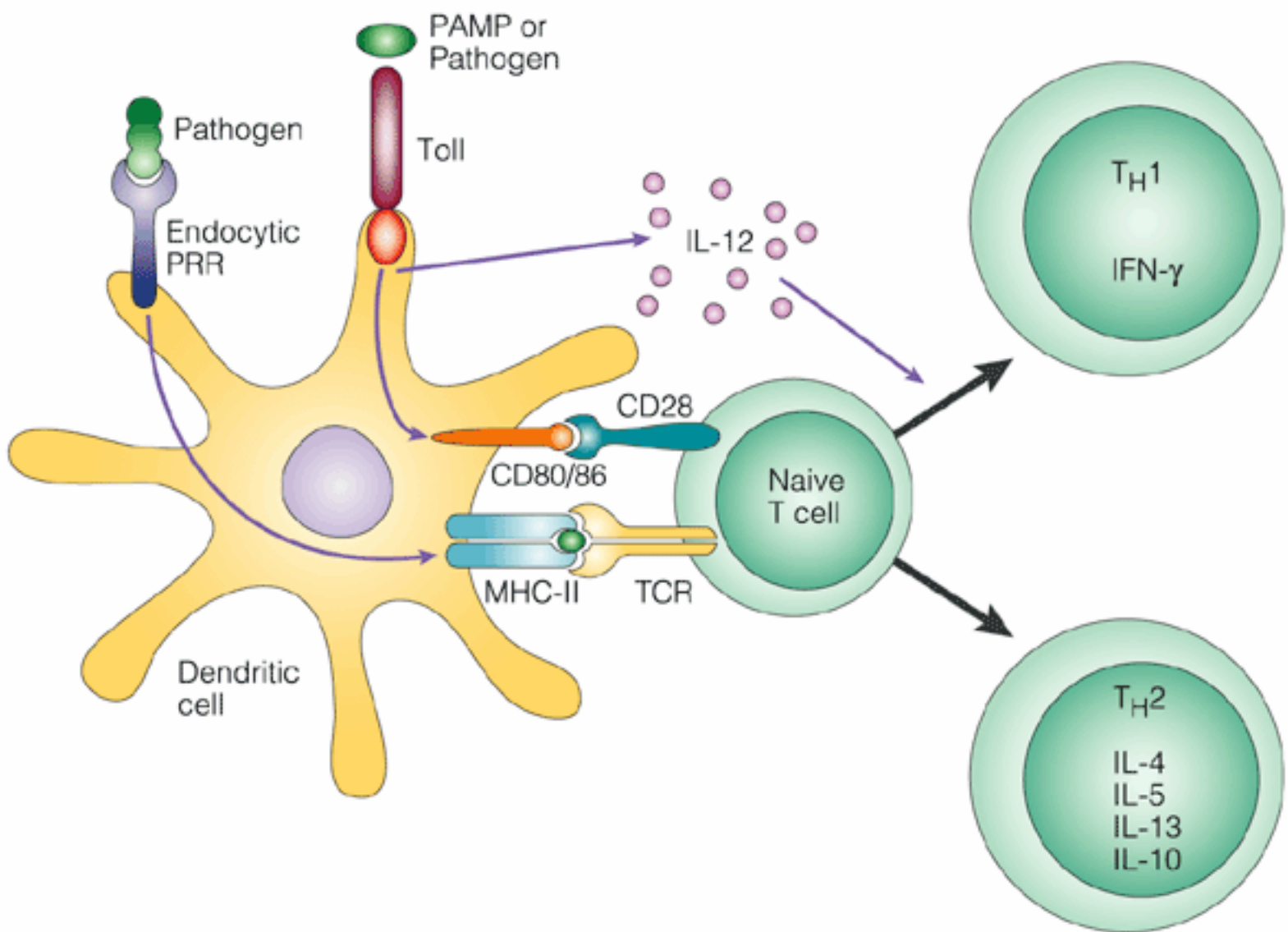


10. T cells II: T cell polarization and cytokine signaling

Learning Objectives and Summary



10. T cells II: T cell polarization and cytokine signaling

Learning objectives:

1. Understand how naive T-cells give rise to polarized effector Th cells
2. Be able to describe functional differences between Th1, Th2, and Th17 helper T-cell subsets
3. Understand the critical role of CD40-CD40-L interactions, in concert with IL-4, in B cell function
4. Be familiar with major components of TCR and cytokine signaling
5. Understand some critical functions of chemokines in immunity

SUMMARY

1. Naive T-cells differentiate into distinct T cell subsets. Among the most important of Th1, Th2, and Th17 cells.
2. Th1 cells secrete IFN- γ and IL-2. IFN- γ is the predominant cytokine that activates macrophages to produce pro-inflammatory cytokines. IFN- γ often synergizes with innate immune stimuli (e.g., LPS). Th1 cells play important roles in acute bacterial and viral infections and are essential effectors of "Delayed Type Hypersensitivity," or DTH, which is characterized by the presence of IFN- γ -activated macrophages. IL-2 is required for proliferation of T-cells. Pathways leading to IL-2 production, especially those that activate NF-AT, are attractive drug targets (e.g., cyclosporin and FK506).
3. B-cells, via CD40 and MHC-peptide, activate T cells to release cytokines that activate B cells (e.g., IL-4). IL-4, in concert with CD40L on activated T-cells, stimulate B-cells to undergo class-switching to IgG and IgE. IL-4, the prototypical Th2 cytokine, is important to immunity against parasites (e.g., helminths)
4. During T-cell polarization, negative feedback loops regulate T-cell differentiation: IL-4 antagonizes the outgrowth of Th1 cells and IFN- γ antagonizes the outgrowth of Th2 cells.
5. Th17 cells stimulate neutrophils during acute bacterial infections and many other cells during chronic inflammation (e.g., in autoimmunity).
6. Chemokines are small proteins that activate G protein-coupled receptors and are essential for leukocyte trafficking. Collectively, they have multiple roles in many cell types besides directing traffic.