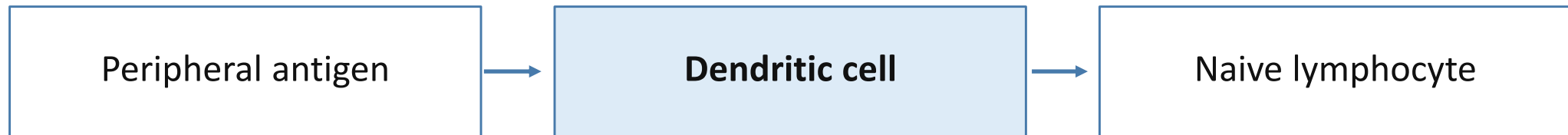


Display and Recognition of Antigens

Normal immune response: mechanisms and clinical correlation



Dr Abu Suraih Sakhri

MBBS, MD (Pathology)

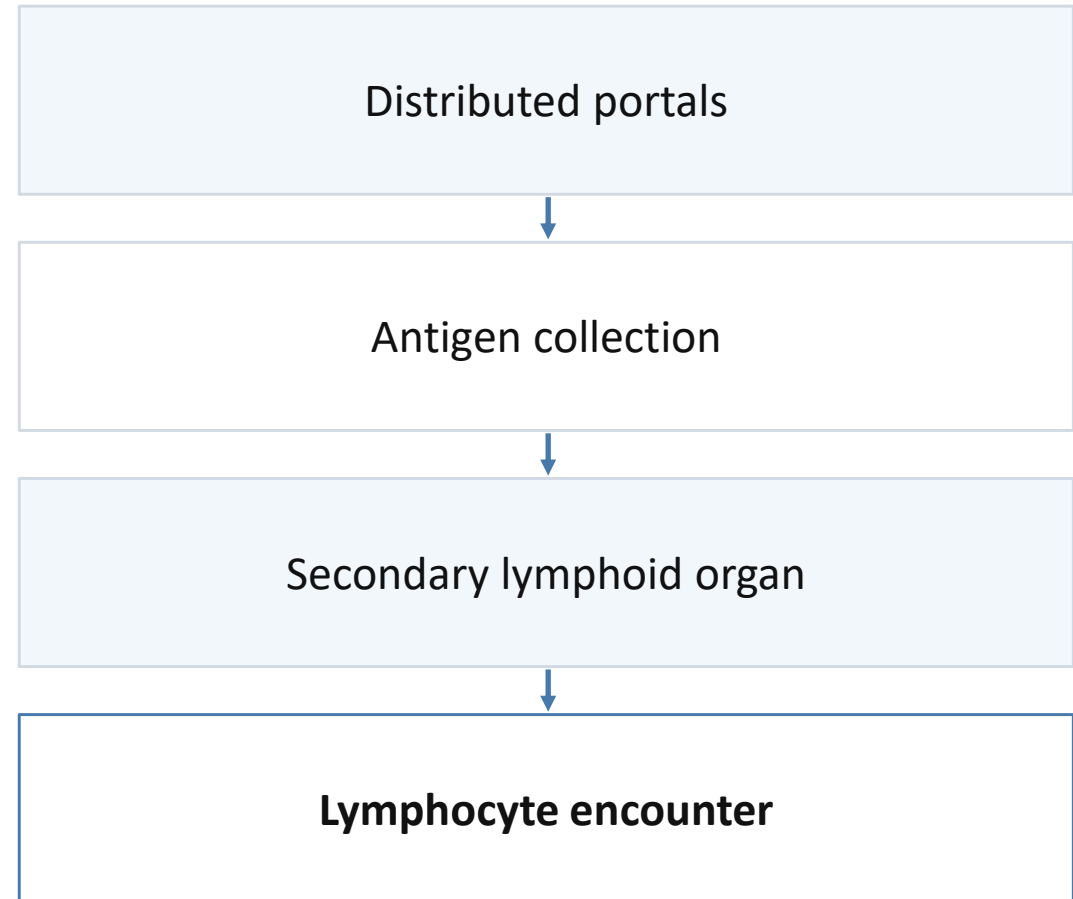
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Learning objectives

- Explain antigen concentration in secondary lymphoid organs.
- Compare MHC I/CD8 and MHC II/CD4 presentation pathways.
- Distinguish TCR recognition of peptide–MHC from BCR recognition of native antigen.
- Explain how innate sensing, B7–CD28 costimulation, and tolerance modify recognition.

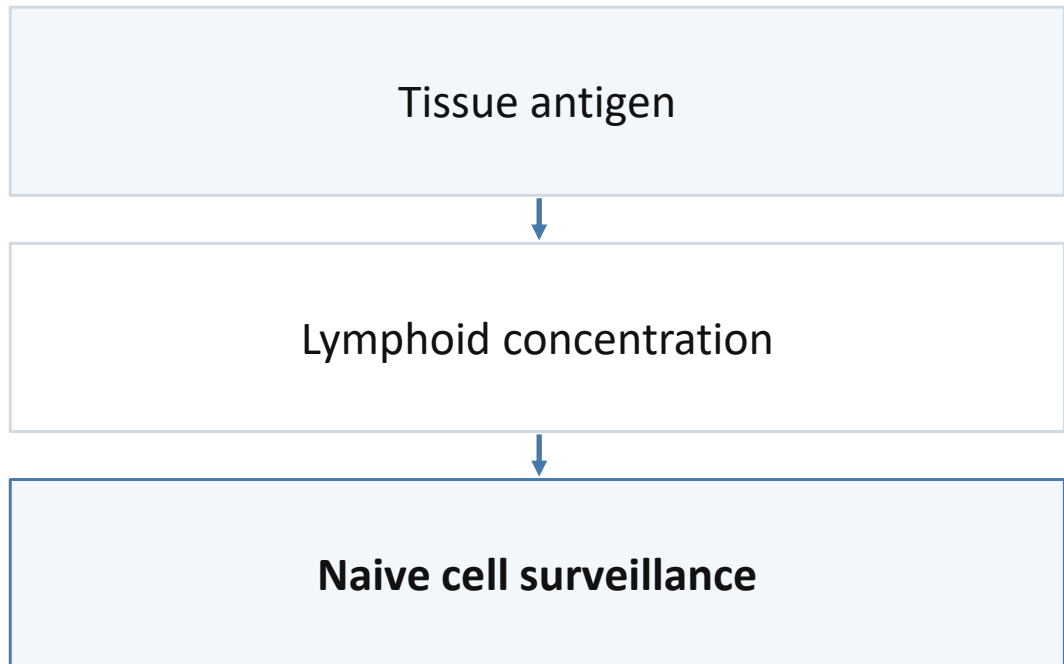
The immune system faces a sampling problem

- Microbes and foreign antigens can enter through many anatomic sites.
- An individual antigen-specific naive lymphocyte is too rare to inspect every site.
- The solution is concentrating captured antigens where recirculating lymphocytes can encounter them.



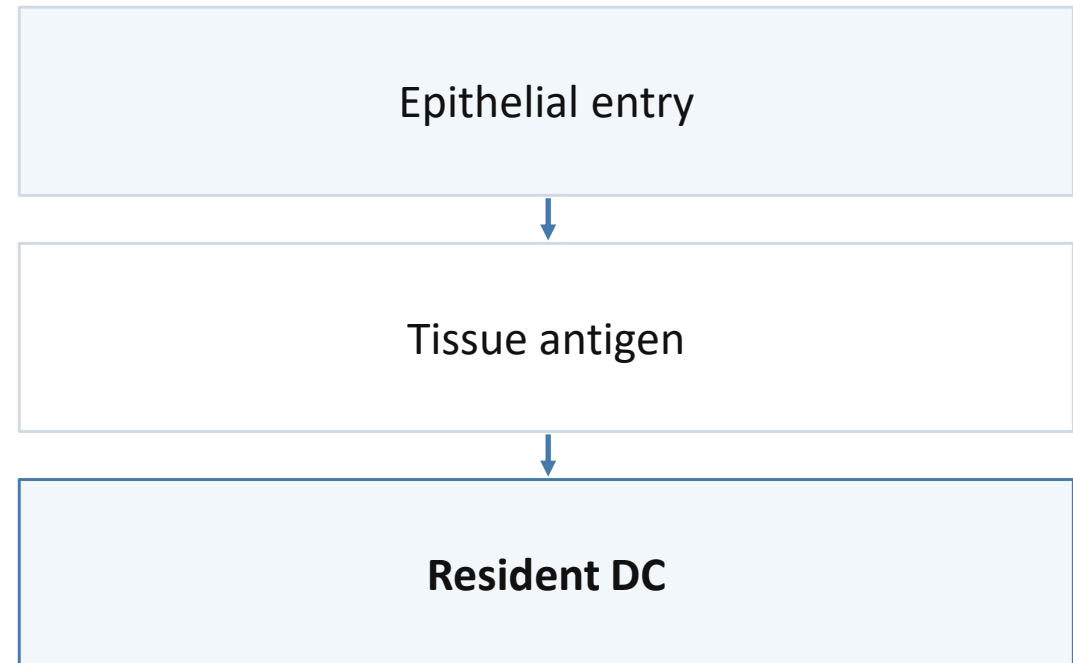
Secondary lymphoid organs concentrate antigens

- Antigens and presenting cells accumulate in regional lymphoid tissues.
- Naive lymphocytes continually pass through these sites.
- Spatial concentration raises the probability of productive recognition.



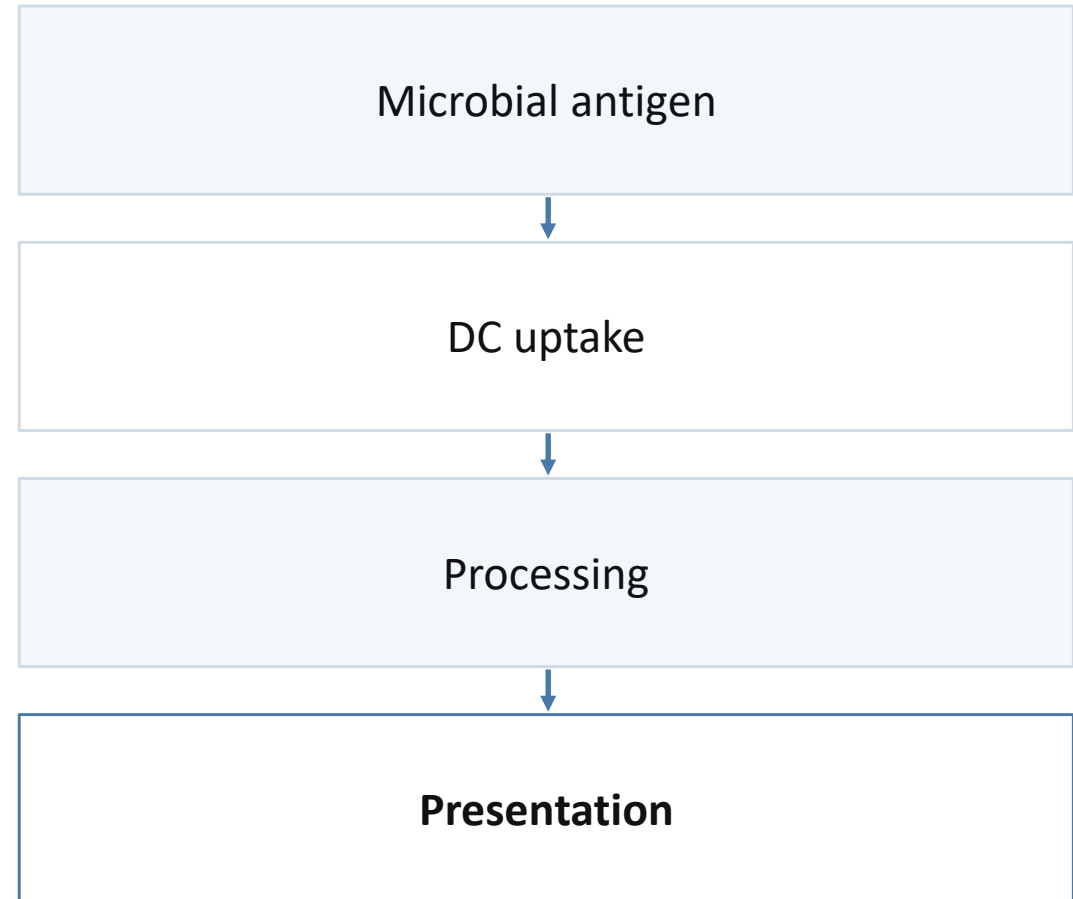
Epithelial surfaces are common portals of entry

- Microbes frequently arrive at epithelial barriers.
- Dendritic cells reside under epithelia and in tissue interstitia.
- These locations make DCs well placed to acquire foreign protein antigens.



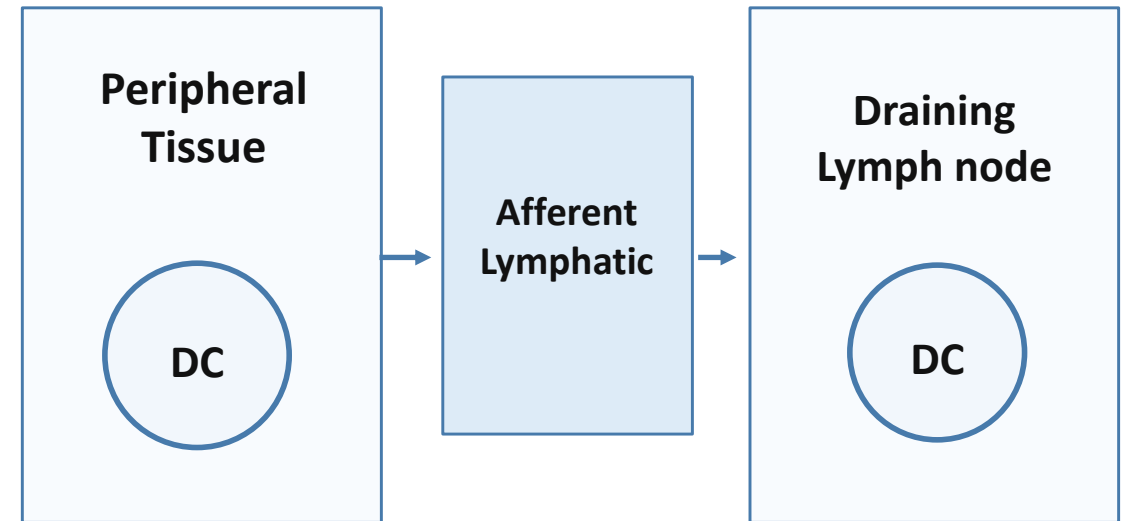
Dendritic cells capture microbial antigens

- Dendritic cells possess receptors for microbial structures, including TLRs and lectins.
- They collect antigens in peripheral tissues.
- Antigen acquisition precedes presentation to naive T cells.



Migrating DCs transport antigenic cargo

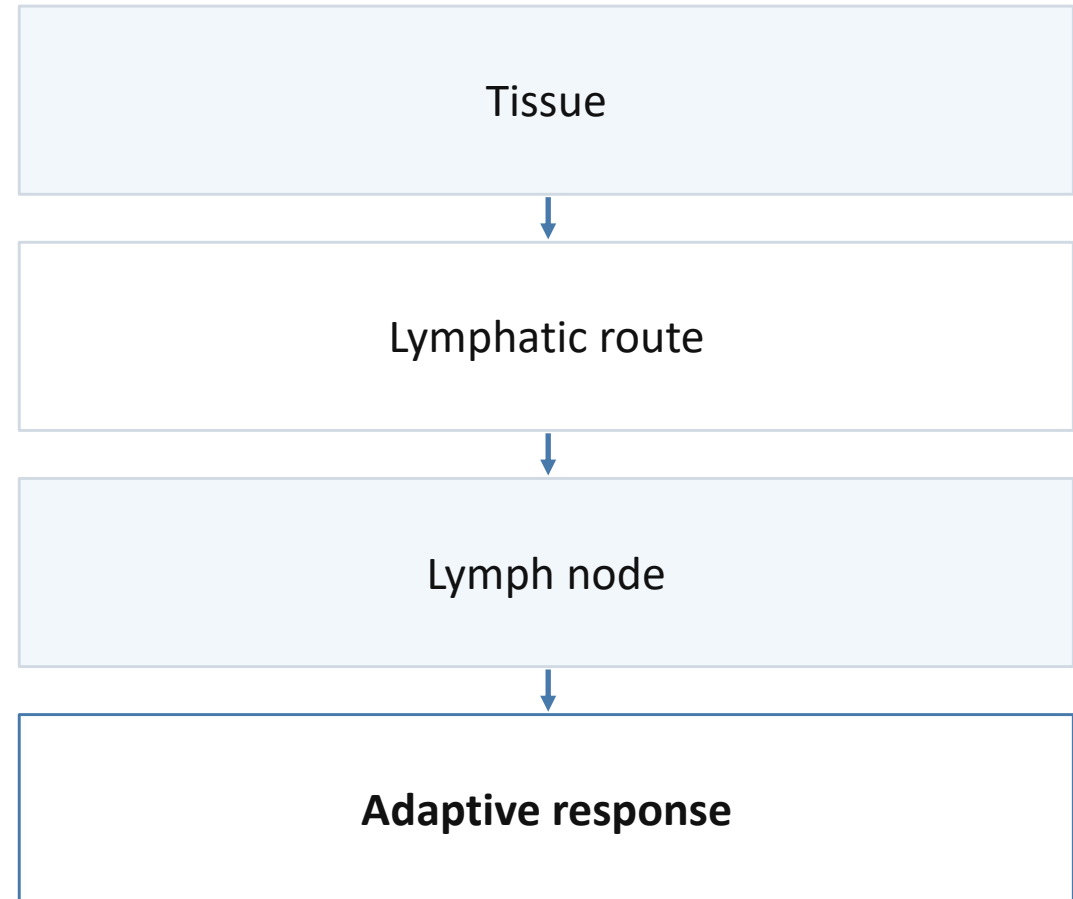
- DCs carrying microbial antigens travel from tissues through lymphatic vessels.
- The destination is the draining lymph node.
- This physically links a peripheral infection with an organized T-cell encounter site.



Migration conveys antigen toward naive T cells

Lymph nodes specialize in tissue-derived antigens

- Lymph draining tissues reaches lymph nodes along lymphatic channels.
- Antigens and antigen-loaded DCs become concentrated in these organs.
- Lymph nodes are key initiation sites for adaptive responses to tissue-entry microbes.



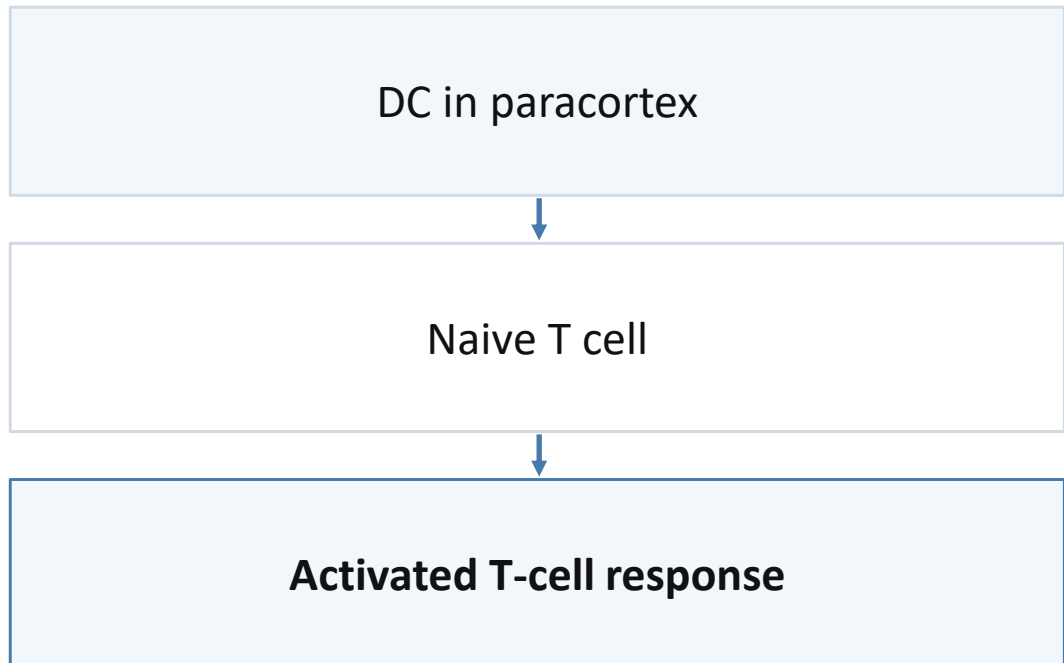
Naive lymphocytes recirculate through lymphoid organs

- Naive lymphocytes search repeatedly through secondary lymphoid tissues.
- Antigen concentration converts a rare receptor–ligand encounter into a feasible event.
- Circulation and antigen transport solve complementary parts of the surveillance problem.

**Antigen delivered to node < Naive cell
Arrives through circulation**

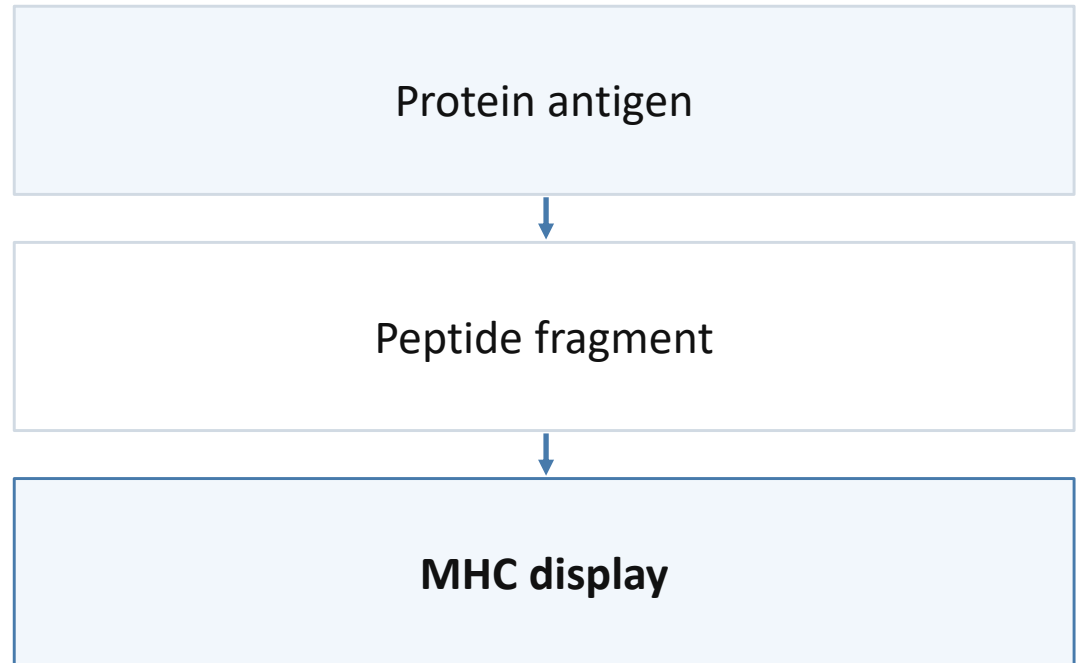
Recognition happens in the correct tissue compartment

- Naive T cells encounter antigen-presenting DCs in T-cell zones of nodes.
- B cells are concentrated in follicles that support humoral responses.
- Regional organization brings each lymphocyte type into contact with its appropriate antigen display.



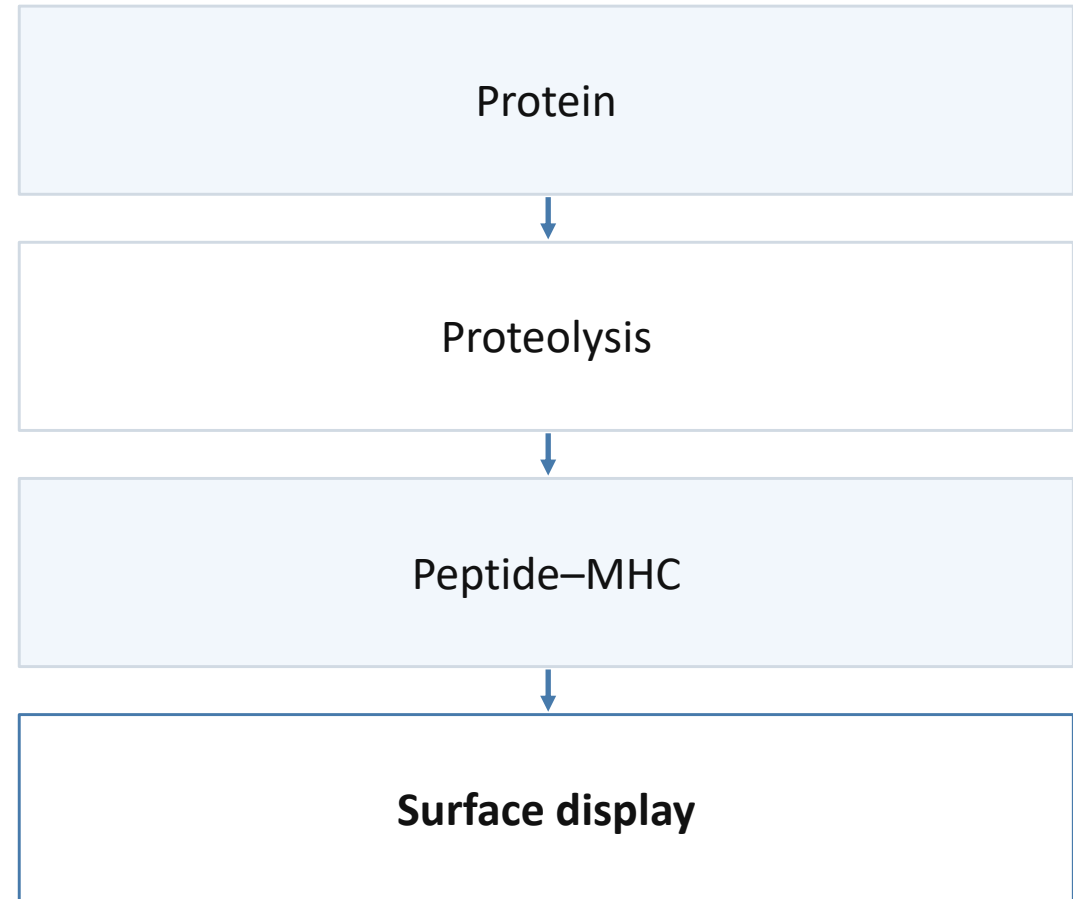
MHC molecules display peptide fragments

- Major histocompatibility complex proteins bind peptides derived from proteins.
- A peptide–MHC complex appears at the cell surface for T-cell scrutiny.
- The antigenic unit recognized by most conventional T cells is peptide plus MHC, not free protein.



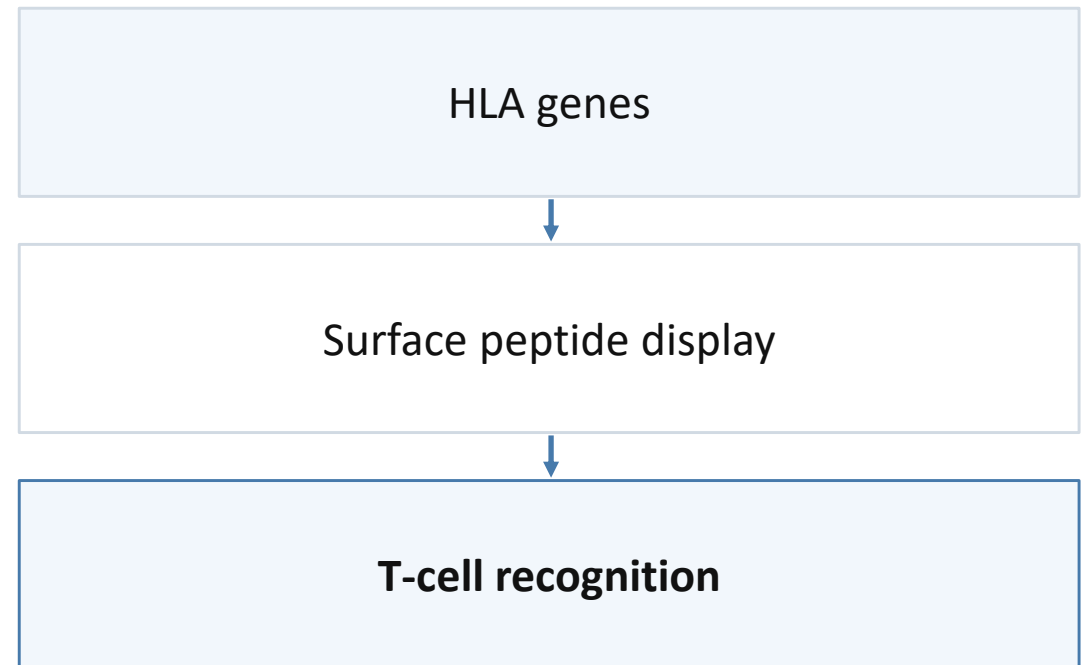
Processing precedes classical T-cell recognition

- Protein antigens are degraded into peptide fragments.
- Peptides associate with MHC proteins inside appropriate cellular compartments.
- Loaded complexes travel to or remain at the plasma membrane for T-cell recognition.



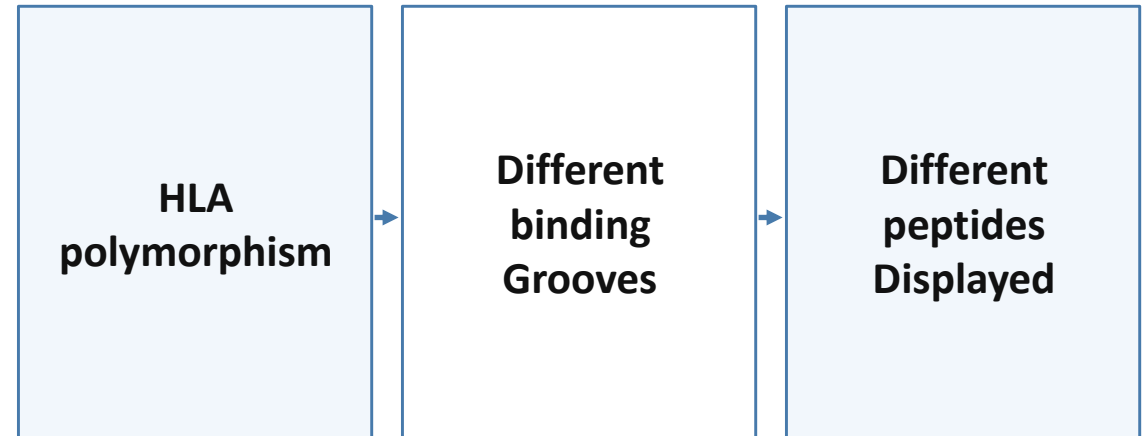
HLA is the human MHC system

- The human major histocompatibility complex is called HLA.
- HLA genes are clustered on chromosome 6.
- Their products were discovered through roles in transplant compatibility.



HLA diversity influences peptide presentation

- MHC genes are highly polymorphic across humans.
- Allelic differences alter which peptides can bind the MHC groove.
- HLA diversity also creates a major biological barrier to organ transplantation.



MHC class I and II divide presentation tasks

- Class I primarily displays peptides from cytosolic proteins to CD8 T cells.
- Class II displays peptides from internalized extracellular proteins to CD4 T cells.
- The separation links antigen origin with appropriate effector-cell selection.

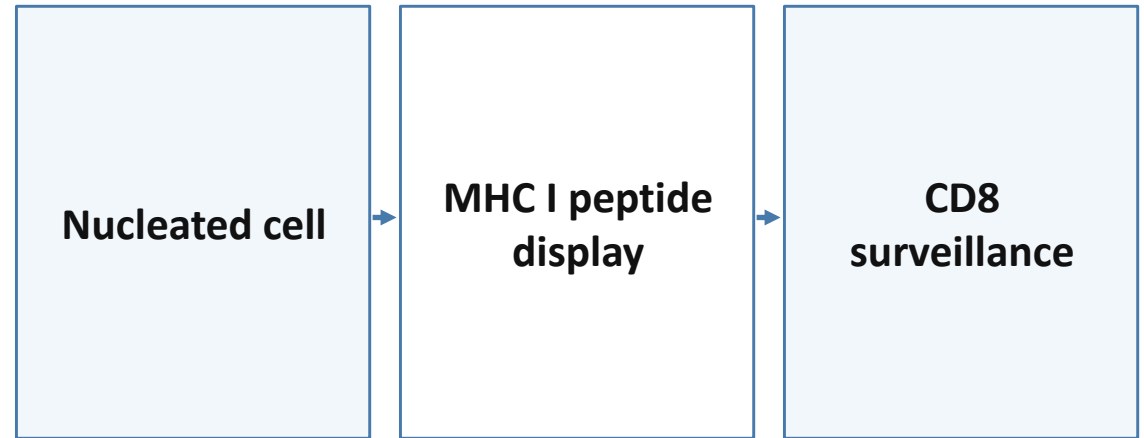
Cytosol → MHC I → CD8

Compared with

Endosome → MHC II → CD4

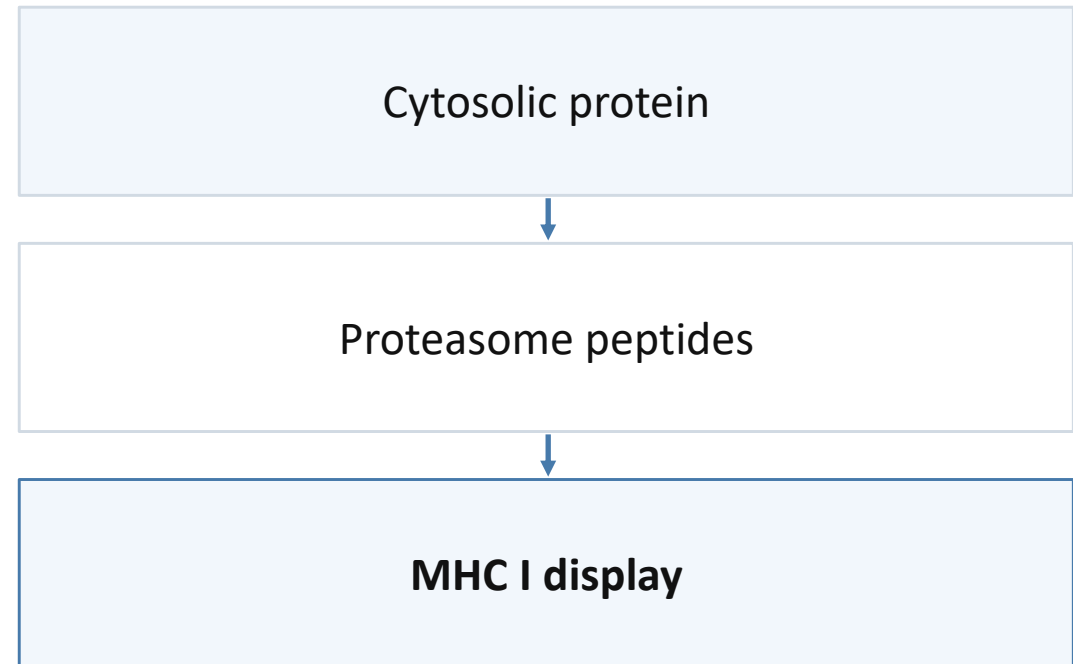
MHC class I distribution supports immunosurveillance

- MHC I occurs on all nucleated cells and platelets.
- Viruses may infect many nucleated cell types, and tumors can arise in them.
- Broad expression enables cytotoxic T cells to inspect diverse tissues.



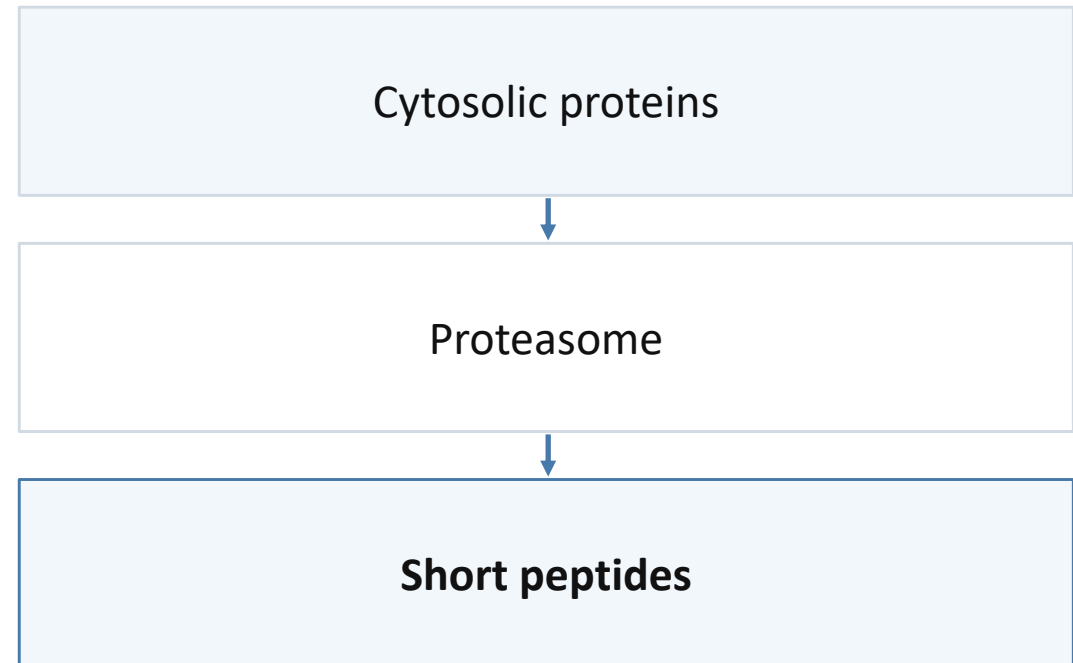
Class I peptides originate in the cytosol

- Cytosolic proteins include viral and abnormal tumor proteins.
- These proteins become substrates for peptide generation.
- The resulting fragments enter the MHC class I presentation pathway.



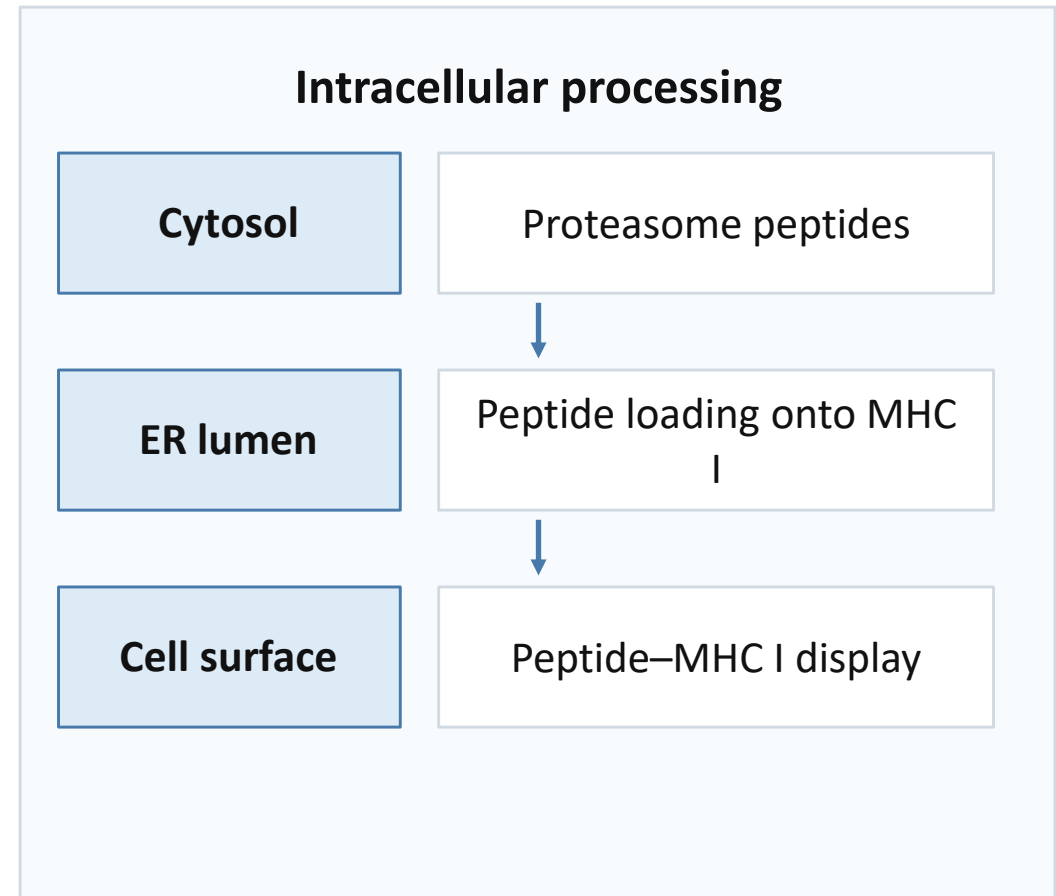
Proteasomes generate class I peptides

- Cytosolic proteins are degraded in proteasomes.
- Peptides produced by this degradation can enter the class I-loading pathway.
- Proteasomal processing is upstream of peptide transport to the ER.



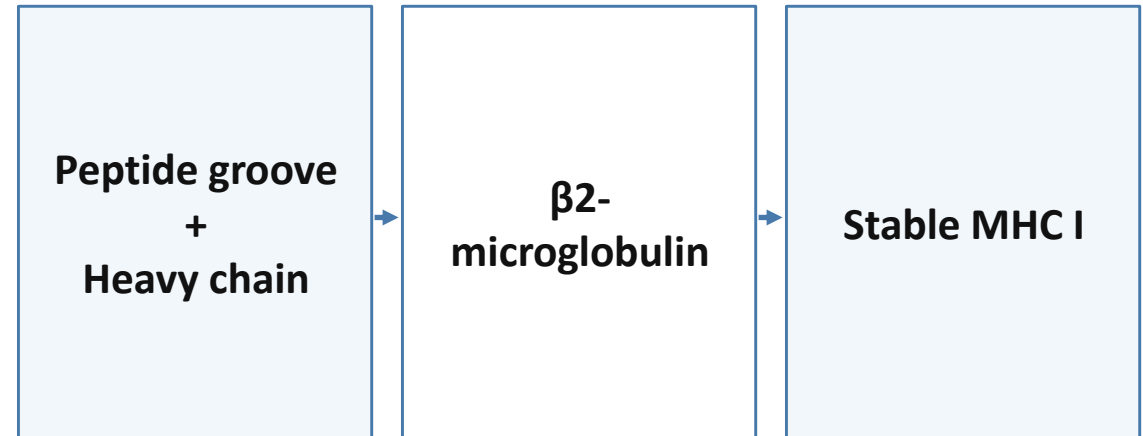
Class I loading occurs in the ER

- Peptides from the cytosol are transported into the endoplasmic reticulum.
- There they associate with newly synthesized MHC I proteins.
- Stable complexes subsequently reach the cell surface.



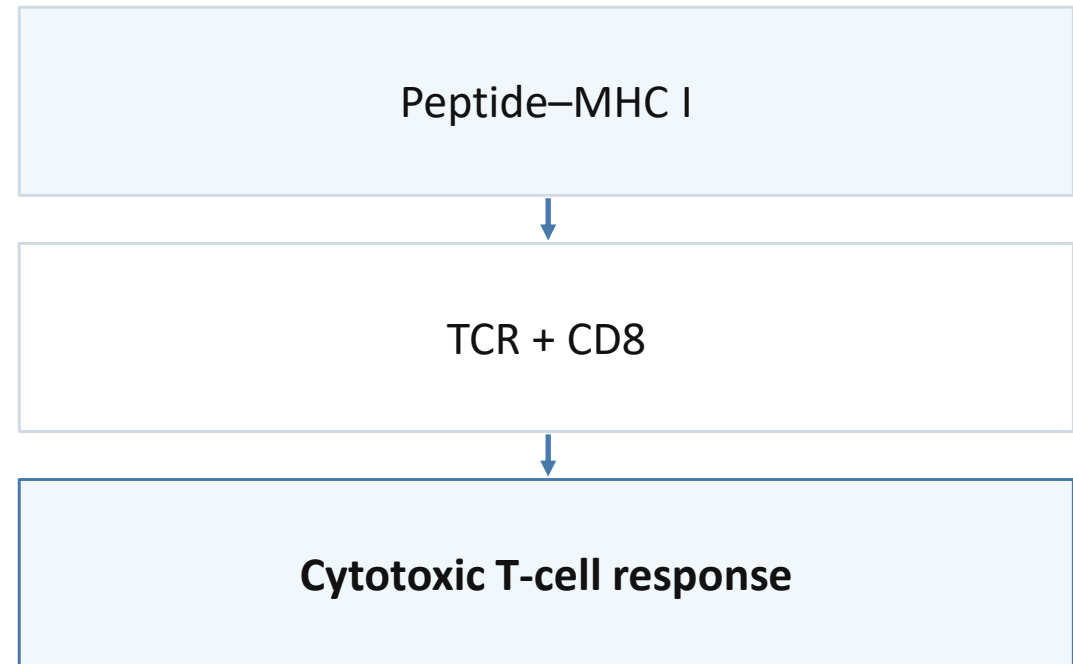
MHC I includes β 2-microglobulin

- The polymorphic MHC I heavy chain associates with β 2-microglobulin.
- The α 1 and α 2 domains form the peptide-binding groove.
- The α 3 domain provides a binding site for the CD8 coreceptor.



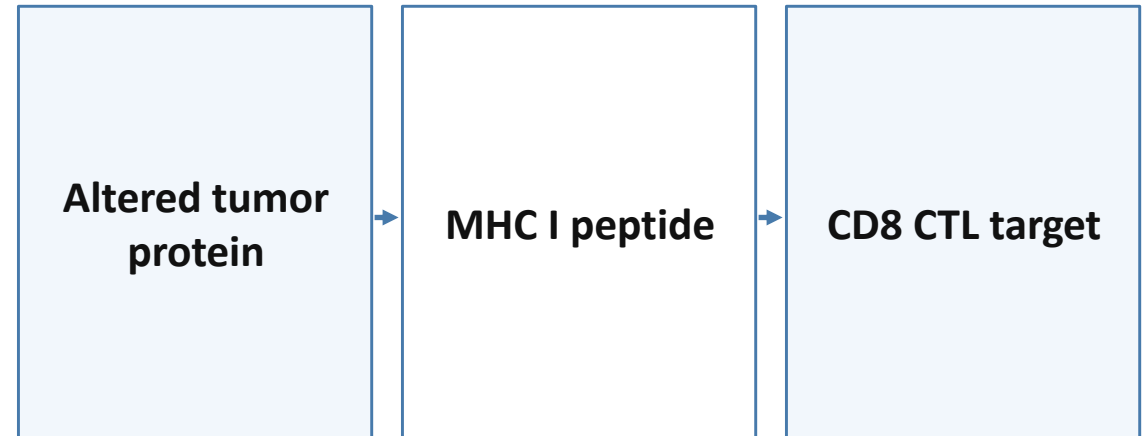
CD8 T cells recognize class I complexes

- A T-cell receptor contacts the peptide–MHC I complex.
- CD8 binds to the nonpolymorphic $\alpha 3$ domain as a coreceptor.
- Recognition can license cytotoxic action after appropriate activation.



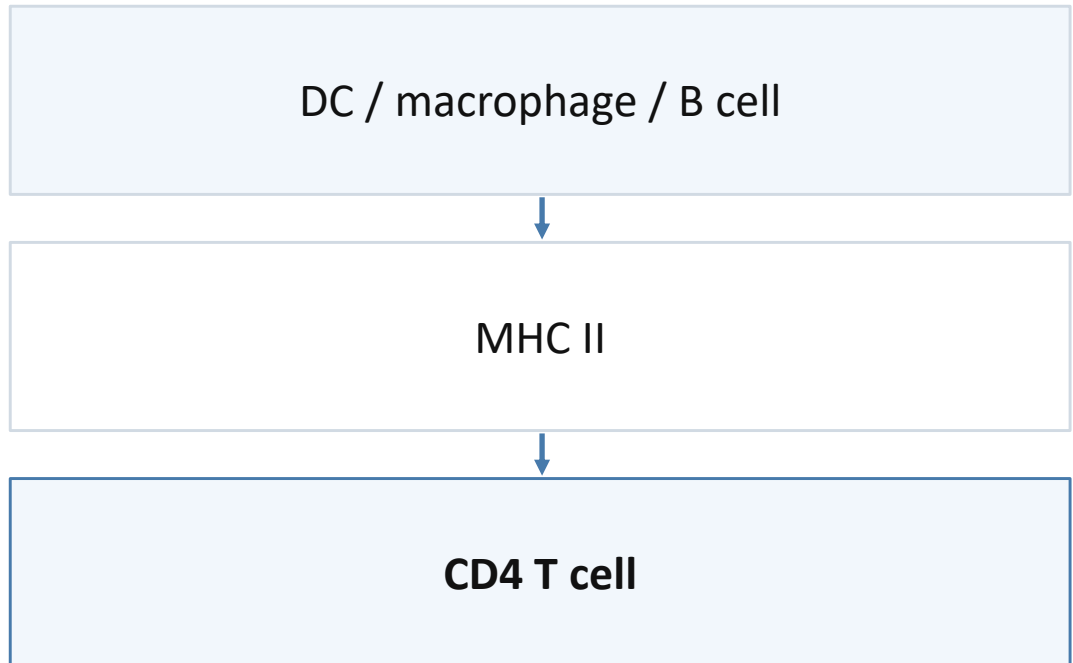
Tumor recognition can use the class I pathway

- Abnormal or mutated proteins in tumor cells can yield antigenic peptides.
- These peptides may be displayed by MHC class I.
- Cytotoxic T lymphocytes can recognize and kill tumor cells displaying such antigens.



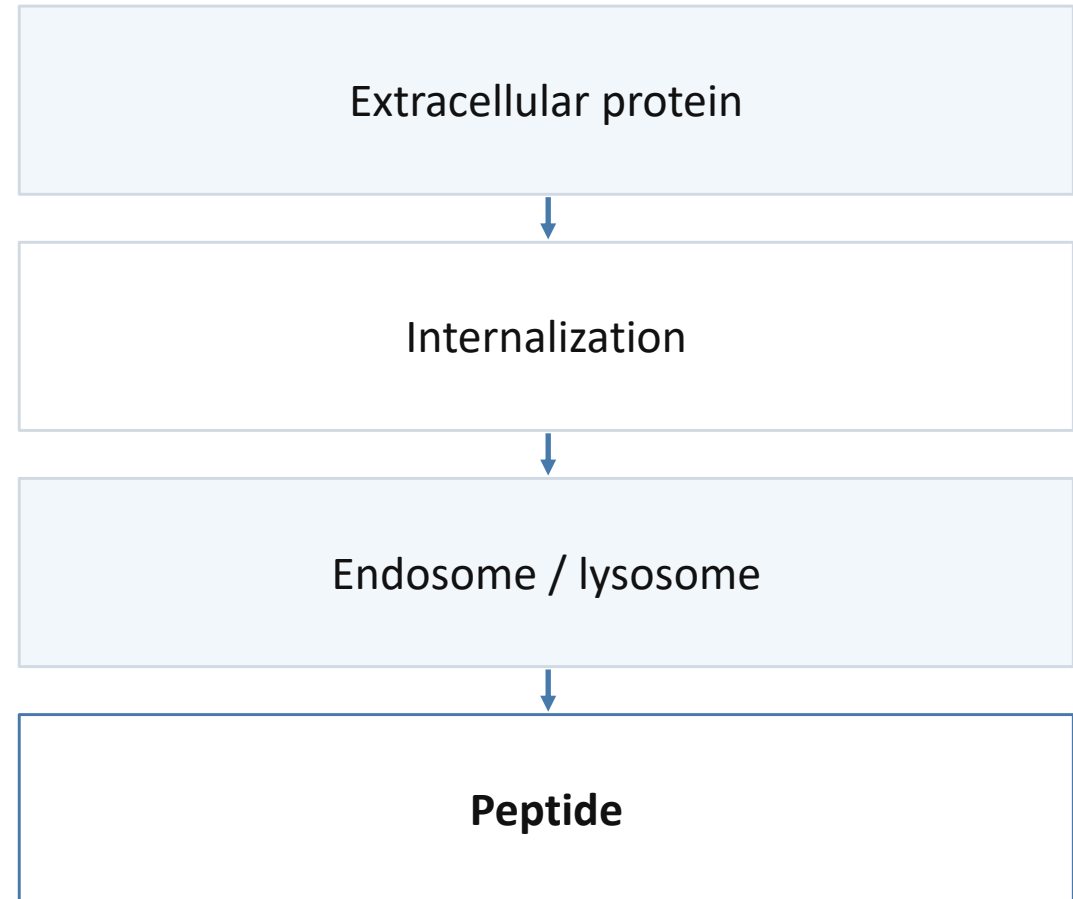
MHC class II expression is more restricted

- MHC II is especially associated with professional antigen-presenting cells.
- Dendritic cells present protein peptides to naive CD4 T lymphocytes.
- Macrophages and B cells can display antigen to helper T cells during effector responses.



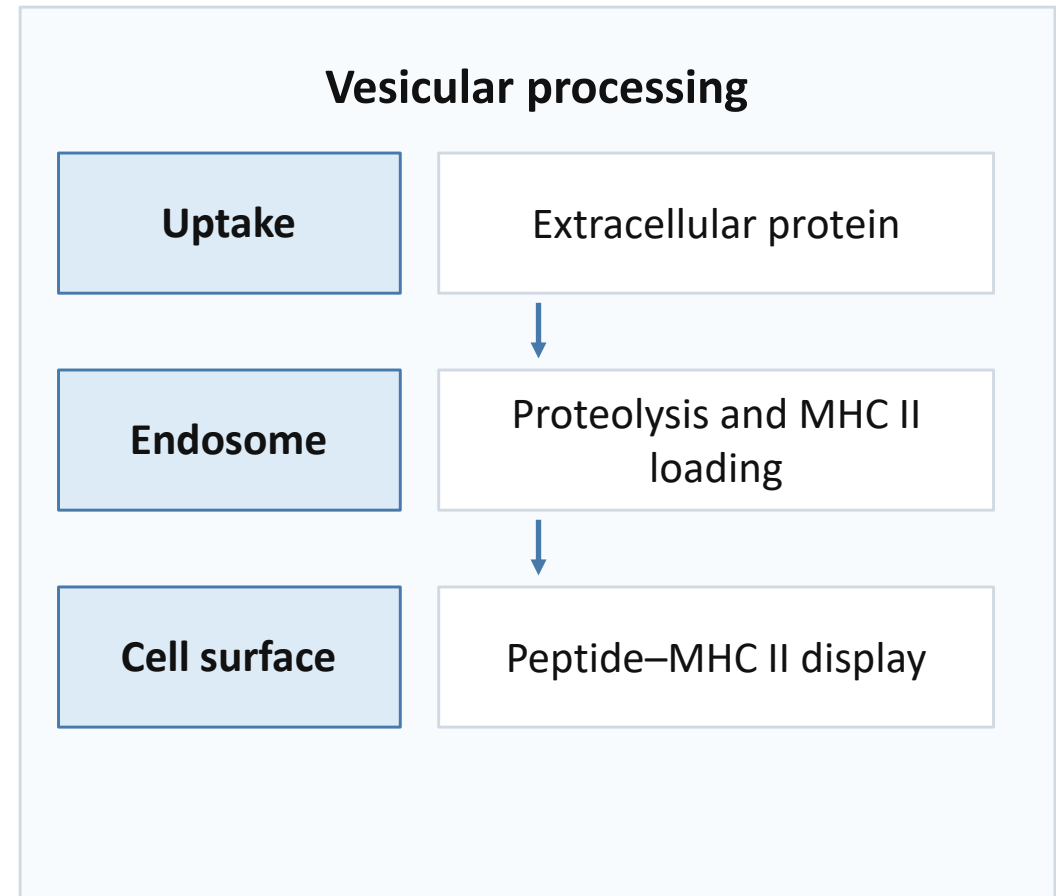
Class II antigen typically starts outside the cell

- Extracellular microbes and proteins can be taken up by presenting cells.
- They are delivered to endosomal or lysosomal compartments.
- Proteolysis there prepares peptides for MHC II binding.



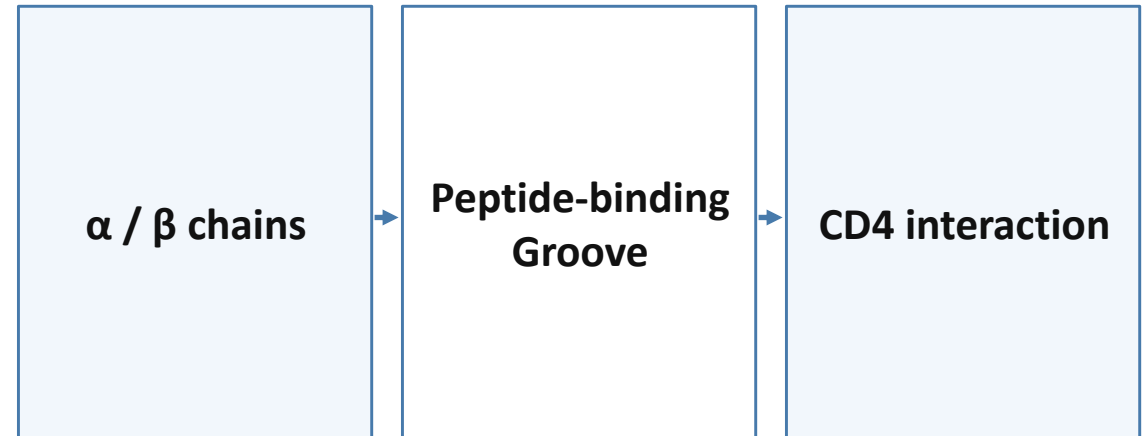
Class II loading occurs in vesicles

- Internalized proteins are broken down in intracellular vesicles.
- The resulting peptides bind MHC II heterodimers.
- Peptide–MHC II complexes then reach the cell surface.



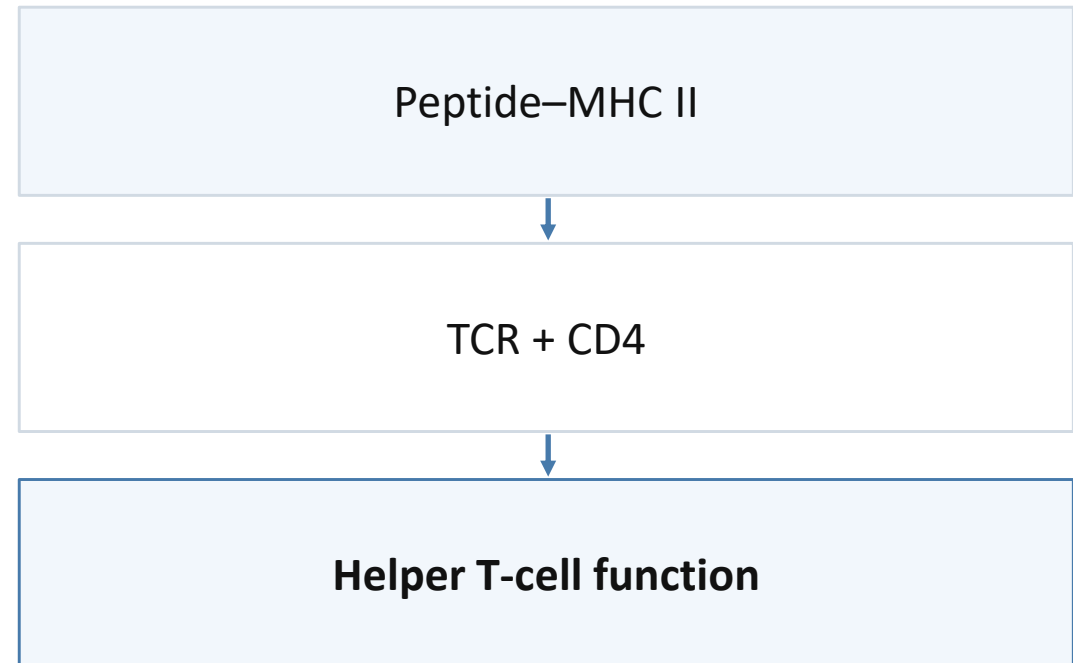
MHC II consists of two polymorphic chains

- Class II proteins contain an α chain and a β chain.
- The $\alpha 1$ and $\beta 1$ domains form the peptide-binding cleft.
- The $\beta 2$ domain supports binding of the CD4 coreceptor.



CD4 T cells recognize class II complexes

- The TCR recognizes the specific peptide–MHC II complex.
- CD4 provides a coreceptor interaction with MHC II.
- Activated helper cells can subsequently signal to macrophages or B cells.



MHC restriction explains T-cell recognition

- CD8 T cells are class I restricted in conventional antigen recognition.
- CD4 T cells are class II restricted in conventional antigen recognition.
- A peptide alone is not equivalent to the peptide–MHC ligand seen by the TCR.

MHC I + peptide → CD8

Compared with

MHC II + peptide → CD4

Endogenous and exogenous antigen pathways

- Endogenous proteins enter the class I proteasome–ER route.
- Internalized extracellular proteins enter the class II vesicular route.
- This is a fundamental organizing principle, not a claim that every pathway lacks exceptions.

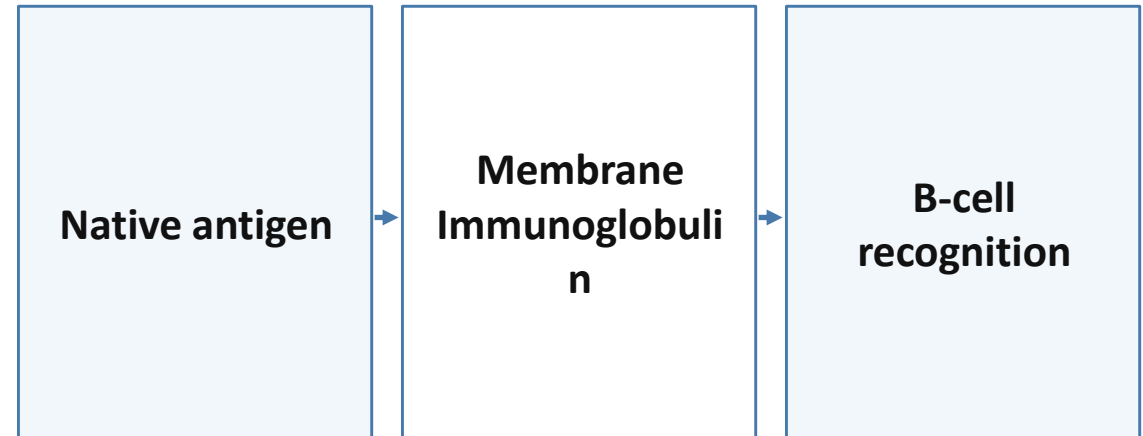
Cytosol/proteasome/ER

Compared with

Endosome/lysosome/MHC II

B cells detect antigen without classical peptide–MHC restriction

- The B-cell receptor is membrane-bound antibody.
- It binds native antigens of several chemical types.
- Recognized antigens may be proteins, polysaccharides, or lipids.



T-cell and B-cell antigen recognition differ

- Conventional T cells recognize processed peptides displayed by MHC.
- B cells recognize native antigen with their membrane immunoglobulin receptor.
- A B cell can later internalize a protein and present peptide–MHC II to helper T cells.

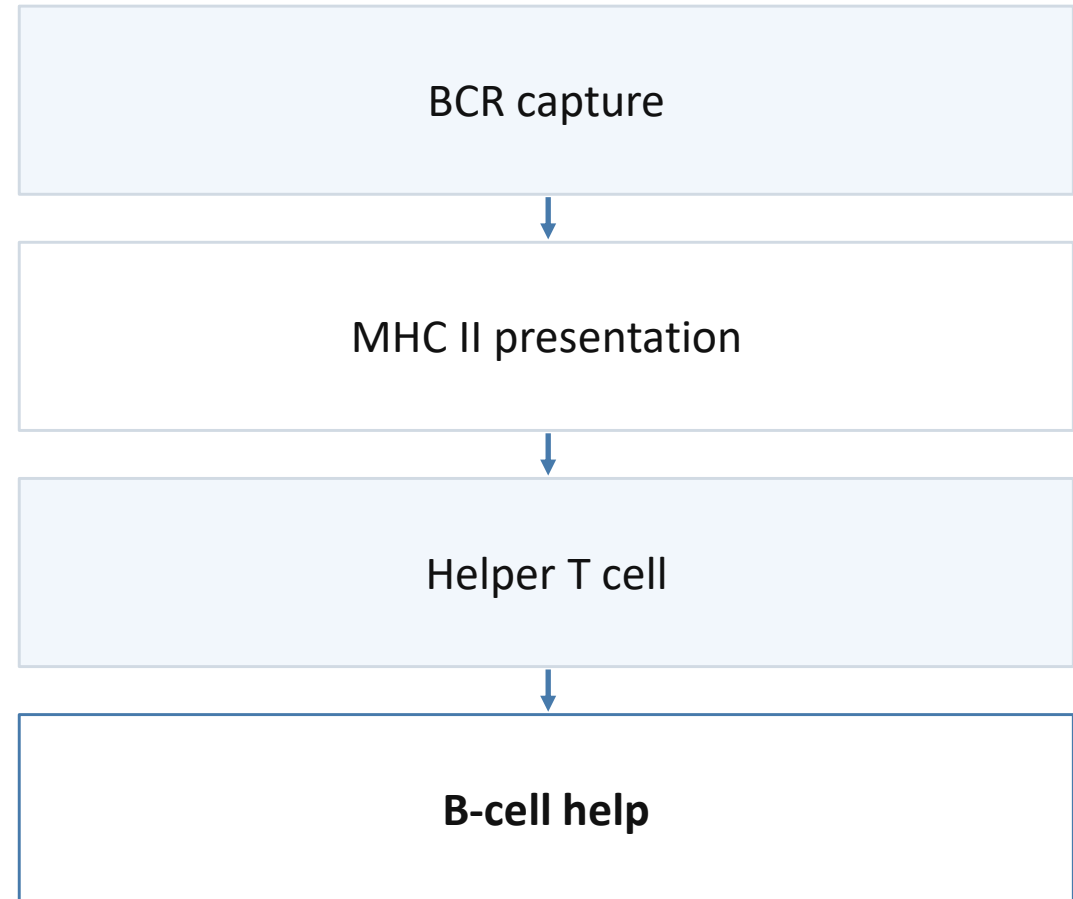
TCR: Peptide–MHC

Compared with

BCR: Native antigen

A B cell can act as an antigen presenter

- The BCR captures a protein antigen recognized by that B cell.
- The protein is internalized, degraded, and displayed on MHC II.
- A helper T cell recognizing the displayed peptide can deliver help.



Classical DCs and follicular DCs are different

- Conventional DCs process antigen and present peptide–MHC to T cells.
- Follicular dendritic cells trap antigen–antibody or complement complexes for B cells.
- Their distinct mechanisms explain their localization in T-cell zones versus follicles.

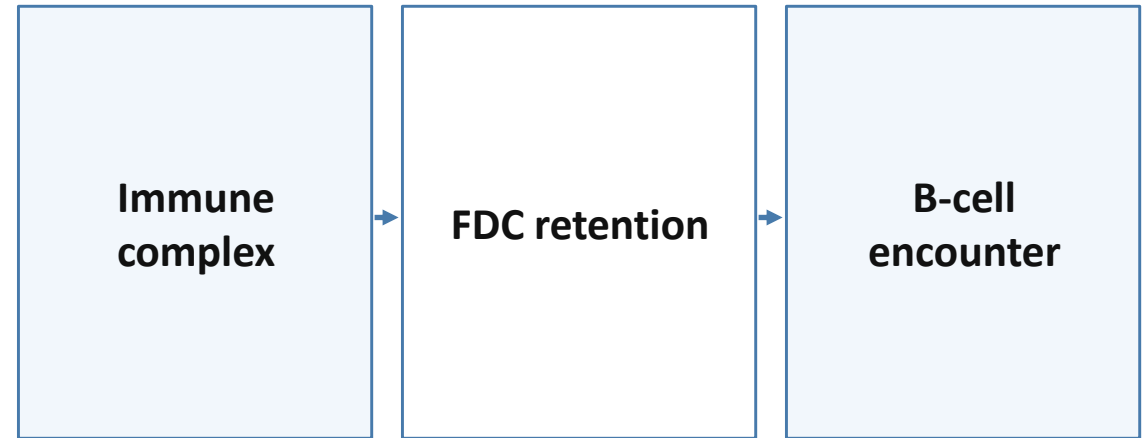
Conventional DC → T cell

Compared with

FDC → B cell

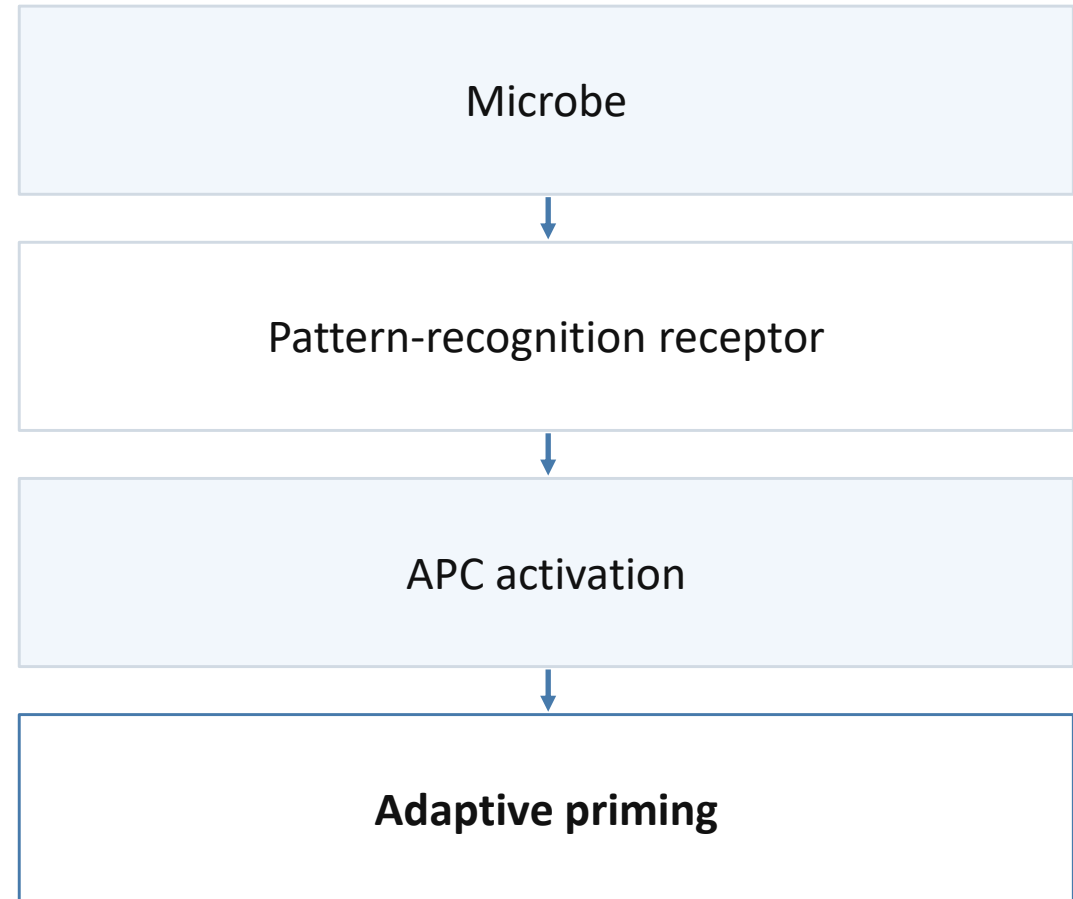
Follicular DCs retain antigen complexes

- FDCs in germinal centers bear Fc receptors and complement-binding receptors.
- They can capture immune complexes containing antigen.
- This supports B-cell selection during antibody responses.



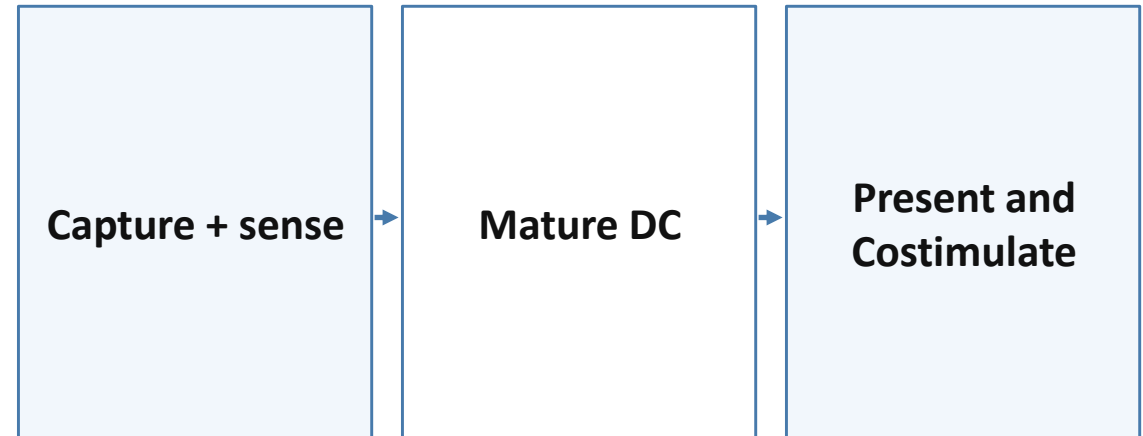
Innate recognition precedes adaptive recognition

- Innate cells use pattern-recognition receptors to sense microbial products.
- This first response provides more than immediate defense.
- It drives APC changes needed to efficiently activate naive lymphocytes.



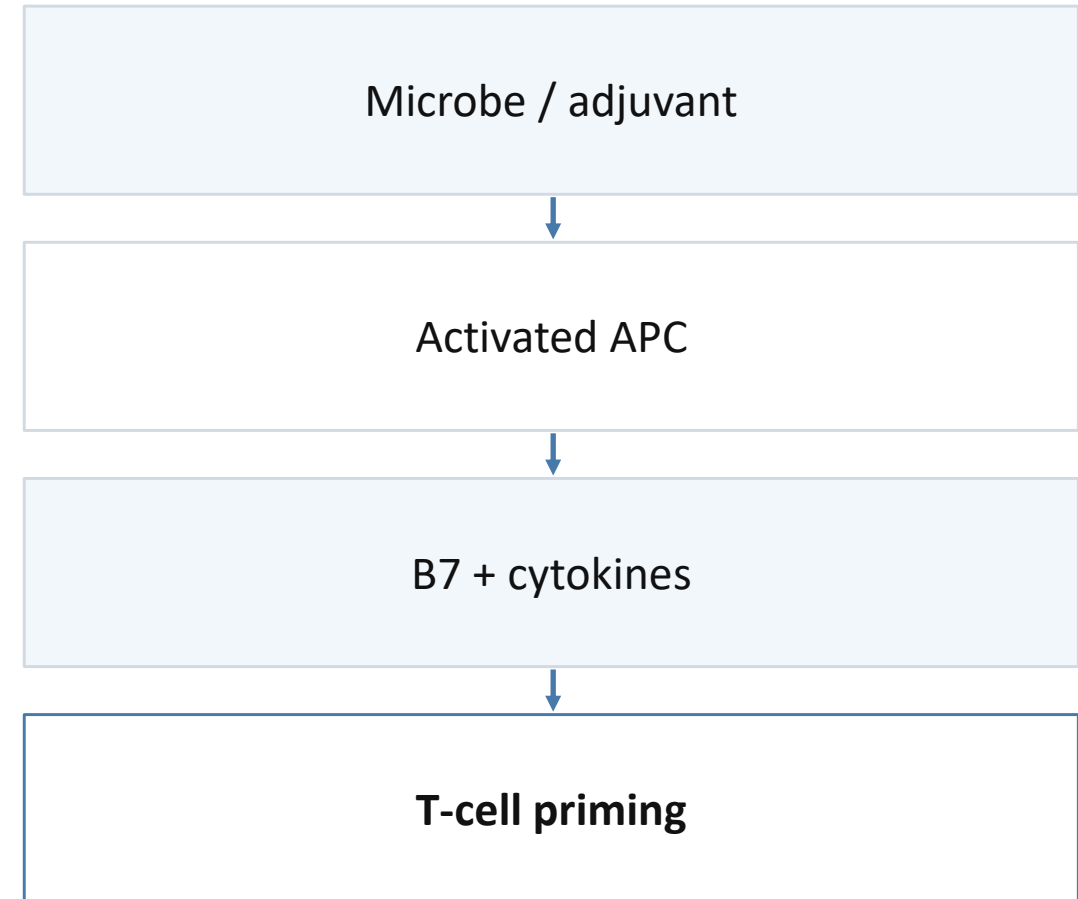
Dendritic cells carry sensors and presentation machinery

- Dendritic cells express pattern-recognition receptors such as TLRs and lectins.
- After microbial activation they increase MHC and activation-associated molecules.
- Their biology unifies antigen capture, sensing, migration, and T-cell stimulation.



Microbial stimuli induce APC maturation

- Microbes or adjuvants trigger innate responses.
- APCs respond by expressing costimulatory molecules and producing cytokines.
- Mature APCs can now provide more than peptide–MHC recognition to naive T cells.



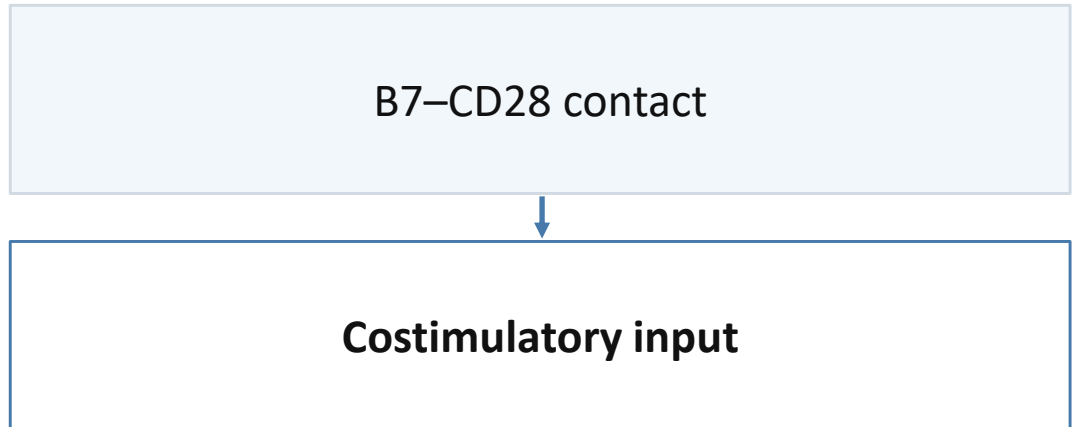
B7 proteins are principal costimulators

- CD80 and CD86 are the B7 proteins highlighted.
- They are expressed by antigen-presenting cells after activation.
- They engage the CD28 receptor on naive T cells.



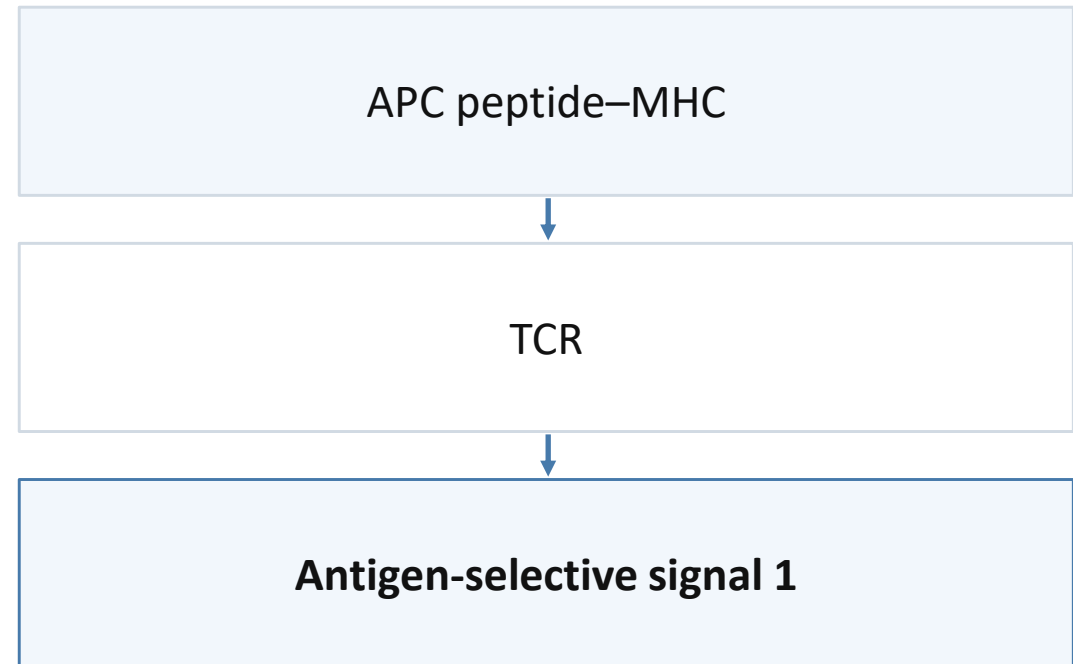
CD28 receives APC costimulation

- CD28 is expressed on naive T lymphocytes.
- Its interaction with B7 occurs alongside antigen recognition.
- CD28 signaling is distinct from the specificity provided by the TCR.



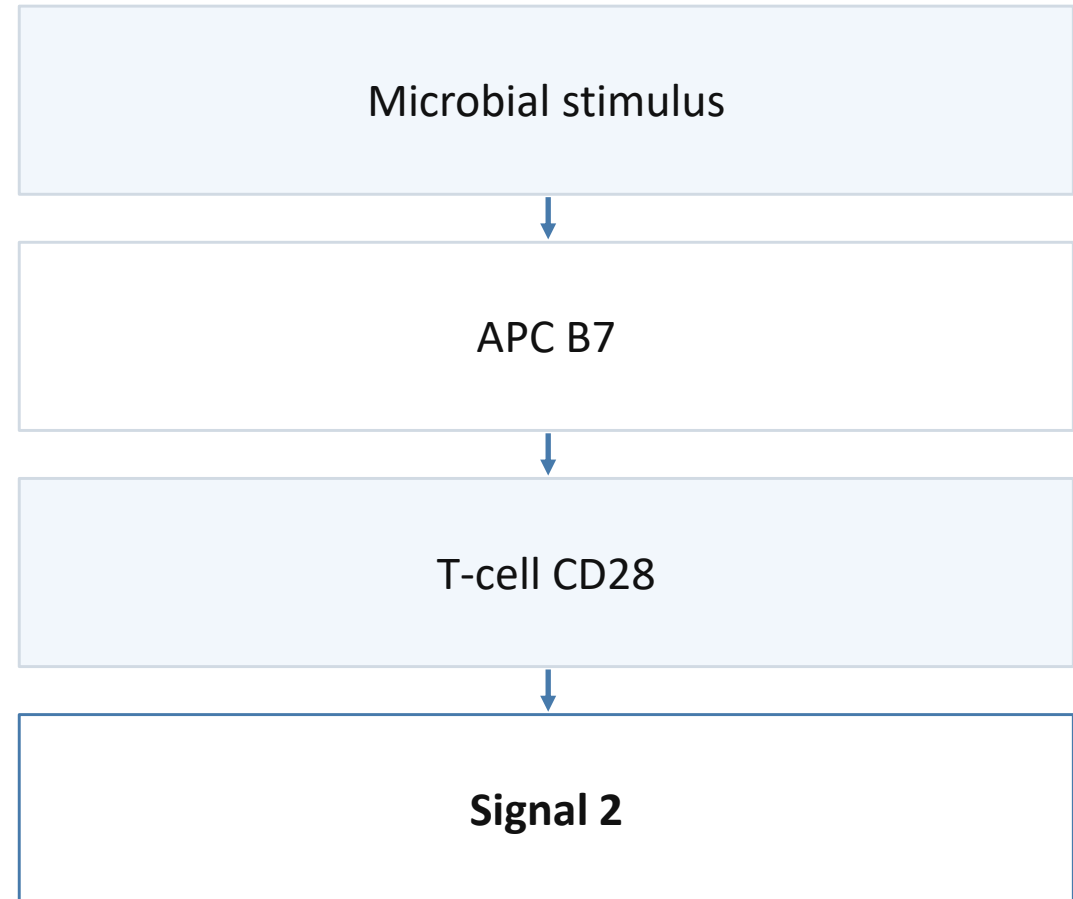
Signal 1 determines antigen specificity

- The TCR recognizes a particular peptide–MHC complex.
- This provides the antigen-selective part of T-cell stimulation.
- Signal 1 alone is not the complete activating context.



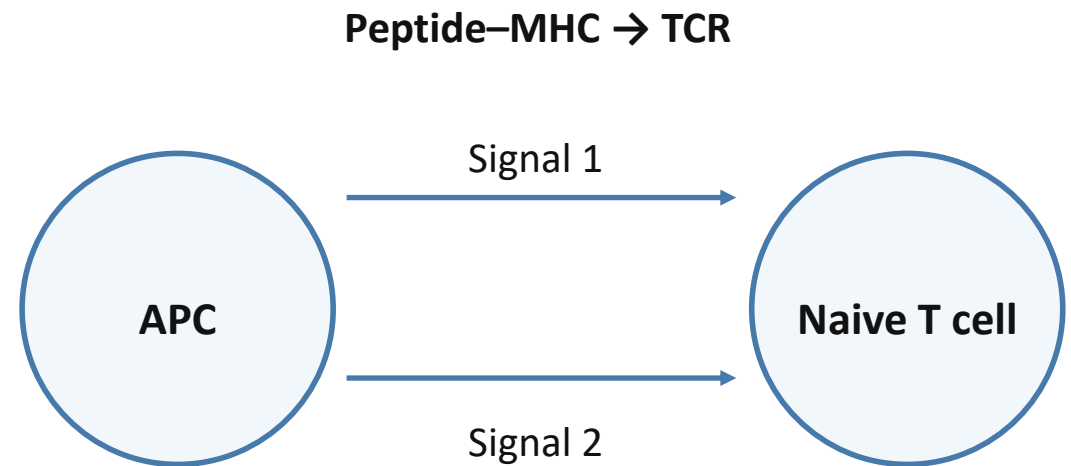
Signal 2 provides activation context

- Activated APCs express CD80/CD86 costimulators.
- CD28 on the naive T cell recognizes these molecules.
- This pathway couples T-cell activation to innate detection of microbial danger.



Naive T cells integrate two cooperating signals

- Signal 1 is antigen presented on an MHC molecule.
- Signal 2 is supplied by APC costimulatory proteins.
- Their cooperation supports antigen-specific lymphocyte activation.



Both inputs act on the same responding T cell

Why microbes activate immunity more reliably than harmless antigen

- Microbial sensing drives APC costimulator expression.
- A harmless protein without equivalent innate activation does not ordinarily produce the same activation context.
- This is an important safeguard, although additional tolerance mechanisms also operate.

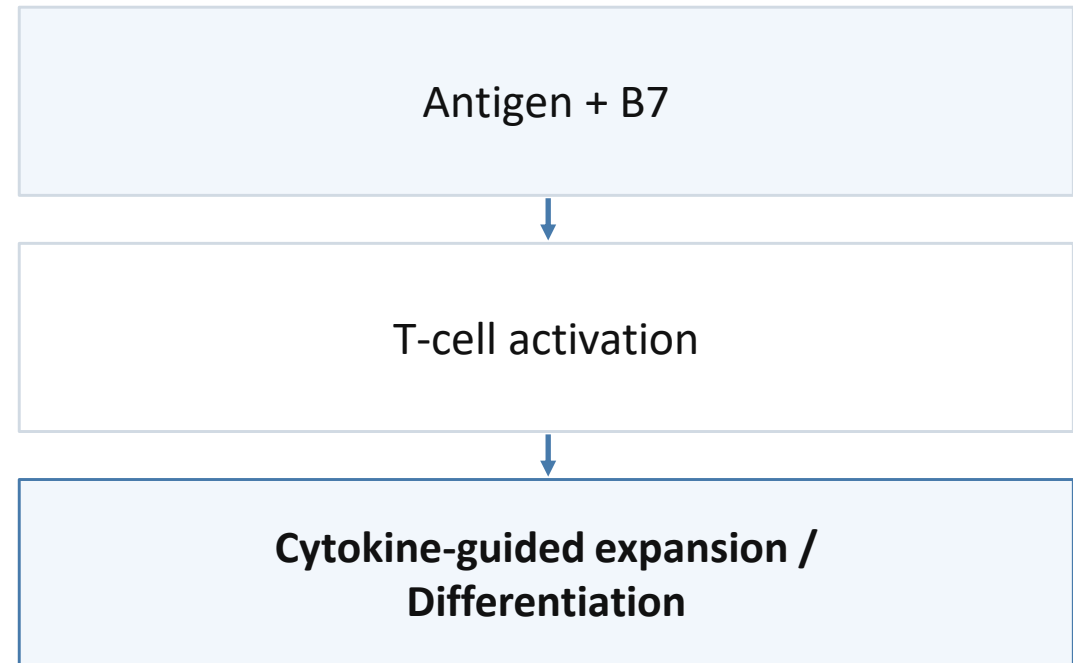
Microbe + costimulation

Compared with

Harmless antigen alone

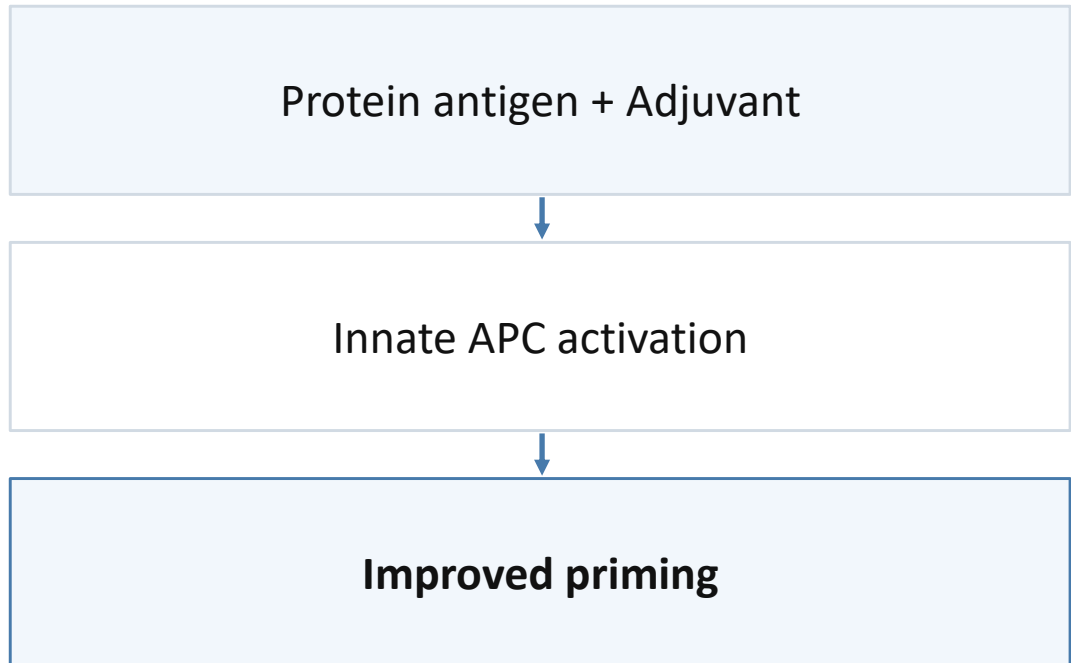
APC cytokines extend beyond costimulation

- Activated APCs not only express B7 but also secrete cytokines.
- Cytokines support the proliferation and differentiation of responding T cells.
- Thus effective priming combines cell-contact and soluble inputs.



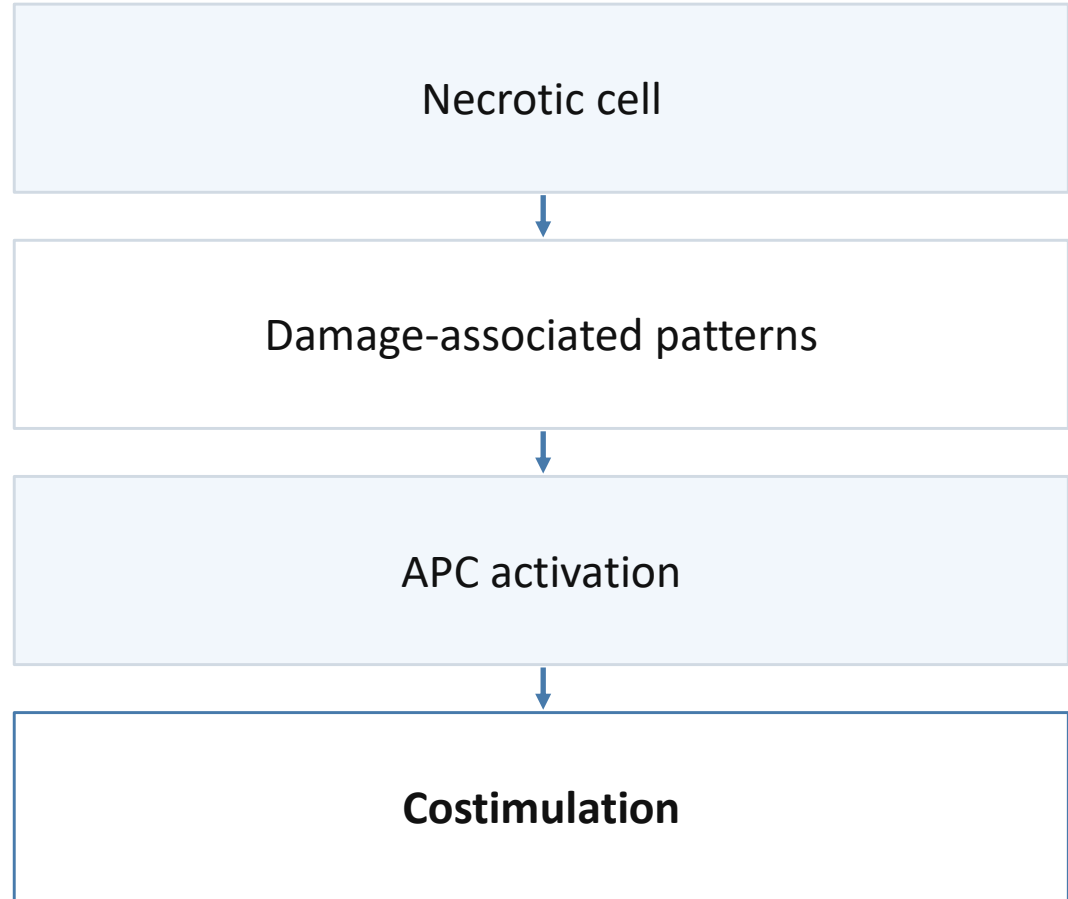
Adjuvants mimic microbial activation cues

- Protein-antigen immunization can include adjuvants.
- Adjuvants stimulate innate immune responses that make antigen presentation more effective.
- They are not simply additional target antigens for the same lymphocyte receptor.



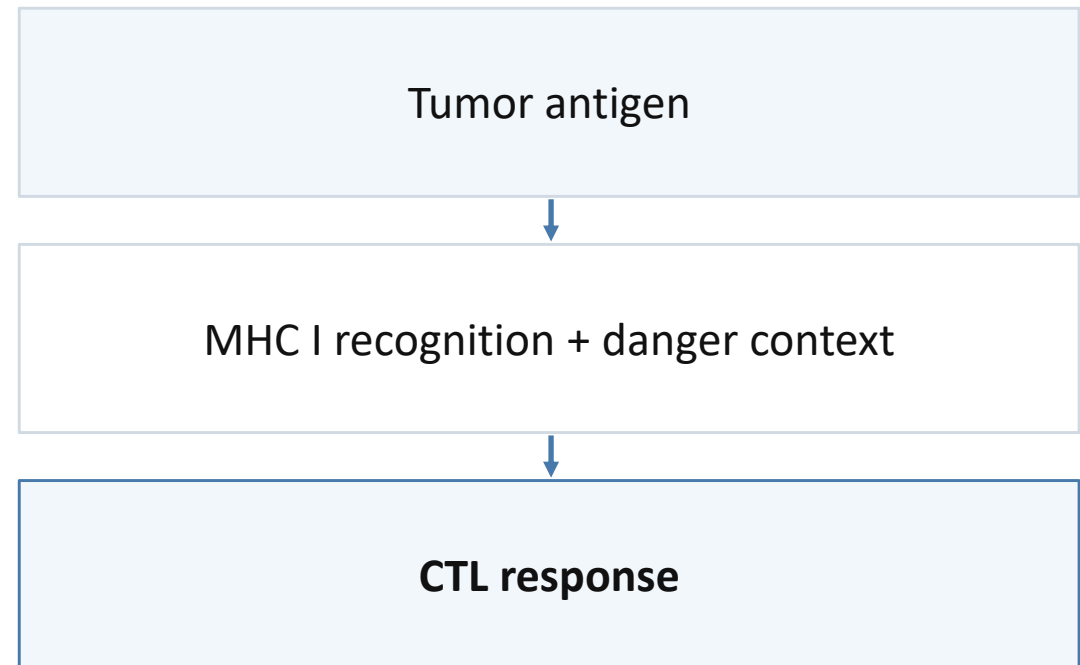
Damage cues can supply activation context

- During tumor or transplant immune responses, signals may arise from injured cells.
- Necrotic cells release damage-associated molecular patterns.
- These signals can help induce costimulators even without microbial infection.



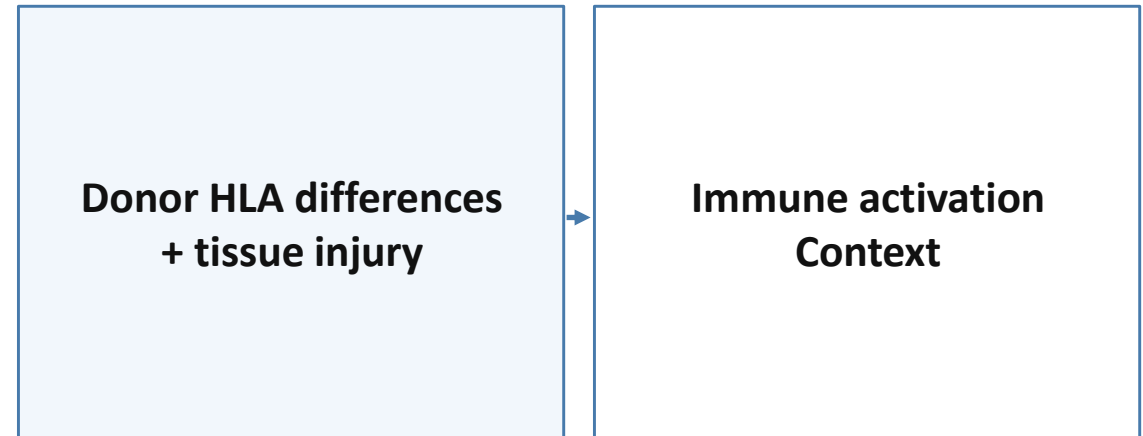
Tumor immunity uses abnormal antigens and danger context

- Tumor cells may produce abnormal cytosolic proteins yielding class I peptides.
- T-cell immunity can recognize tumor-associated peptide–MHC displays.
- Local injury-related danger signals can contribute to immune activation context.



Transplants create both antigenic and innate stimuli

- HLA diversity makes donor tissues immunologically distinct from recipients.
- The source notes damage-associated signals in immune responses to transplants.
- Antigen presentation and inflammatory context are both relevant to alloreactivity.



Costimulation does not abolish self-tolerance

- Self antigens may be displayed by APCs even during infection.
- Increasing costimulator expression alone does not ordinarily cause a self-directed response.
- Powerful immune control mechanisms restrain inappropriate recognition.

Self peptide display + APC activation



Additional tolerance safeguards

Antigen recognition is necessary but not the whole story

- Specific receptor engagement explains which lymphocyte is selected.
- Costimulation and cytokines explain whether and how that lymphocyte responds.
- Regulatory controls determine whether responses to self are permitted.

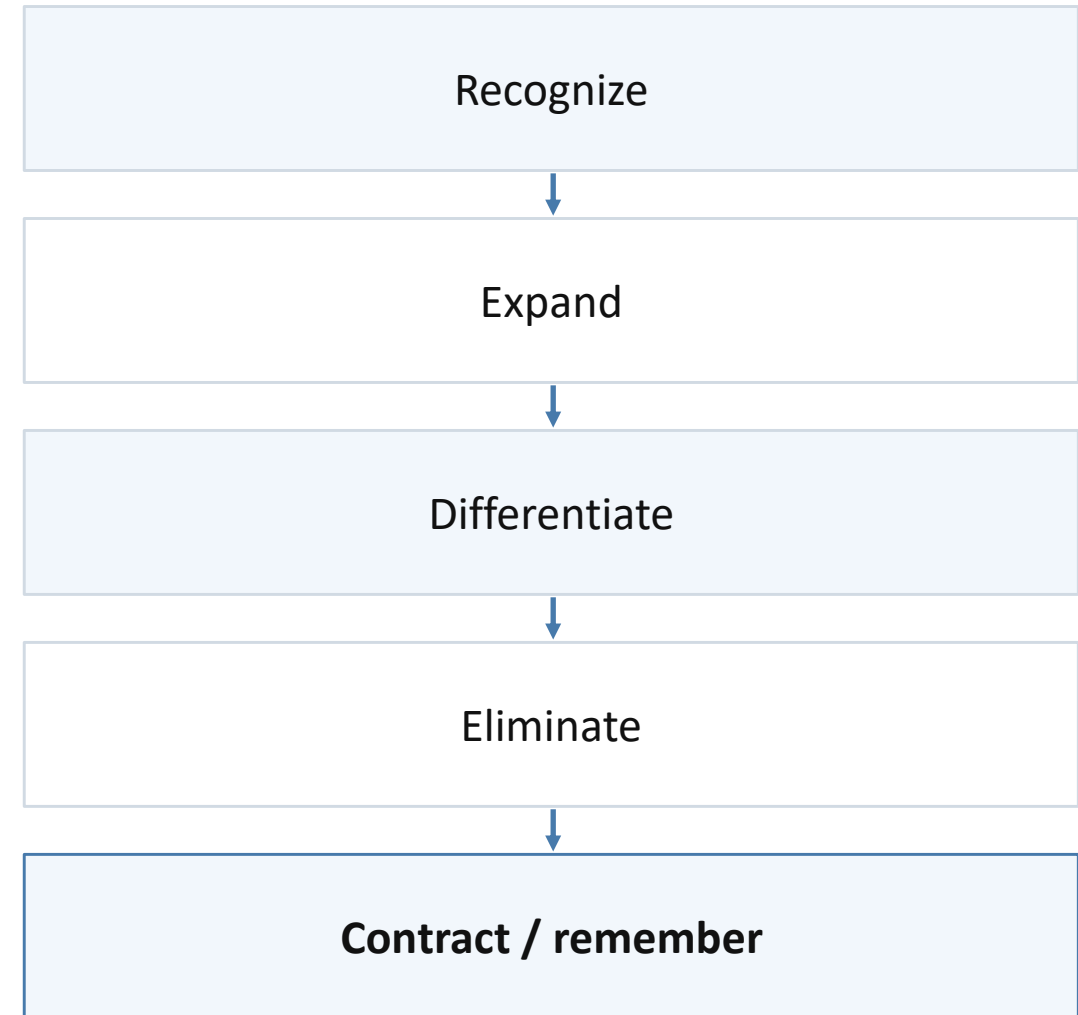
Specificity · Activation context

Compared with

Control

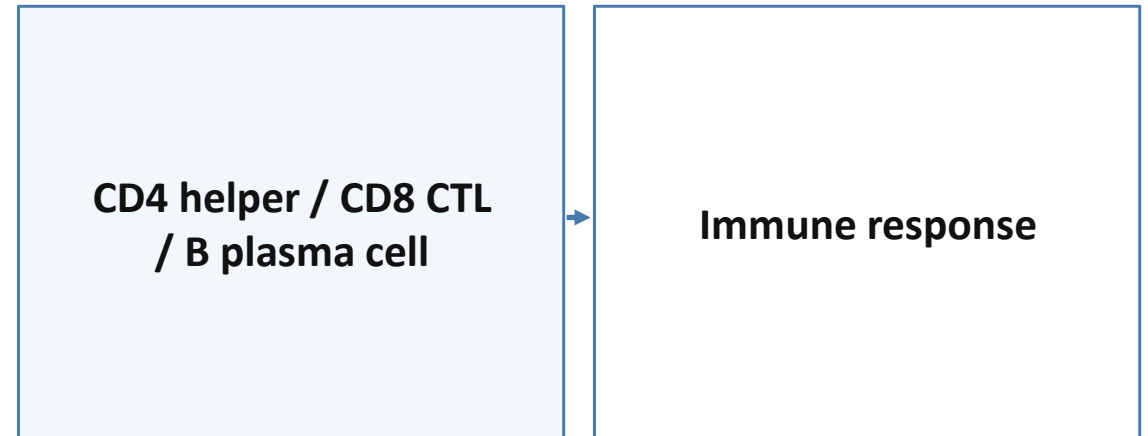
Adaptive immunity follows an ordered response sequence

- Recognition precedes lymphocyte proliferation and differentiation.
- Effector and memory cells emerge after activation.
- Antigen elimination is followed by contraction while memory cells persist.



Activated T cells and B cells perform different tasks

- Activated CD4 cells direct other cells through contact signals and cytokines.
- Activated CD8 cells can differentiate into cytotoxic lymphocytes.
- Activated B cells can develop into antibody-secreting plasma cells.



Lymph node versus spleen antigen capture

- Lymph nodes concentrate antigens carried from tissues in lymph.
- The spleen captures antigens circulating in the blood.
- Both are secondary lymphoid organs supporting adaptive initiation.

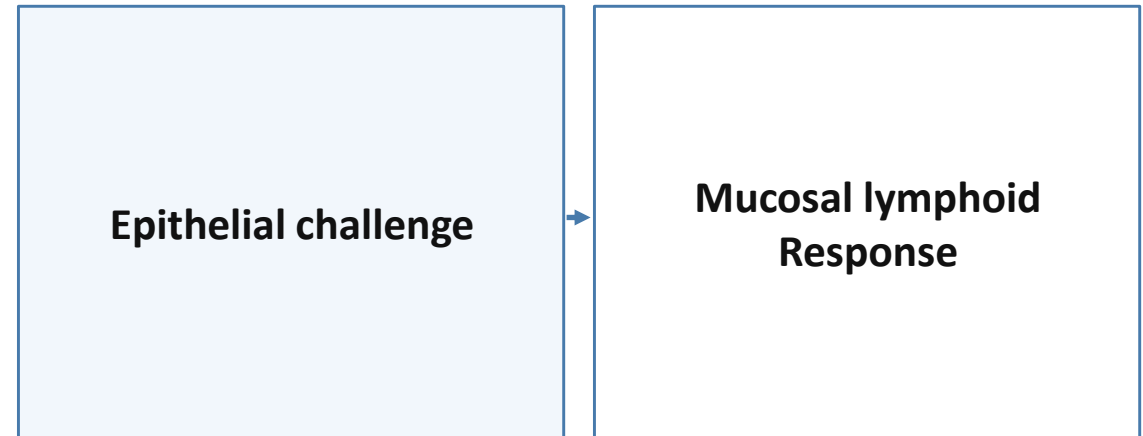
Lymph-borne → node

Compared with

Blood-borne → spleen

Mucosal lymphoid tissues survey epithelial entry

- Lymphoid tissue lies beneath mucosal and cutaneous barriers.
- These regions respond to microbes crossing epithelial surfaces.
- Tonsils and Peyer patches are anatomically defined mucosal lymphoid tissues.



Primary and secondary lymphoid organs serve different roles

- The thymus and bone marrow are primary organs of lymphocyte development.
- Nodes, spleen, and mucosal/cutaneous tissues support antigen-driven responses.
- Maturation and antigen encounter are distinct stages of lymphocyte biology.

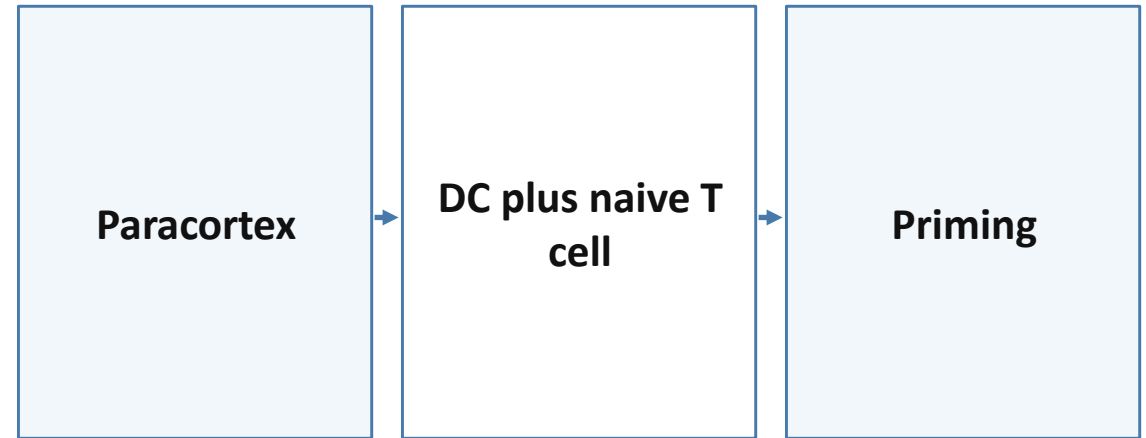
Primary: Development

Compared with

Secondary: Antigen-driven activation

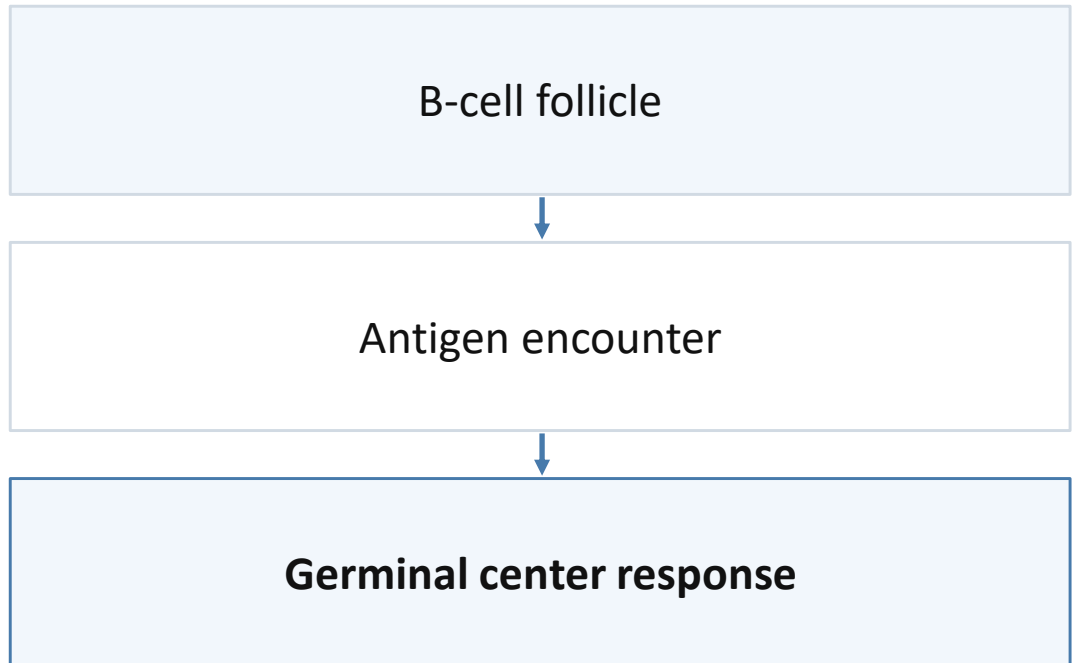
T-cell zones optimize DC–T-cell encounters

- DCs accumulate where naive T cells patrol, such as the lymph-node paracortex.
- These contacts enable recognition of displayed peptide–MHC.
- Cellular localization is as important as the binding specificity.



Follicles optimize B-cell responses

- B cells are enriched in cortical lymphoid follicles.
- Follicular dendritic cells retain antigens for B-cell interaction.
- Germinal centers appear when follicles contain activated responding B cells.



Antigen display must be distinguished from activation

- A surface peptide–MHC complex can be displayed without ensuring full activation.
- Naive T-cell activation also depends on appropriate costimulation.
- Activated T cells later use cytokines and contacts to produce effector outcomes.

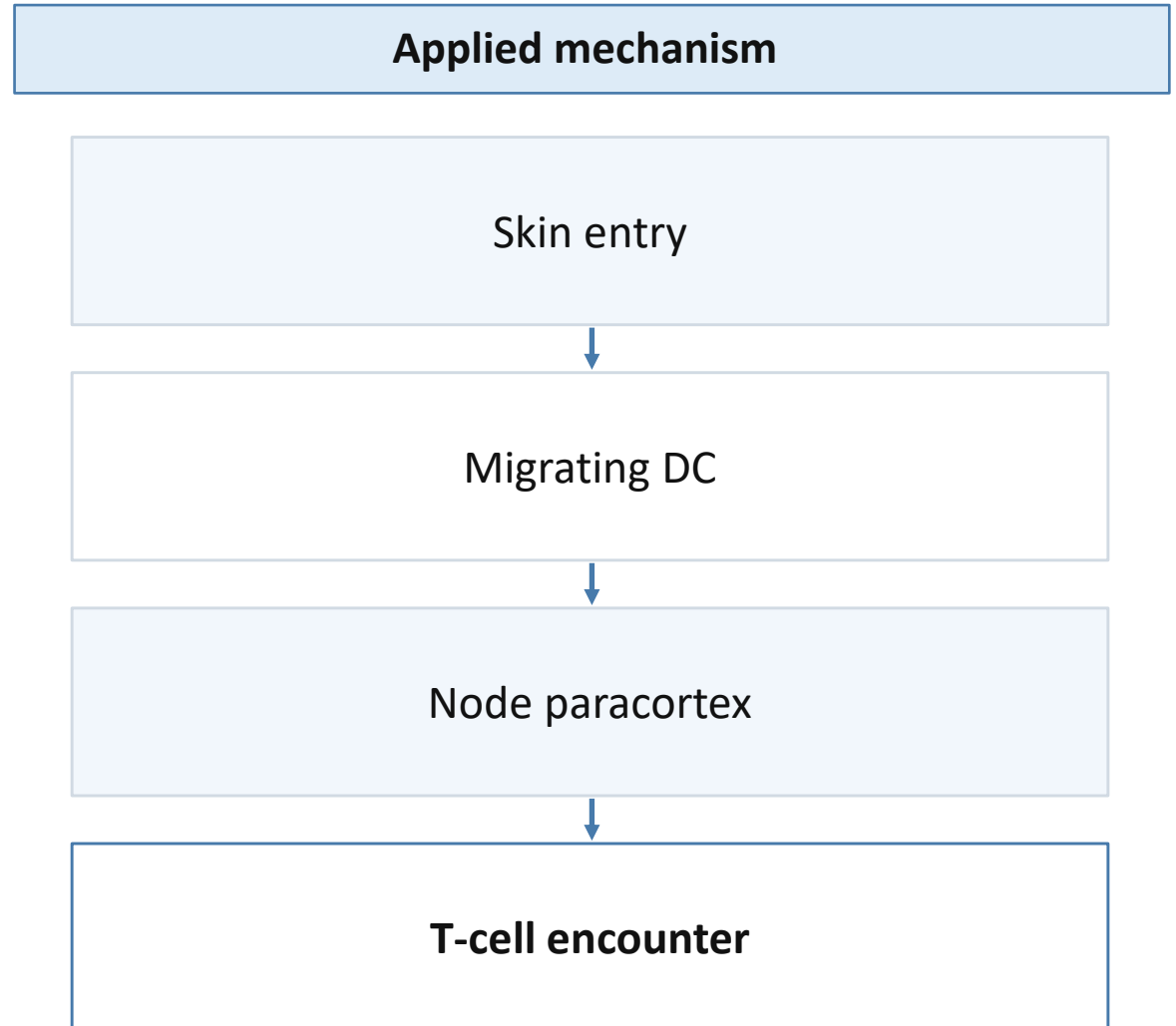
Display: Peptide–MHC

Compared with

Activation: Signal 1 + signal 2

Case: Antigen enters through a skin wound

- A microbial protein enters peripheral tissue beneath an epithelium.
- Resident dendritic cells carry the antigen to draining lymph nodes.
- Recognition by naive T cells is most likely where antigen and recirculating cells converge.



Case: A virus produces proteins inside a cell

- A viral protein is produced in the cytosol of a nucleated cell.
- The class I pathway delivers cytosolic peptides to the surface.
- CD8 T cells recognize the displayed peptide–MHC I complex.

Applied mechanism

Viral protein



MHC I



CD8 T cell

Case: A vaccine protein is given with an adjuvant

- An injected protein supplies antigen for adaptive recognition.
- The adjuvant stimulates innate activation of APCs.
- B7 expression and cytokine release help make priming effective.

Applied mechanism

Protein + adjuvant



Activated APC



T-cell priming

Case: Infection occurs alongside self-antigen display

- An infected tissue contains APCs that display both foreign and self peptides.
- Microbial activation may upregulate costimulators on those APCs.
- Costimulation alone does not override immune tolerance to self.

Applied mechanism

Infection



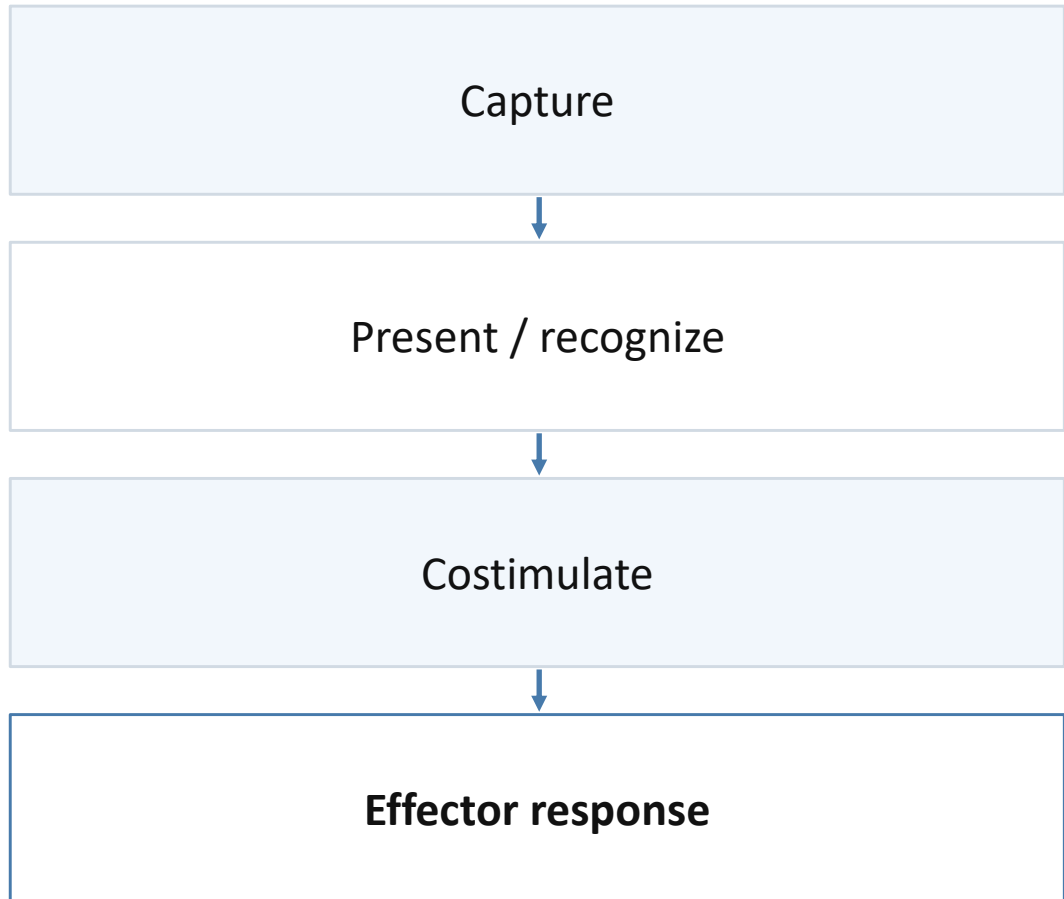
APC activation



Self-tolerance safeguards remain

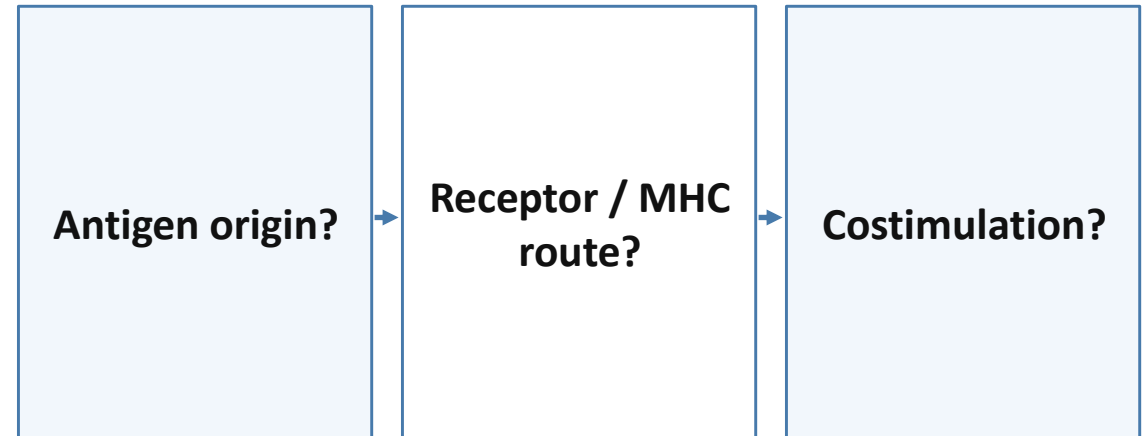
Integrated antigen-recognition model

- Antigens are transported or concentrated in secondary lymphoid organs.
- T cells inspect peptide–MHC with a requirement for appropriate activation context.
- B cells recognize native antigen and may enlist T-cell help after processing protein antigens.



Three questions to diagnose a presentation pathway

- Where did the antigenic protein originate:
Cytosol or extracellular space?
- Which receptor sees it: Peptide–MHC-specific TCR or native-antigen-specific BCR?
- Was the required APC context supplied to activate a naive T cell?



Synthesis: Use the mechanism to interpret immunity

- Antigen concentration solves the problem of rare antigen-specific lymphocytes.
- MHC pathways determine which T-cell subset inspects a protein-derived peptide.
- Antigen recognition, costimulation, and immune regulation jointly determine the response.

Selected source material

Robbins, Cotran & Kumar: Pathologic Basis of Disease, 11th edition (2026)

- Chapter 6: Display and Recognition of Antigens.
- Related sections: Major Histocompatibility Complex Molecules; Tissues of the Immune System.
- Text content derived from the supplied chapter Markdown; textbook figure files not reproduced.