas those in lymph nodes are called **mature dendritic cells** or **activated dendritic cells**. On maturation, the finger-like processes called dendrites, for which the dendritic cell is named, become highly elaborated, which facilitates extensive interaction with T cells in the cortex of the lymph node.



Although CD28 is the only B7 receptor on **naive T cells**, an additional and complementary B7 receptor is expressed once T cells are **activated**. This receptor, called **CTLA4**, is structurally similar to CD28 but binds B7 twentyfold more strongly and functions as a brake on CD28. Whereas B7 binding to CD28 activates a T cell to divide, the engagement of CTLA4 inhibits both the activation and proliferation of T cells.

CTLA-4 is a checkpoint for the production of IL-2

Naive CD8 T cells require stronger activation than naive CD4 T cells

CD4 helper T cells are functionally diverse but interact with relatively few target cell types: lymphocytes, phagocytes, and granulocytes. In contrast, cytotoxic CD8 T cells are functionally homogeneous but have to interact with a wide range of target cells. Because of the inherently destructive nature of CD8 T cells, the activation of naive CD8 T cells in the secondary lymphoid tissues is not done lightly and requires stronger co-stimulatory activity than the activation of naive CD4 T cells.
Naive CD8 T cells recognize antigens presented on the MHC class I molecules of mature dendritic cells.

For some viral infections **(CD4 independent activation)**, the interaction of a virus-specific naive CD8 T cell with a dendritic cell that presents the pep- tide:MHC class I complex is sufficient for activation and differentiation to proceed. When activated by antigen and the dendritic cell's co-stimulatory molecules, the naive CD8 T cells —> IL-2, and high-affinity IL-2 receptor —> which together induce the CD8 T cells to proliferate and differentiate.

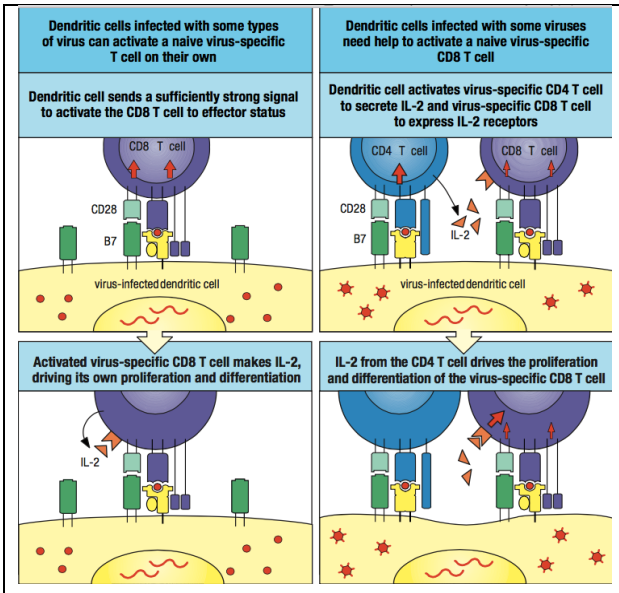
For other viral infections **(CD4 dependent activation),** DCs alone are insufficient to activate naive CD8 T cells, and they solicit the help of virus-specific effector CD4 T cells, which give the necessary IL-2 to 'jump-start' the activation. The dendritic cell must interact simultaneously with both the naive CD8 T cell and the effector CD4 T cell, the former recognizing a viral-peptide:MHC class I complex on the dendritic cell surface and the latter a viral-peptide:MHC cell class II complex (Figure 8.17, right panels). The effector CD4 T cell is activated to make and secrete IL-2, which then binds to the IL-2 receptors induced on the CD8 T cell by its antigen-specific interaction with the dendritic cell. The combination of intracellular signals generated from the IL-2 receptor, the T-cell receptor, the CD8 co-receptor, and the CD28 co-stimulatory receptor then drives the naive CD8 T cell to proliferate and differentiate.

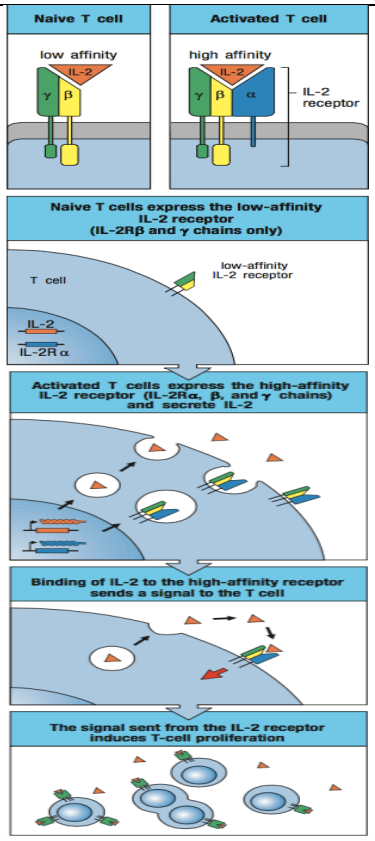
Cytotoxic T cells kill their target cells by inducing apoptosis

Effector T_H1 CD4 cells induce macrophage activation

The principal function of T_H1 CD4 cells is to help macrophages at sites of infection to become more proficient in the uptake and killing of pathogens. If the antigen receptor of a T1 cell recognizes its antigen on a macrophage surface, the T_H1 cell and the macrophage form a conjugate pair with a synapse at which information and material are exchanged. Cytokines secreted by the T_H1 cell induce changes in the macrophage that improve its performance —> **macrophage activation**.
Benefits: (1) phagosomes containing captured pathogens fuse more efficiently with lysosomes (2) increased synthesis of oxygen radicals, nitric oxide (NO), and proteases, which work together to destroy the captive pathogens.

Two signals for Macrophage activation: (1) **IFN-γ**, the characteristic T_H1 cytokine, when it binds to the IFN-γ receptor on macrophages. (2) **CD40 ligand**, a membrane-bound cytokine of the T_H1 cell that binds to its receptor, **CD40**, on the macrophage. (1,2)—> induces the changes in gene expression that activate the macrophage.





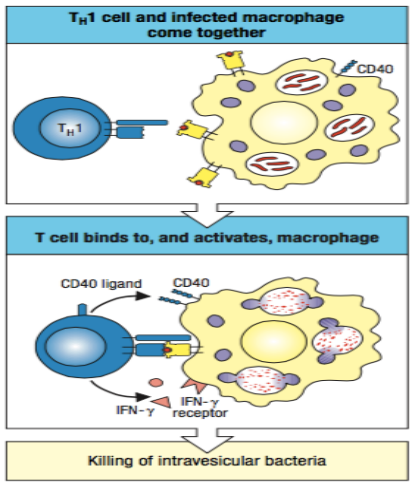


Figure 8.27 T_H1 CD4 cells activate macrophages to become highly microbicidal. When a T_H1 cell specific for a bacterial peptide contacts a macrophage that presents the peptide, the T_H1 cell is induced to secrete the macrophage-activating cytokine interferon-γ (IFN-γ) and also to express CD40 ligand at its surface. Together, these newly synthesized proteins activate the macrophage to kill the bacteria living inside its vesicles.