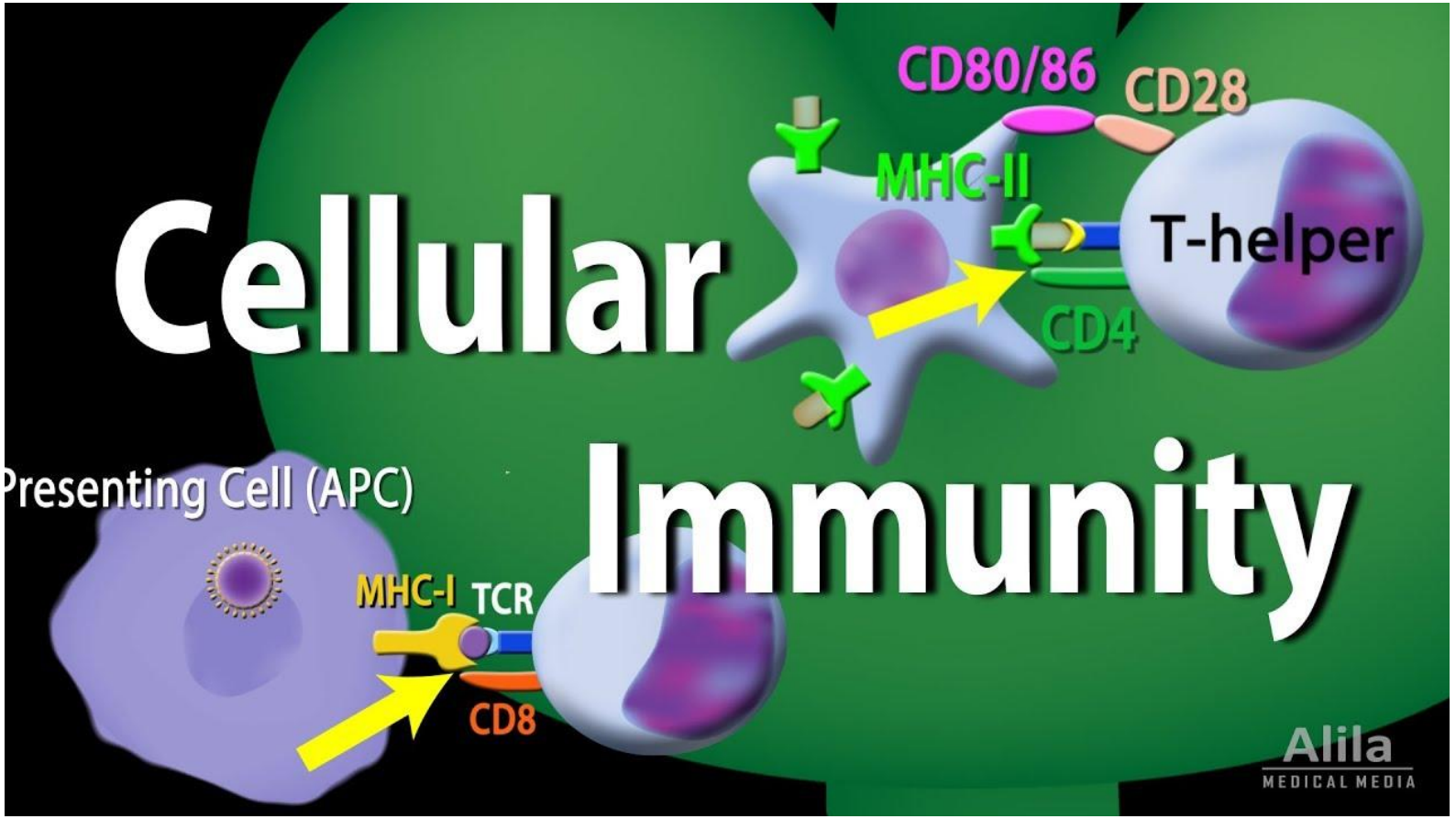
Adaptive Immunity
Cellular Immunity



Objectives

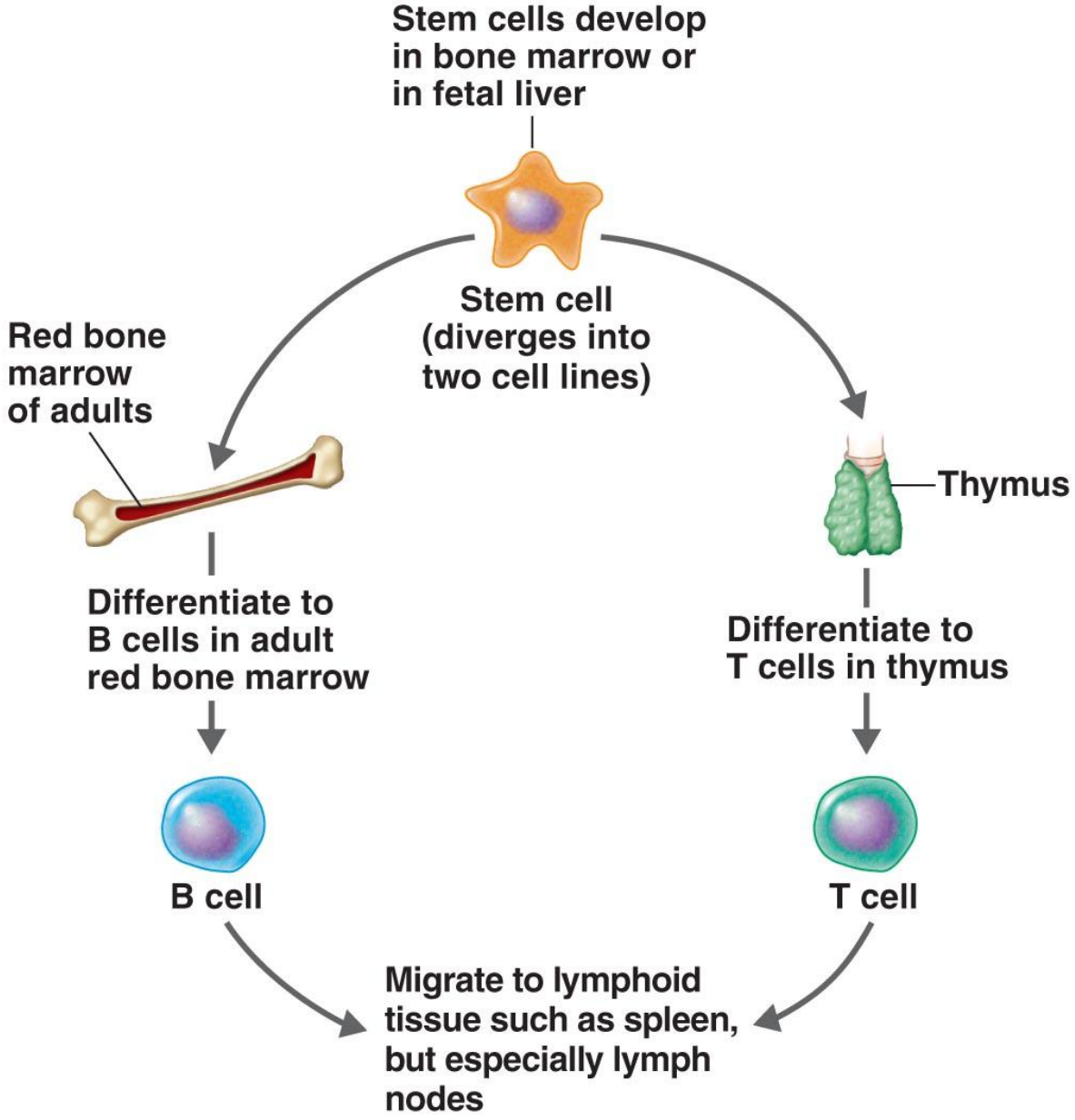
- Explain the principles of adaptive immunity
- Introduce the immune cells that mediate adaptive immunity and their specific roles
- Discuss the differences between cell-mediate immunity and humoral immunity
- Explain what interactions are required for activation of T cells and B cells
- Discuss the stages of cellular and humoral immunity
- Discuss immunological memory and outline the differences between primary and secondary responses
- Compare and contrast the innate and adaptive immune response

Adaptive Immunity

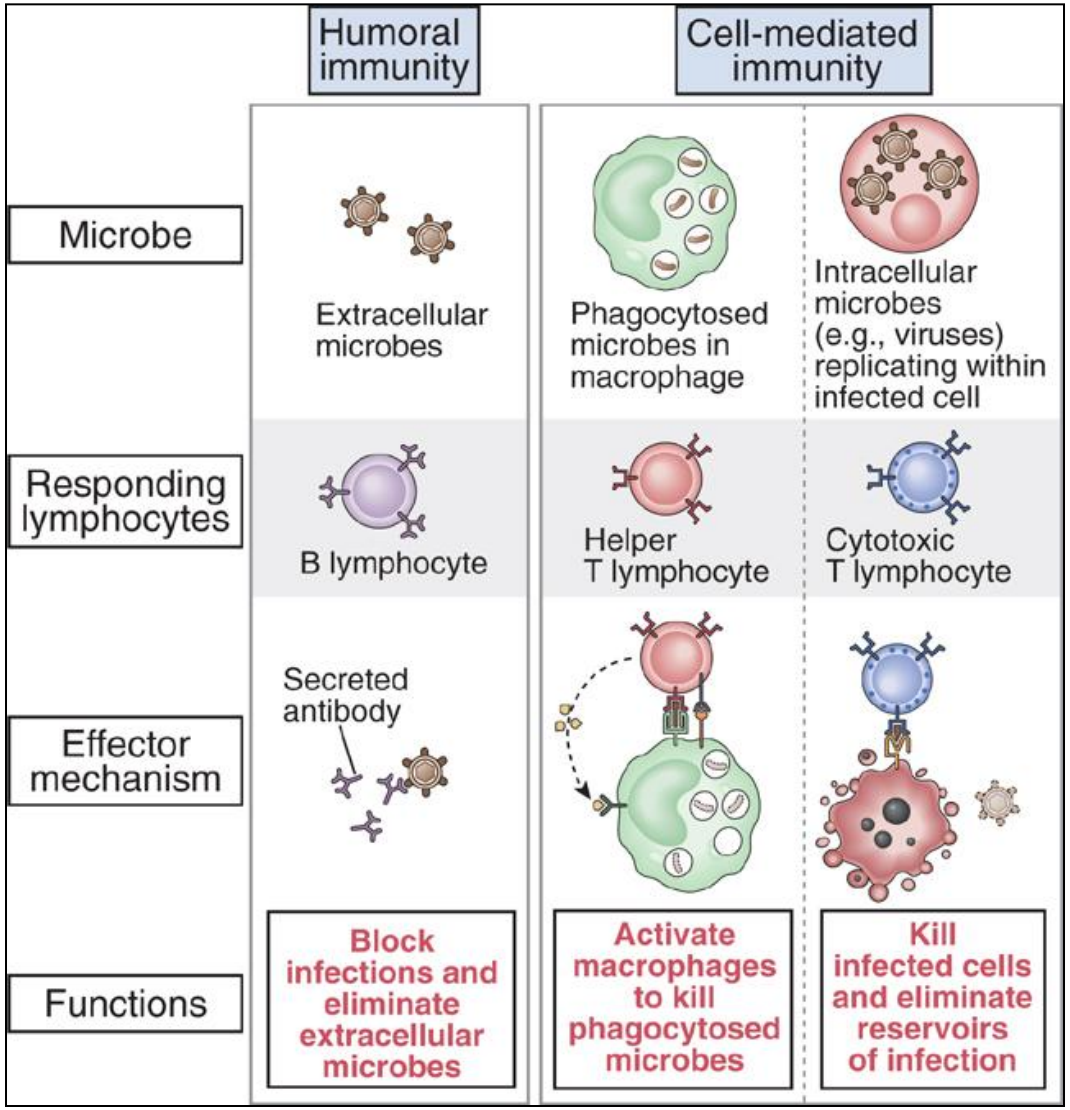
- **Adaptive immunity**:
  - Induced resistance to a specific pathogen
  - Learnt by experience
  - Confers pathogen-specific immunity
  - Enhanced by second exposure
  - Has memory
  - Is poorly effective without innate immunity

1. **Humoral immunity:** B cells and antibodies
2. **Cellular immunity:** Due to T cells and cytokines

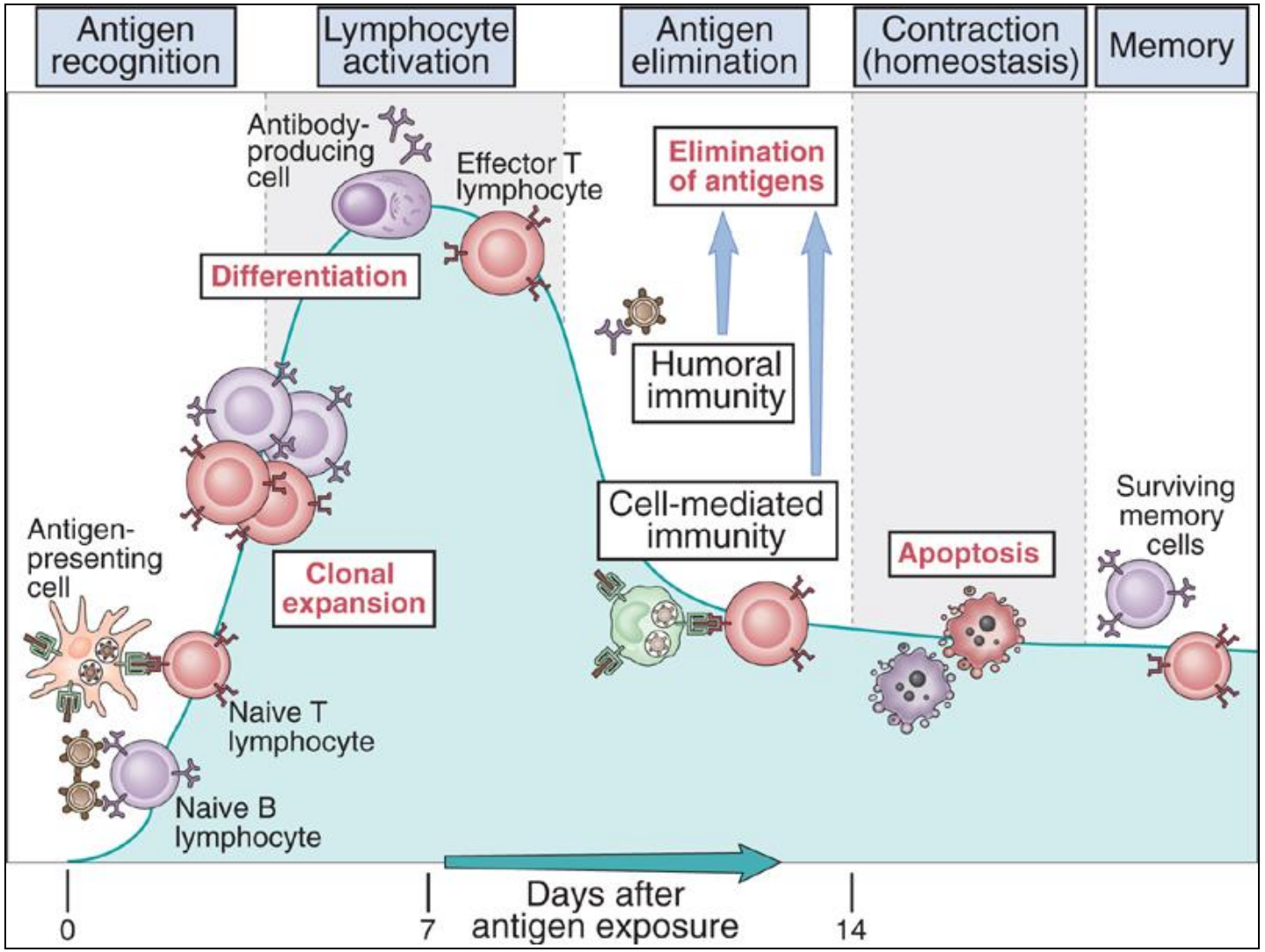
Dual Nature of Adaptive Immunity



Types of Adaptive Immunity



Phases of Adaptive Immune Responses



Cellular Immunity

T Cells and Cellular Immunity

- This type of immunity is performed by T cells to compate infection by intracellular microbes
- Intracellular infections include:
  - Microbes ingested by macrophage that resist microbicidal activity of macrophage
  - Viruses that binds to cells receptors and replicate in the cytoplasm of these cells
- T cells help B cells to produce antibodies
- T cells interact with other cells of the immune system
- Types of T cells:
  1. Helper T cells
  2. Cytotoxic T cells
  3. Regulatory T cells

Stages of Cellular Immunity

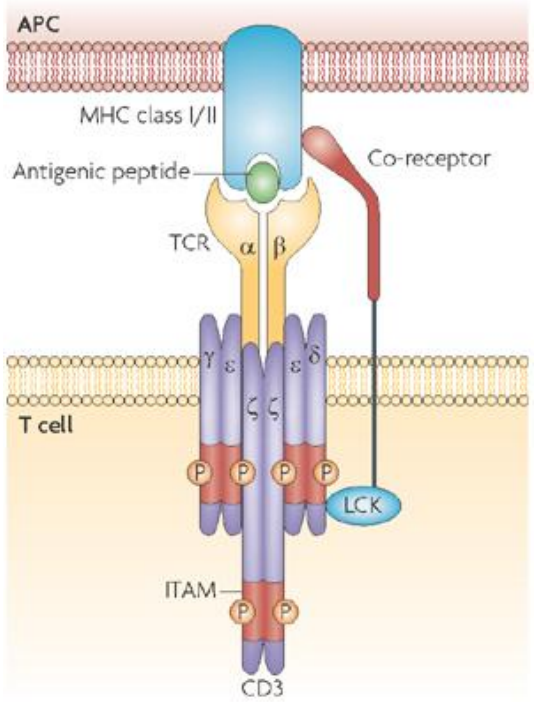
1. Antigen processing and presentations (APC's and MHC's)
2. T cells recognize and bind to Ag by T-cell receptors **(TCRs)**
3. Activation and signaling
4. Clonal expansion and differentiation of T cells
5. Effector functions
6. Shut down of immune response and formation of T memory cells

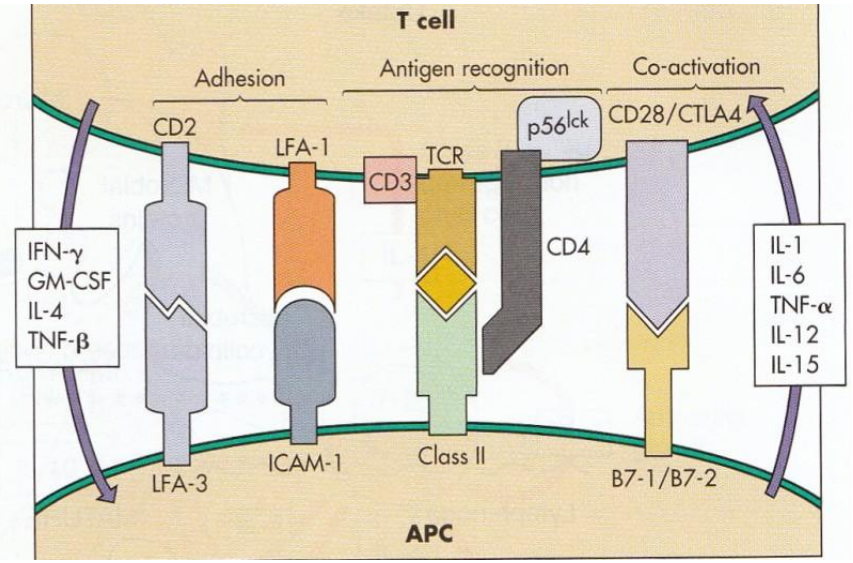
1. Antigen Processing and Presentation

- Naïve T cells can not recognize antigens directly before processing
- The antigens need to be processed and displayed by MHC molecules on professional antigen presenting cells
- For details see lecture on antigen presentation and processing

2. Recognition and Binding

- Naive T cells circulate through peripheral lymphoid organs
- T cells posses specific receptors that bind antigen ligands on APCs these receptors called TCR
- TCRs bind epitopes associated with a MHC protein
- Adhesion molecules strengthen the binding of T cells to APCs through integrin, selectins, LFA (leukocyte function-associated antigen)-1, CD2 adhesion molecules



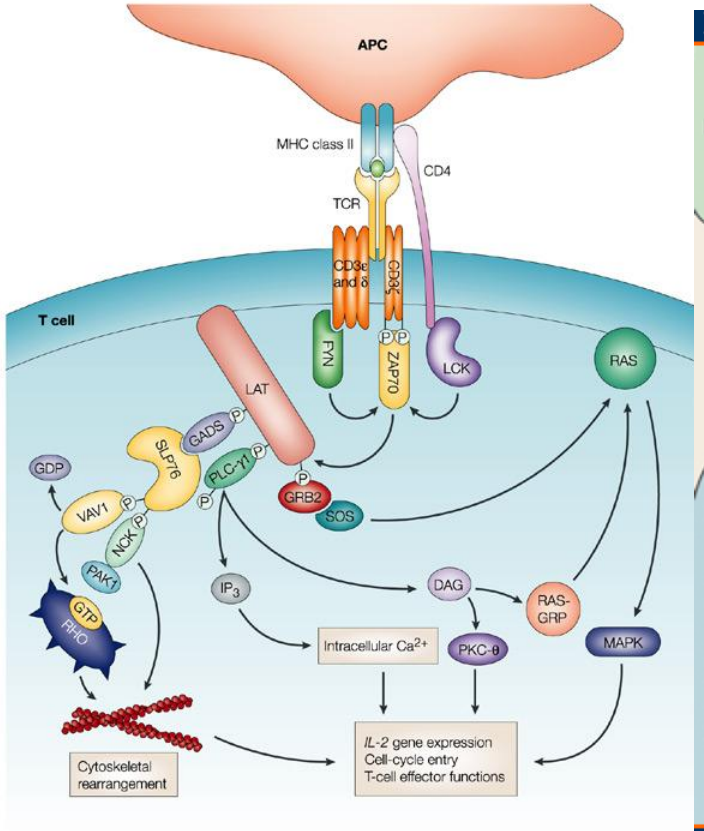


3. Signaling and Activation

1. MHC + antigen – TCR binding and activation of CD3 and zeta chain do the function of signaling (**TCR complex**)
2. Co-receptors including CD4 and CD8 play role in signaling
3. Other accessory molecules including CD45 and CD2 participate in signaling
4. Co-stimulatory signal
   - B7 on APC interacts with CD28 on lymphocyte
   - Receptors for co-stimulation recognize second signal provided by APCs
   - Without co-stimulation T cells remain **not active** (anergy)

T cell Activation

1. Antigen recognition, primary and secondary signaling leads to T cells activation
2. Release of biochemical mediator and active enzymes that end by activation of transcription factors
3. This results in influx of calcium into the cell
4. Calcium activates calcineurin
5. Calcineurin activates gene for IL-2 and its receptor necessary for T cells proliferation and differentiation and cytokine release



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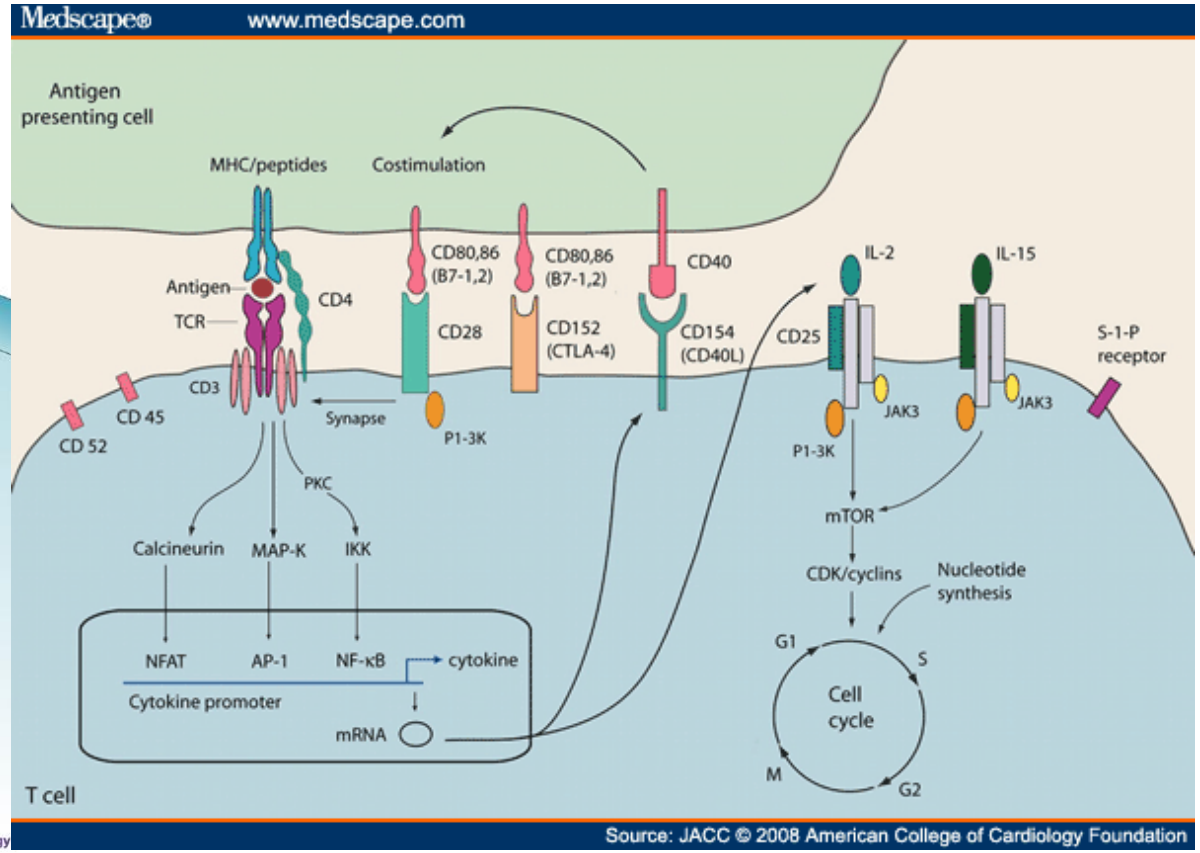
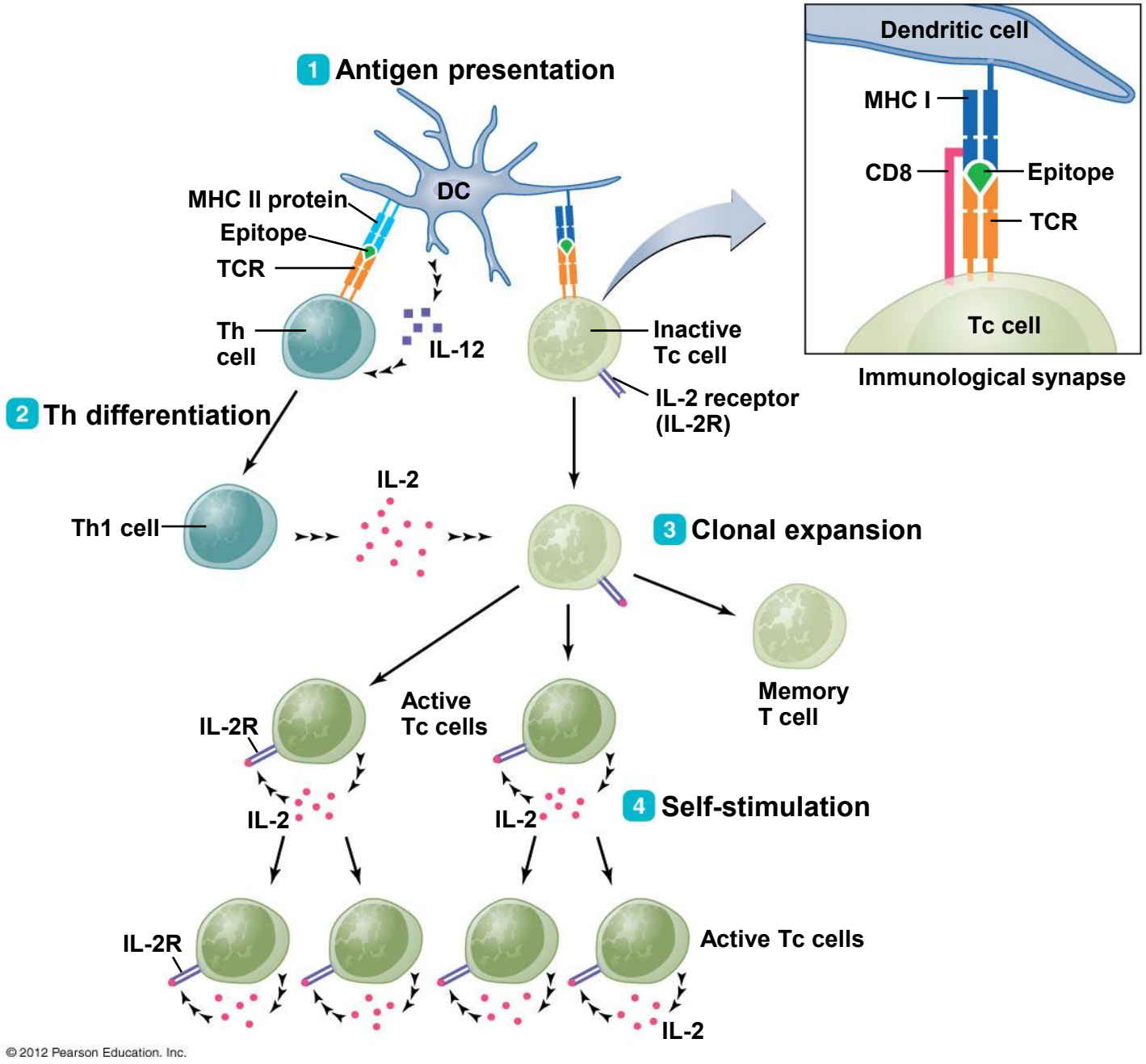


4. Proliferation and Differentiation

- As a result of T cells activation and Interleukins secretion T cells start to proliferate resulting in expansion of antigen specific cells or clones (1-2 days)
- after 4-5 days T cells differentiate and expand to yield enough numbers of functional T cells (effectors cells)
- These cells leave the peripheral lymphoid tissue and migrate to site of infection
- A small subset of T cells will differentiate into memory T cells



5. Effector Mechanisms

- Effector mechanisms are responsible of the final killing of microbes
- The main effector function of T cells include:

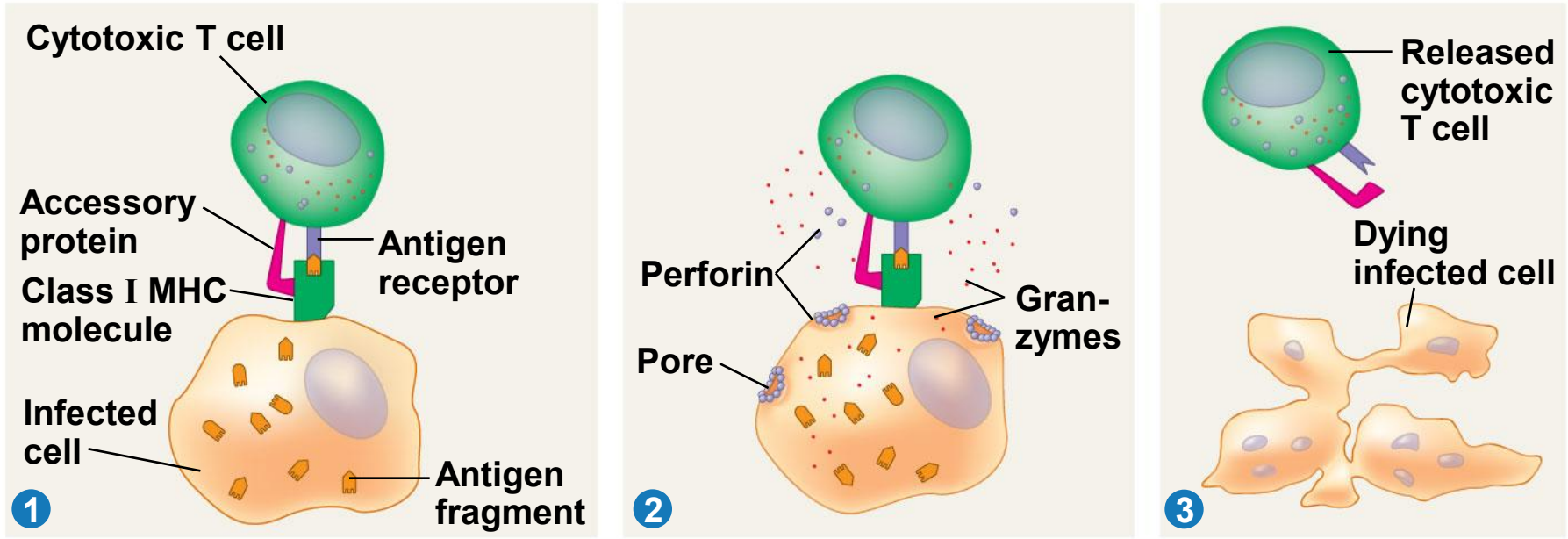
1. Activation of macrophage
2. Activation of cytotoxic T cells
3. Activation of B cells and humoral response

T Helper Cells

- **$CD4^+$** or **T_H** cells
  - T_H cells produce cytokines and differentiate into
    - T_H1
    - T_H2
    - T_H17
    - Memory cells
- TH1 produces IFN-gamma which activates cells related to cell-mediated immunity, macrophages, and Abs
- TH2 activate eosinophils and B cells to produce IgE

T Cytotoxic Cells

- **$CD8^+$** or **T_C** cells
- Target cells are self carrying **endogenous antigens**
- Activated into **cytotoxic T lymphocytes (CTLs)**
  - CTLs recognize Ag + MHC I
  - Induce **apoptosis** in target cell
- Cytotoxic T cells kills microorganism by:
  - Perforins
  - Granzymes – degrading enzymes
  - Fas-Fas Ligand interaction - apoptosis
  - Antibody dependent cellular cytotoxicity



6. Shut down of Immune Response and Formation of T Memory Cells

- T_{reg} cells (have CD4 and CD25 on surface): Suppress T cells and shut down the T cells immune response after the microbe is eradicated
- As the infection is cleared proliferated immune cells are deprived of survival factors and the cells die by programmed cells death (apoptosis)
- A fraction of antigen-activated T cells differentiate into long lived memory T cells
- Memory T cells do not produce any cytokines and they do not kill microorganism, they recognize the same antigen if it enters the body again and activate the immune response faster in the second attack of microorganism