

Antigen Presentation Dendritic Cells

Mark S. Anderson
UCSF

FOCiS

UCSF

University of California
San Francisco

advancing health worldwide™



Lecture outline

- Dendritic cells: antigen capture and presentation
- The role of the MHC
- Antigen processing pathways

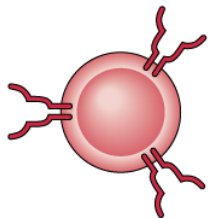
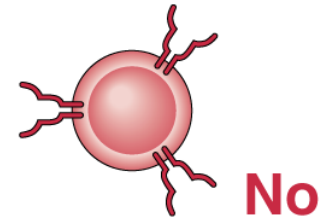
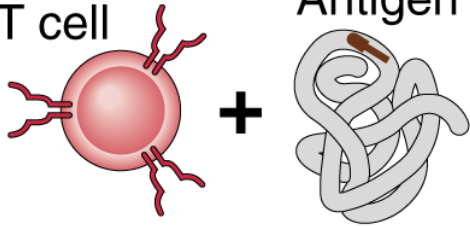
What do T cells see?

Antigen recognition

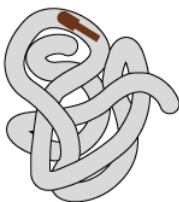
T cell response

CD4⁺
T cell

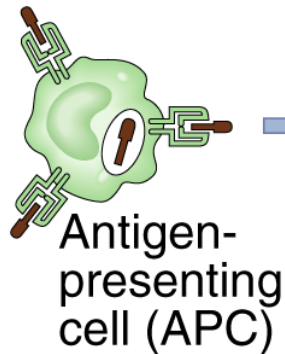
Antigen



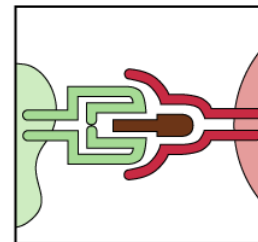
+



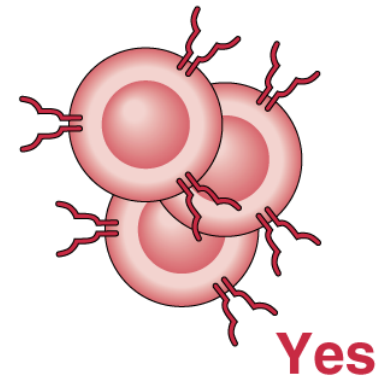
+



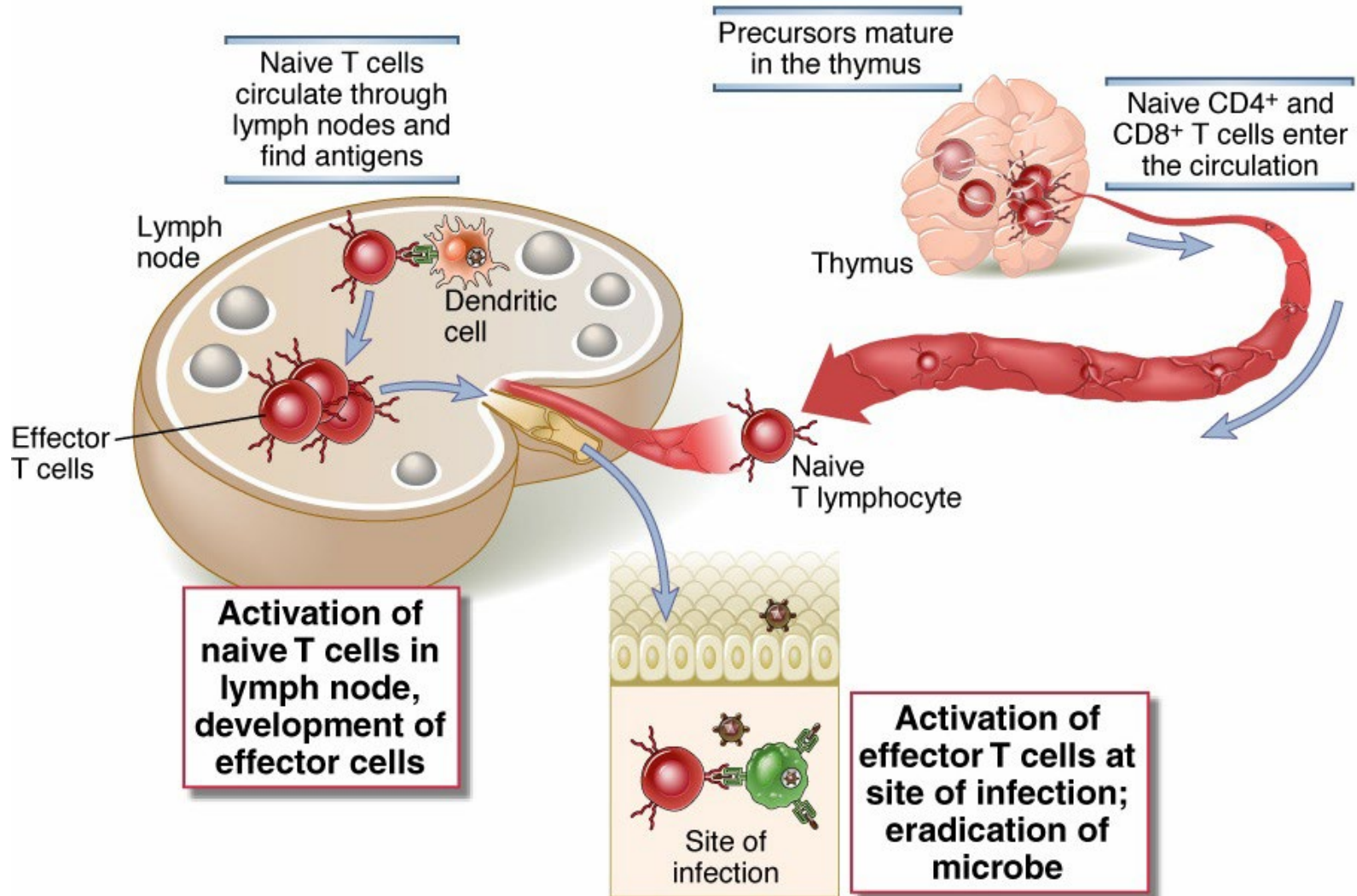
Antigen-
presenting
cell (APC)



Peptide epitope of
antigen presented
by APC



The life history of T lymphocytes



The challenge of finding antigens

- Antigens can enter through any epithelium or be produced in any tissue
- Very few naïve lymphocytes are specific for any one antigen
 - Specificity and diversity of antigen receptors: T and B lymphocytes recognize $10^6 - 10^9$ antigens; total number of cells is about 10^{12} ; therefore, few naïve lymphocytes with the same receptors
 - Too few cells to patrol all epithelia and tissues

The challenge of finding antigens

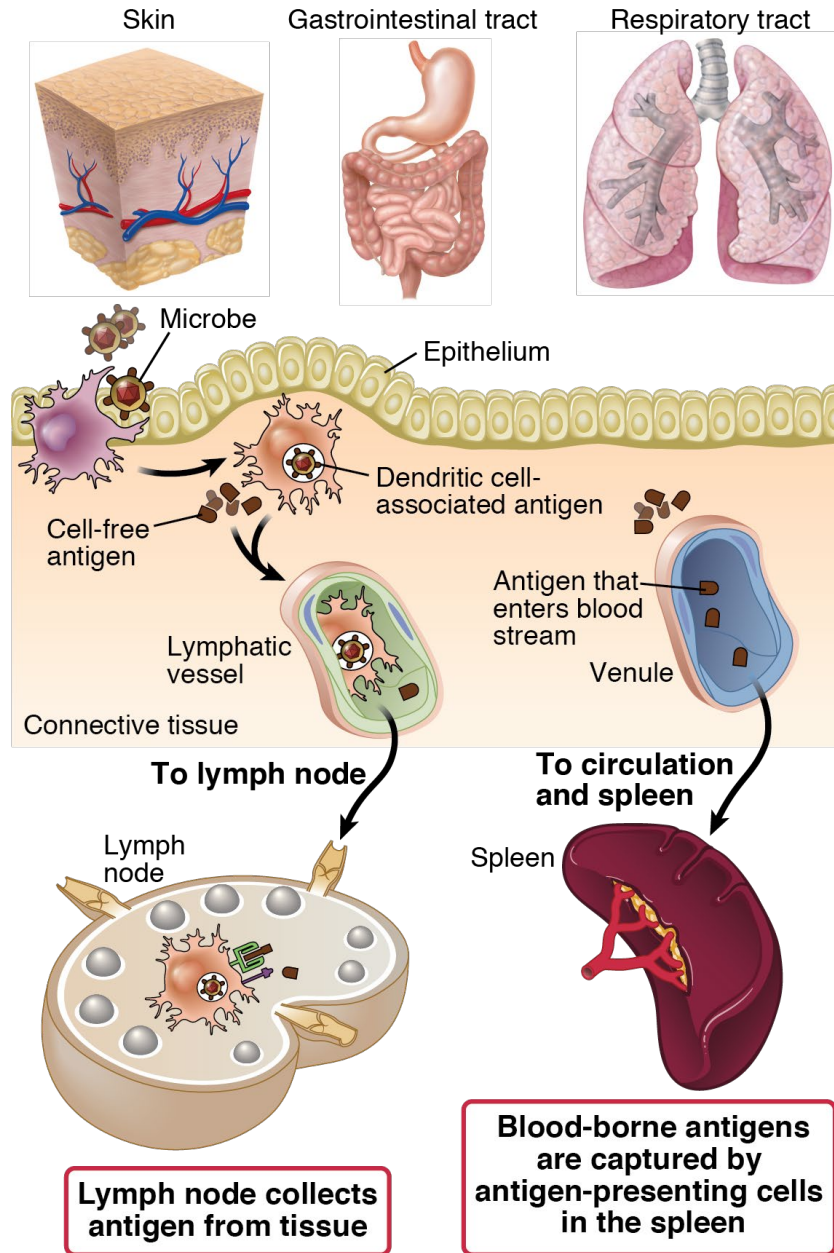
- Therefore, antigens and naïve lymphocytes have to be brought together to begin the immune response
 - The function of secondary lymphoid organs, especially lymph nodes
- Two key adaptations:
 - Dendritic cells capture antigens and take them to lymph nodes
 - Naïve T cells express homing receptors that force them to circulate through lymph nodes

Capture of antigens

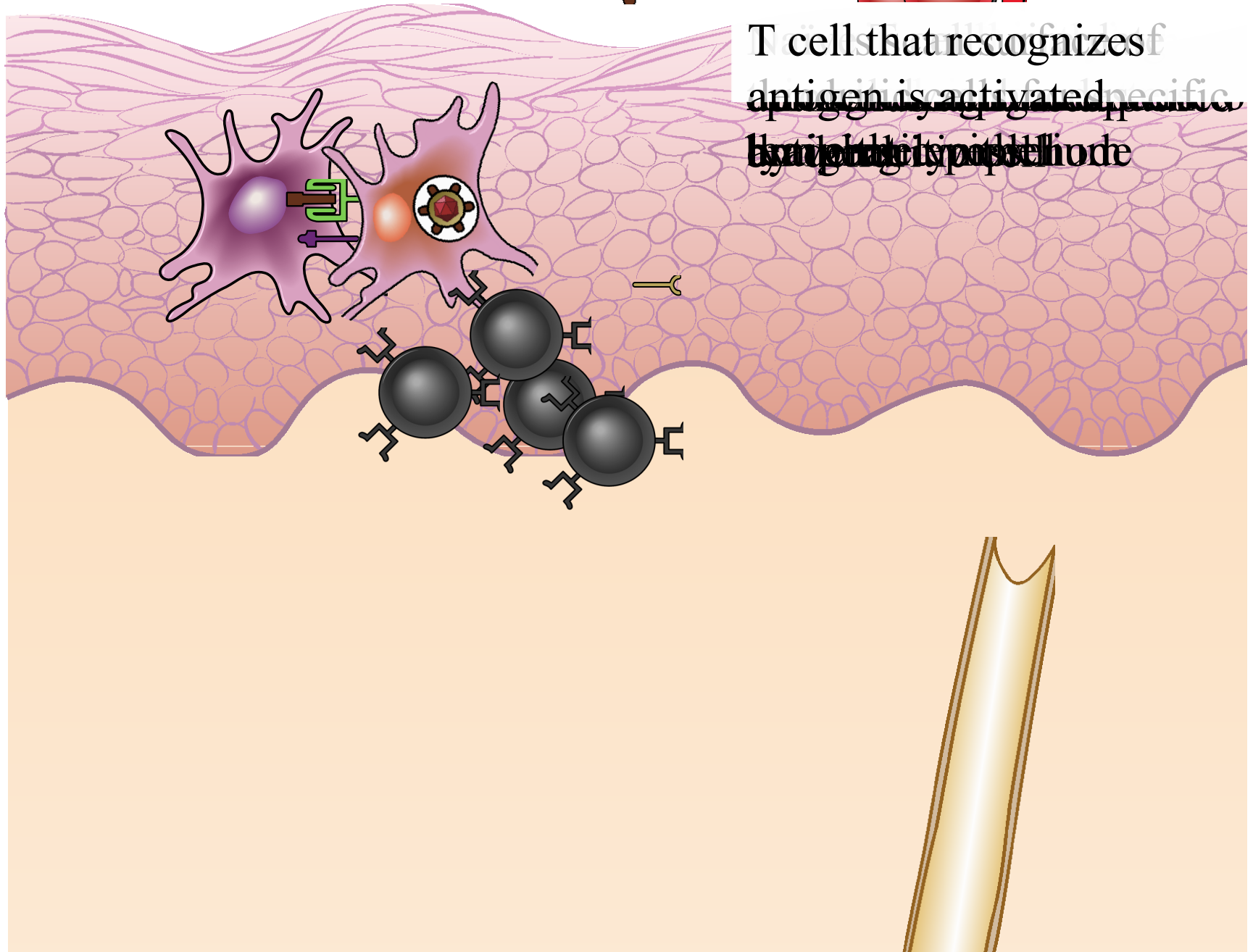
Sites of antigen entry

Sites of initial antigen capture

Sites of antigen collection and capture



Capture and presentation of antigens by dendritic cells



T cell that recognizes specific antigen is activated by dendritic cell

Why are dendritic cells the most efficient APCs for initiating immune responses?

- **Location:** at sites of microbe entry (epithelia), tissues
- **Migration to T cell zones of lymphoid organs**
 - Role of CCR7
 - Co-localize with naïve T cells
- **Receptors for capturing and reacting to microbes:** Toll-like receptors, other receptors
- **Practical application:** dendritic cell-based vaccines for tumors

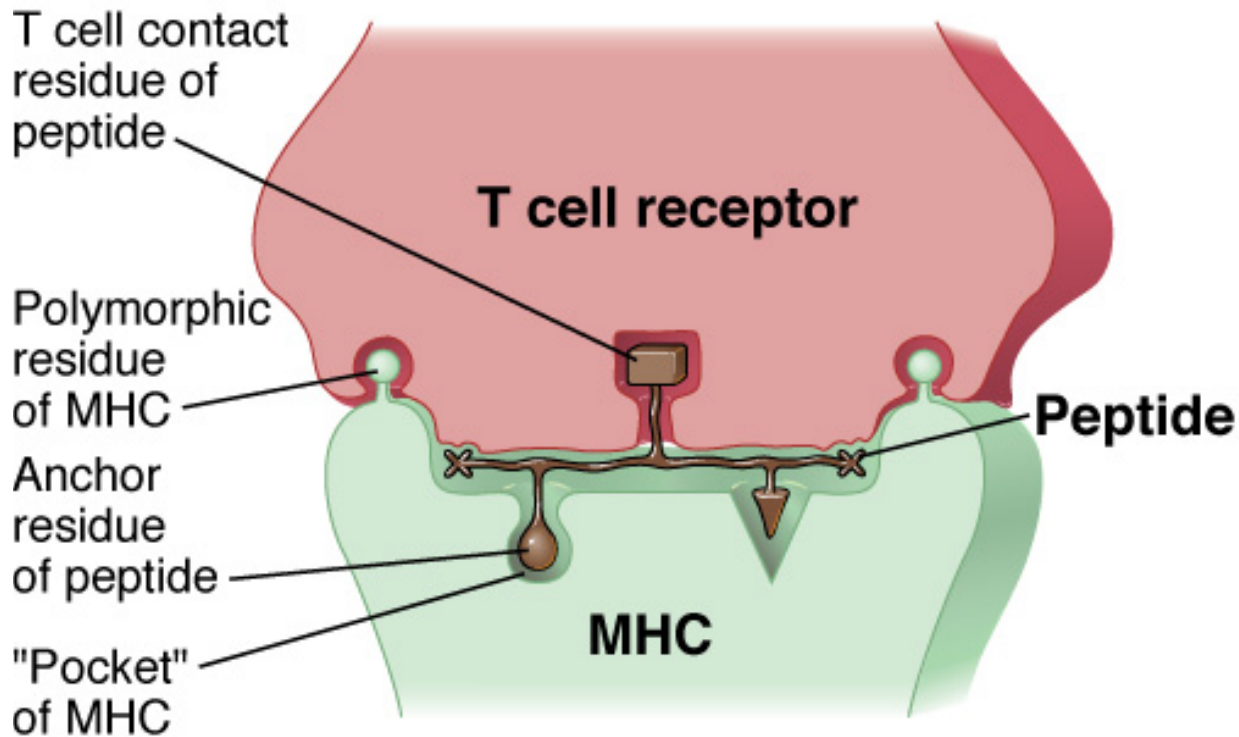
Dendritic cell subsets

- **Conventional (Classical)**: located in epithelia (site of microbe entry) and tissues, role in capture and presentation of most antigens
 - Type 1 (**cDC1**): cross-presentation to CD8+ T cells
 - Type 2 (**cDC2**): presentation of ingested antigens to CD4+ T cells
- **Plasmacytoid**: source of type I IFN (anti-viral); capture of antigens in blood
- **Monocyte derived**: in inflammatory reactions; physiologic role?

What do T cells see?

- **T cells respond to intracellular microbes; how can antigen receptors see antigens inside cells**
 - Intracellular antigens are displayed on the cell surface in a form that can be recognized by T cell antigen receptors (peptide-MHC complexes)
 - MHC also determines what types of antigens are seen by CD4+ and CD8+ T cells
- **Different classes of T cells see antigens from different sources**
 - CD4+ helper T cells recognize antigens that are ingested from the outside
 - CD8+ cytotoxic (killer) T lymphocytes recognize antigens that are produced inside cells

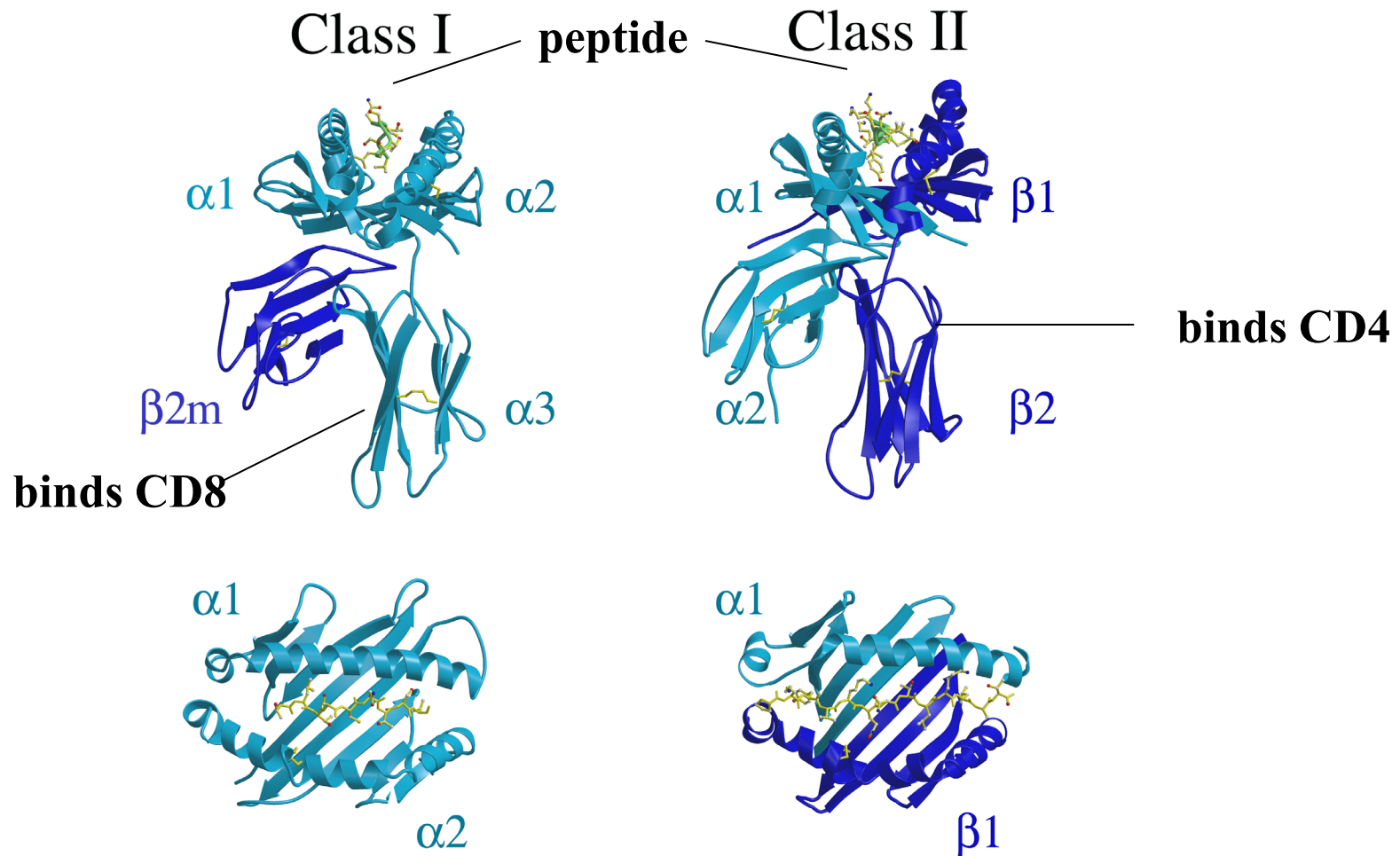
A model of T cell recognition of peptide displayed by an MHC molecule



Human MHC = HLA

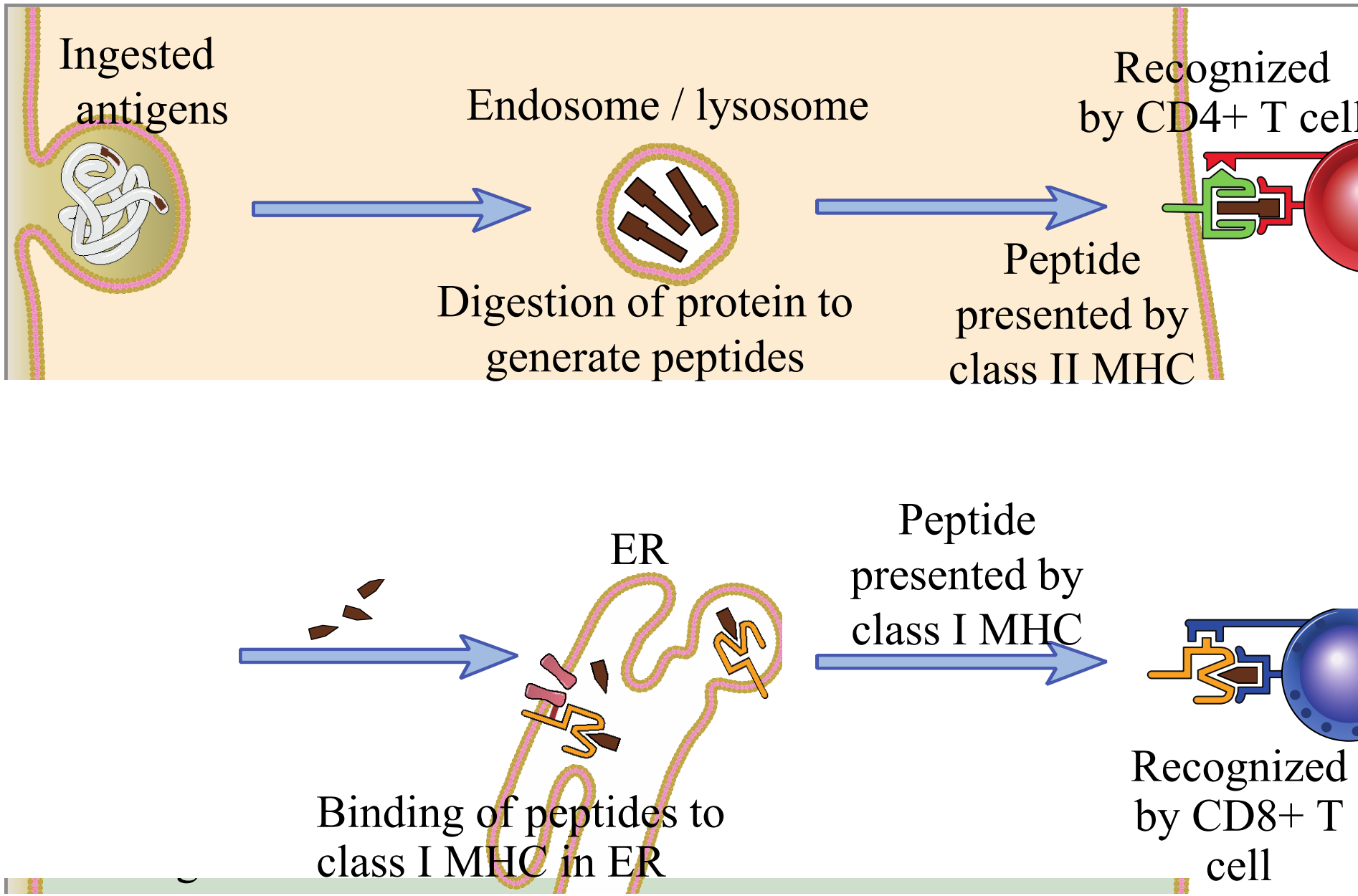
Because MHC molecules are on cells and can display only peptides, T lymphocytes can recognize only cell-associated protein antigens

MHC Structures

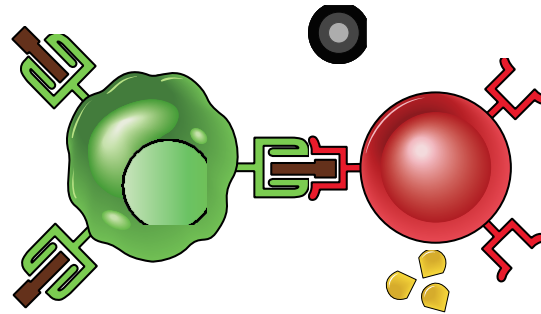


All MHC molecules have a similar basic structure: the cleft at the N-terminal region binds peptide antigens and is recognized by T cell receptors and the membrane-proximal domain binds CD4 or CD8.

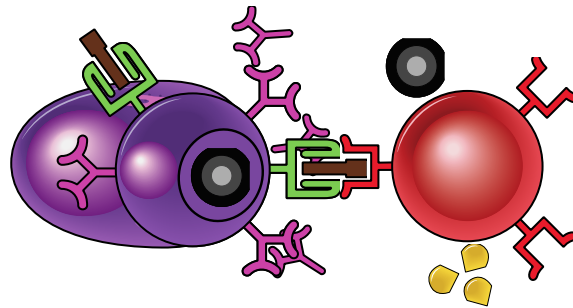
Pathways of antigen processing



Functional importance of class II MHC-associated antigen presentation

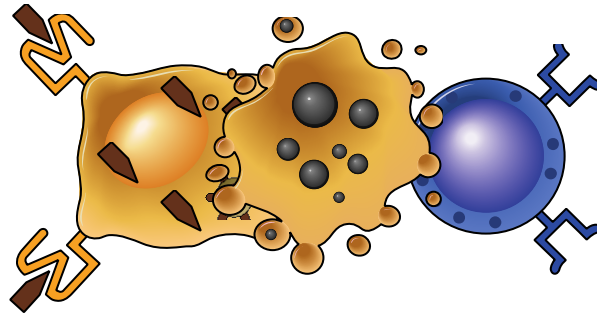


CD4+ T cells secrete cytokines that activate macrophage to destroy
 Microorganisms and present antigens by class II MHC
 ingested microbe



CD4+ T cells secrete cytokines that activate B cells to
 Antigen presentation by class II MHC
 differentiate into antibody secreting plasma cells

Functional importance of class I MHC-associated antigen presentation

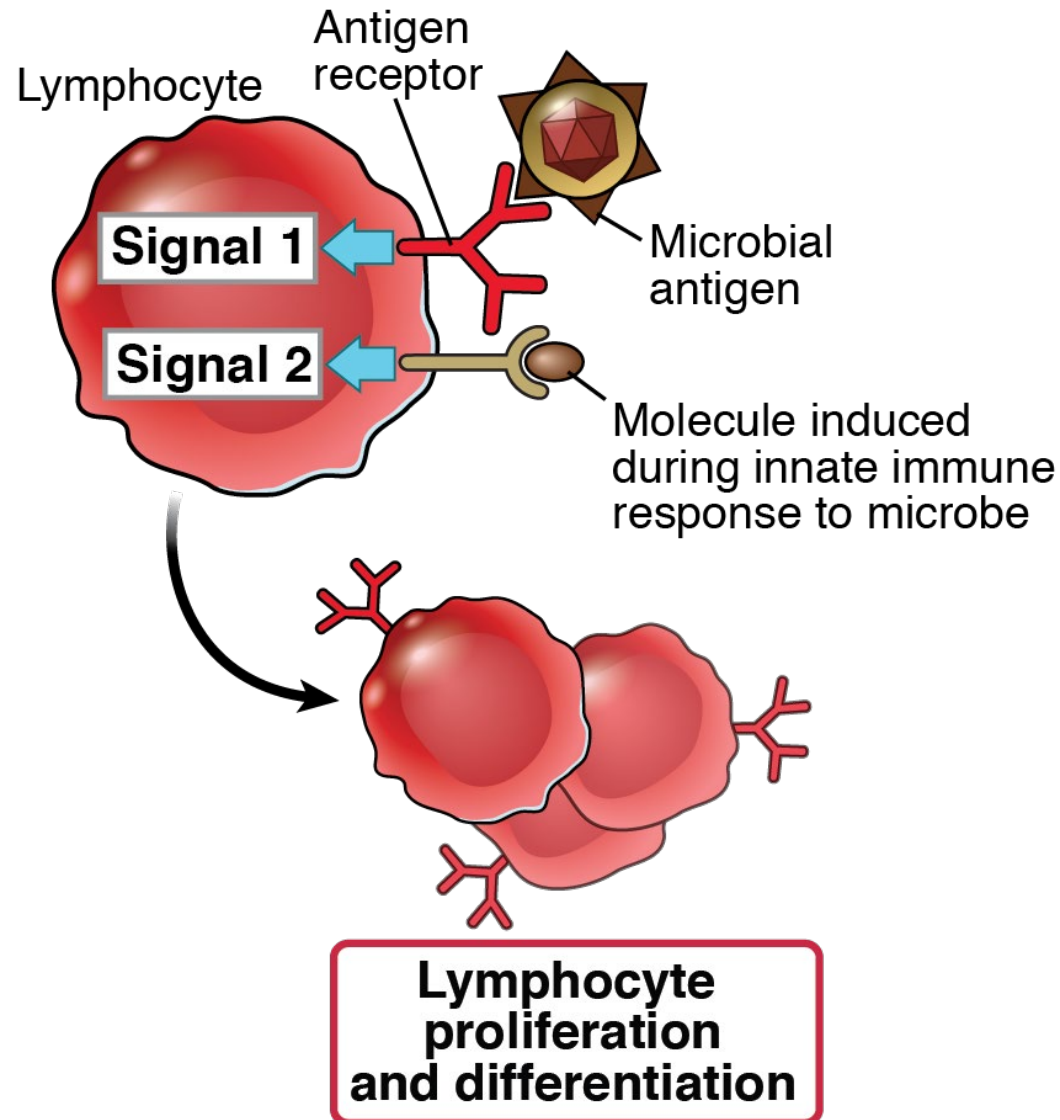


Antigen presentation by class I MHC to CD8⁺ cytotoxic T cells (CTLs)

Functions of antigen-presenting cells

- Capture antigens and take them to the "correct" place
 - Antigens are concentrated in peripheral lymphoid organs, through which naïve lymphocytes circulate
- Display antigens in a form that can be recognized by specific lymphocytes
 - MHC-associated peptides: cytosolic peptides to class I, vesicular peptides to class II
- Provide "second signals" for T cell activation
 - Critical for initiation of responses

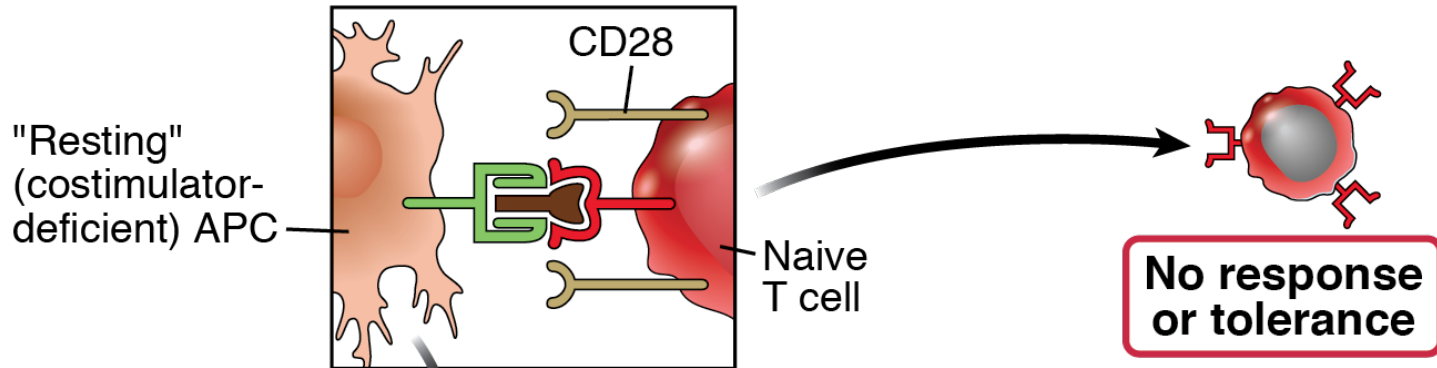
The two-signal requirement for lymphocyte activation



Role of costimulation in T cell activation

Antigen recognition

T cell response



Activation of APCs by microbes, innate immune response

