ANTIGEN PROCESSING AND PRESENTATION

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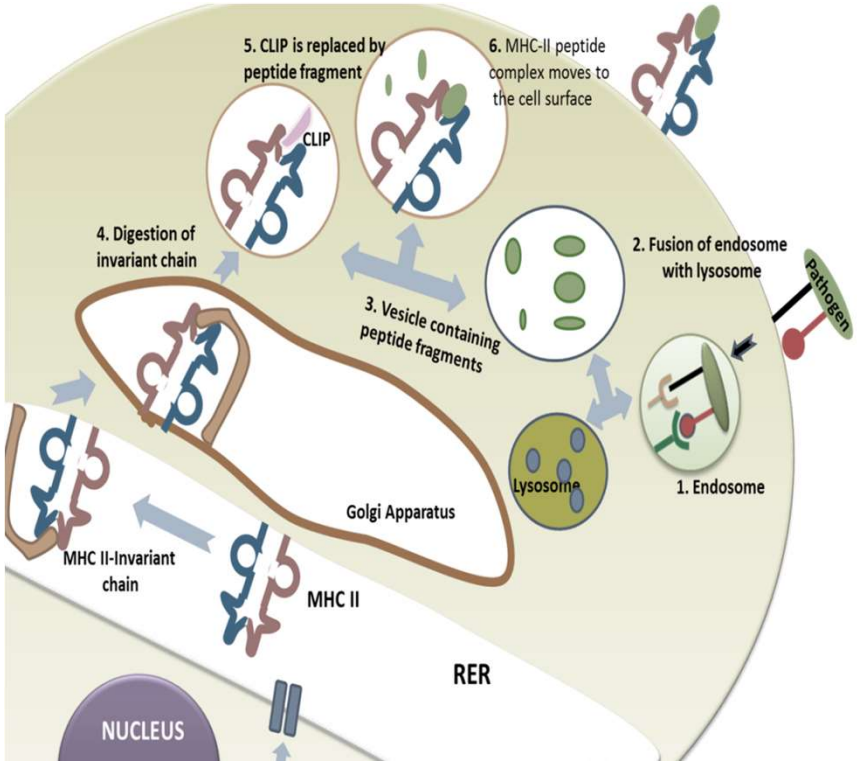
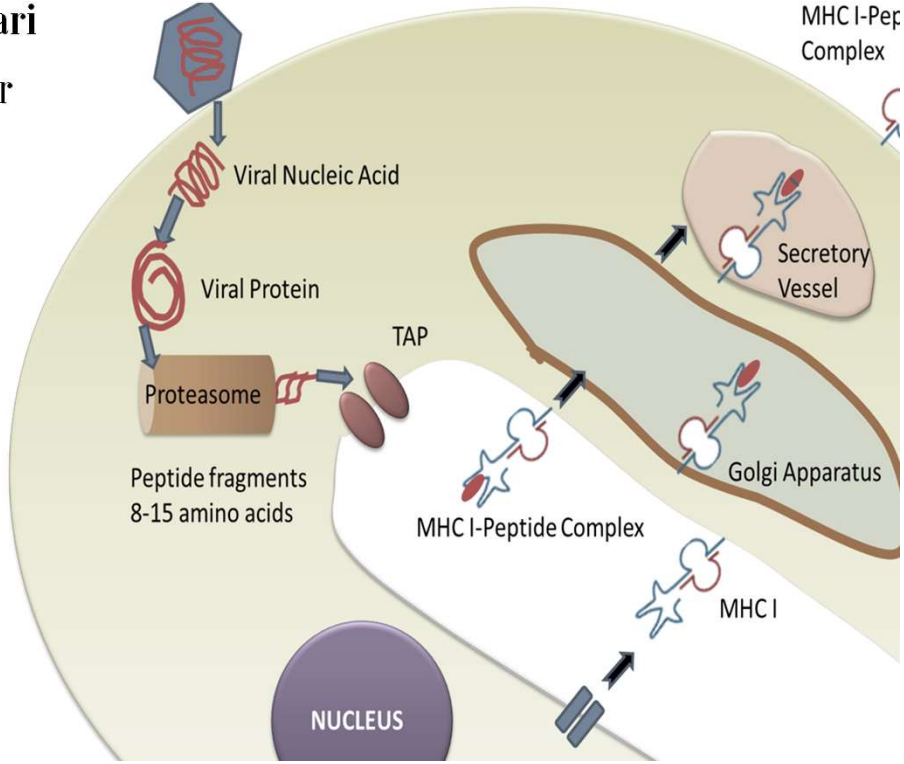
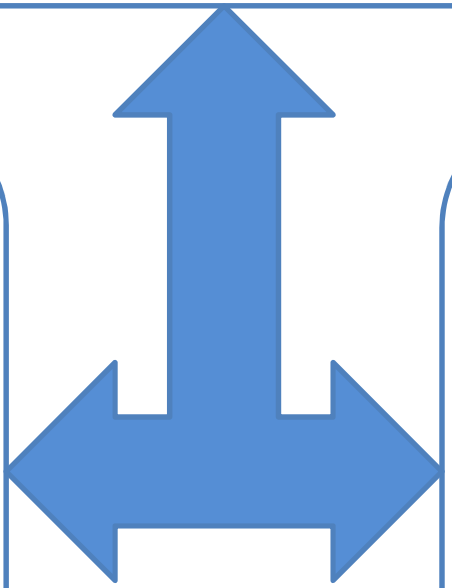




INTRODUCTION

- T cells recognise processed peptides displayed with Histocompatibility Complex class I (MHC-I) and class II (MHC-II) molecules.
- Processed peptides from pathogens or transformed cells are displayed with MHC-I and MHC-II.
- Processed peptides from self antigens are presented with MHC-I.
- Two pathways for antigen processing and presentation are:
  - Endogenous pathway
  - Exogenous Pathway

ANTIGEN PROCESSING AND PRESENTATION



- ✓ Endocytic or exogenous processing pathway
- ✓ MHC II binds peptides and present to CD4_ T Cells

- ✓ Cytosolic or endogenous processing pathway
- ✓ MHC I binds peptides and present to CD8+ T Cells

STEPS OF ANTIGEN PROCESSING IN ENDOGENOUS OR EXOGENOUS PATHWAY

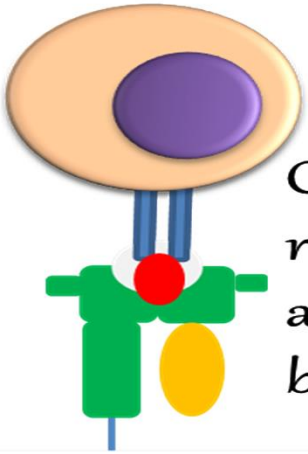
- **Uptake:**
  - Self antigens and pathogens are accessed and taken up by intracellular pathways of degradation.
- **Degradation:**
  - Controlled processing of antigens to peptides through proteolysis.
- **Peptide: MHC Complex Formation:**
  - Loading of the processed peptides onto MHC molecules.
- **Presentation of the Peptide: MHC Complex:**
  - Movement of MHC: Peptide Complexes on surface of cells for recognition by T-Cells.

RECOGNITION OF ANTIGENS BY B AND T-CELLS

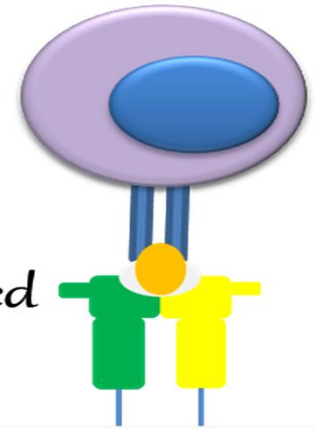
- ✓ B-Cells recognize variety of antigens
  - ✓ Proteins
  - ✓ Polysaccharides
  - ✓ Lipids
  - ✓ Nucleic acids

- ✓ T-Cells recognize only protein antigens which are displayed in antigen binding cleft of MHC.

RECOGNITION OF ANTIGENS BY B AND T-CELLS



Cytotoxic T-cells recognize antigens displayed by MHC 1



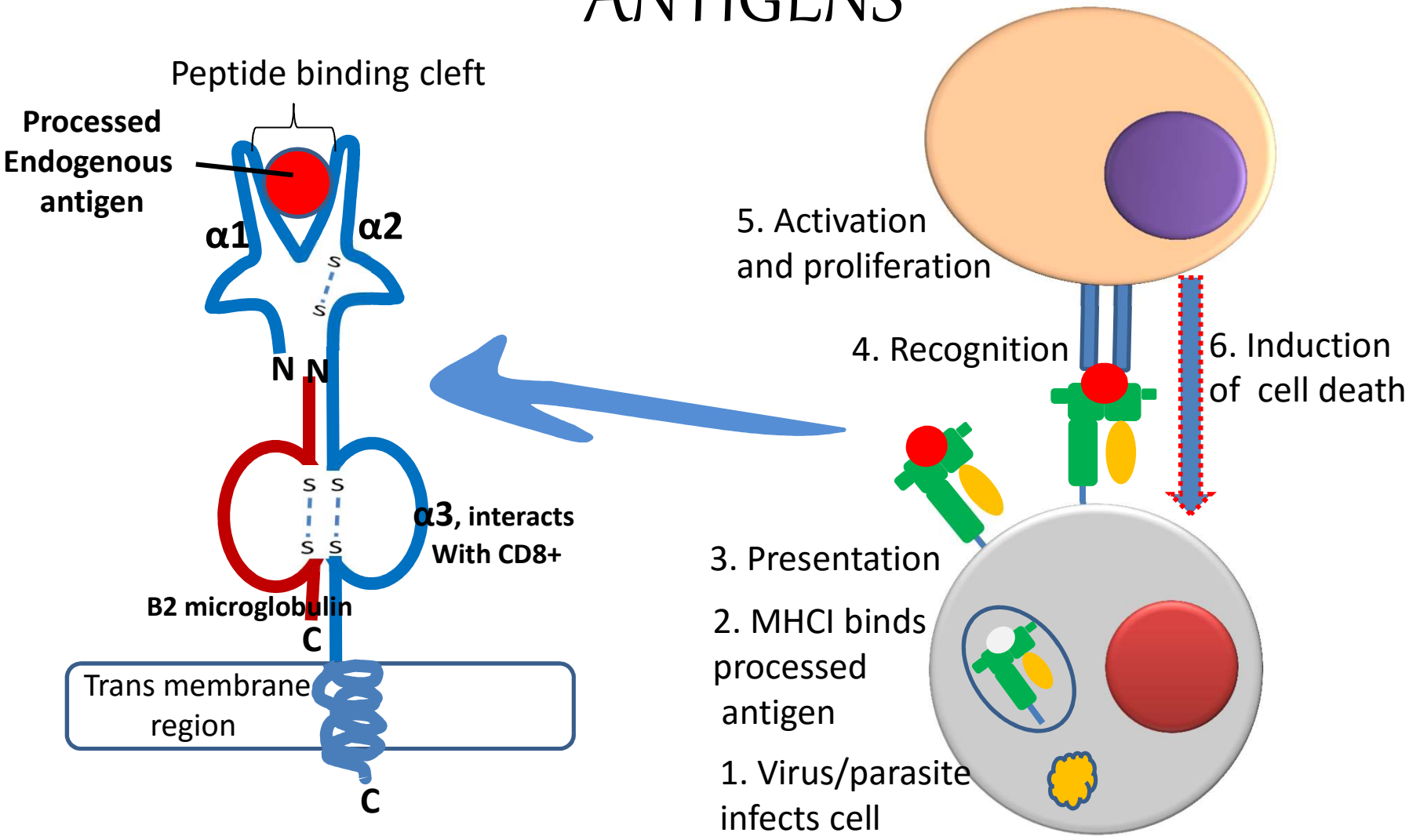
T Helper Cells recognize antigens displayed by MHC 11

MHC Class 1 is expressed on all nucleated cells and express endogenous antigen

MHC Class 11 is expressed on all antigen presenting cells such as dendritic cells, macrophages, B--Cells

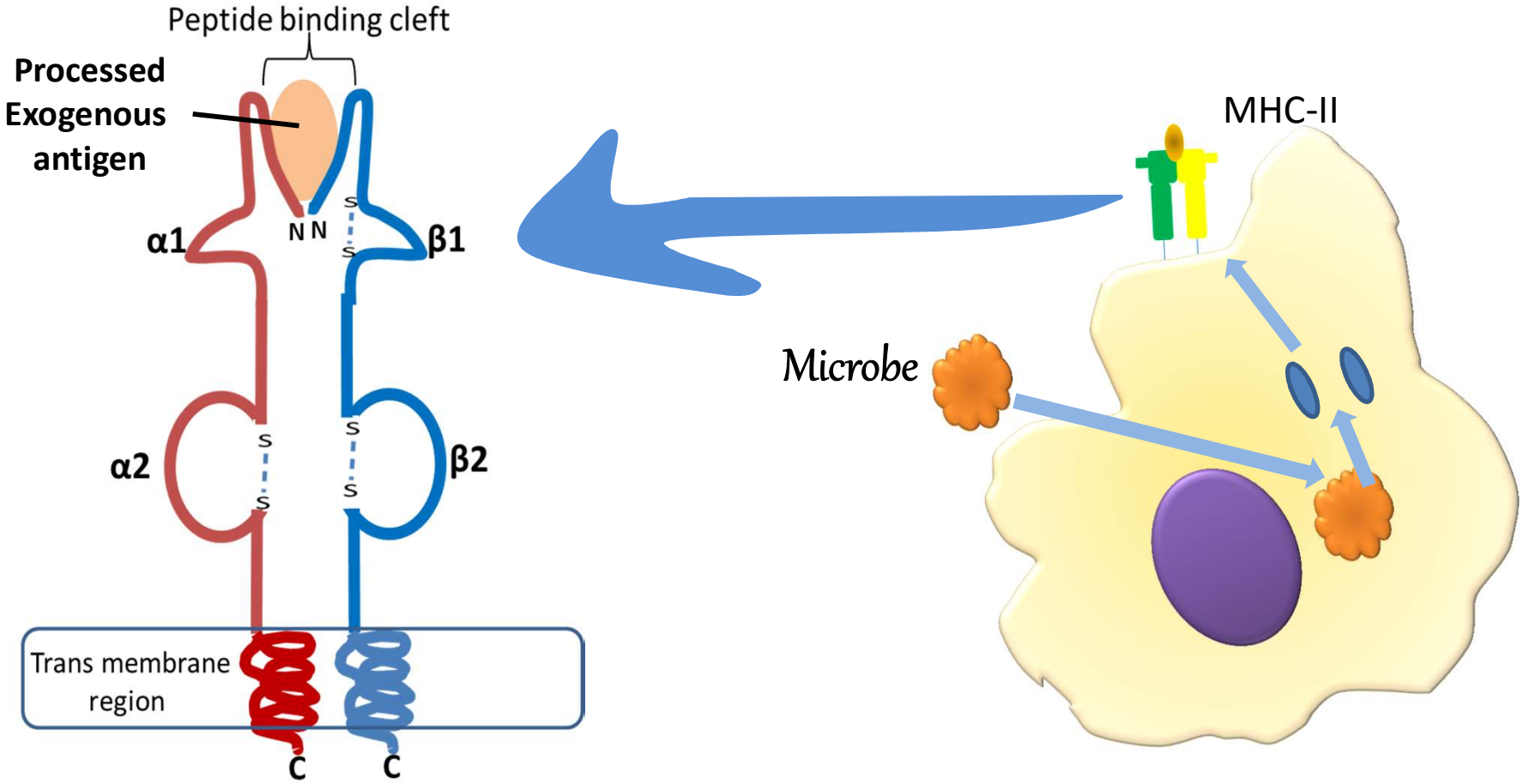
- ✓ Antigen presentation is a decisive step in the adaptive immune response
- ✓ It permits self/non self discrimination by T-cells, eventually facilitating the recognition of pathogens.

MHC CLASS I PRESENT ENDOGENOUS ANTIGENS



MHC 11 PRESENT EXTACELLULAR OR EXOGENOUS ANTIGENS

Extracellular live and replicate outside host cells and endocytosed by macrophages and dendritic cells, processed and presented with MHC11.



- ✓ Process by which pathogens or their products are degraded to process peptide antigens is known as
- ✓ ANTIGEN PROCESSING

- ✓ These peptide fragments bind with MHC molecules inside the cell

- ✓ The MHC peptide complex thus formed displays the processed peptide antigen and this is known as
- ✓ ANTIGEN PRESENTATION

- ✓ How peptide fragments from pathogens and their products are produced
- ✓ How these processed peptide antigens are combined with MHC
- ✓ How MHC: peptide complex is processed to the T-Cells

PROCESSING & PRESENTATION OF INTRACELLULAR OR ENDOGENOUS ANTIGENS

PROCESSING & PRESENTATION OF INTRACELLULAR ANTIGENS

- ✓ Endogenous proteins are presented by MHC-I.
- ✓ Cytosolic or endogenous proteins move to the proteasome complex and get processed into short peptides.
- ✓ These short peptides then move into ER via TAP for display with MHC-I.

ANTIGENIC PEPTIDE BINDING TO MHC-1

- ✓ α-chain assemble with β_2m to form MHC-1 in the presence the chaperone calnexin (CNX) in ER.
- ✓ Peptides after proteasomal degradation of endogenous proteins enter ER via TAP.
- ✓ Peptides longer than the 8-10 residues undergo trimming by ER amino-peptidases known as ERAAP/ERAP1 and ERAP2.
- ✓ Peptides having high affinity and of right size complex with MHC-1 by a tapasin-mediated editing process.
- ✓ MHC-1-peptide complexes move to the cell surface.

MHC I ANTIGEN PRESENTATION PATHWAY

1. Viral Nucleic acid enters host cell

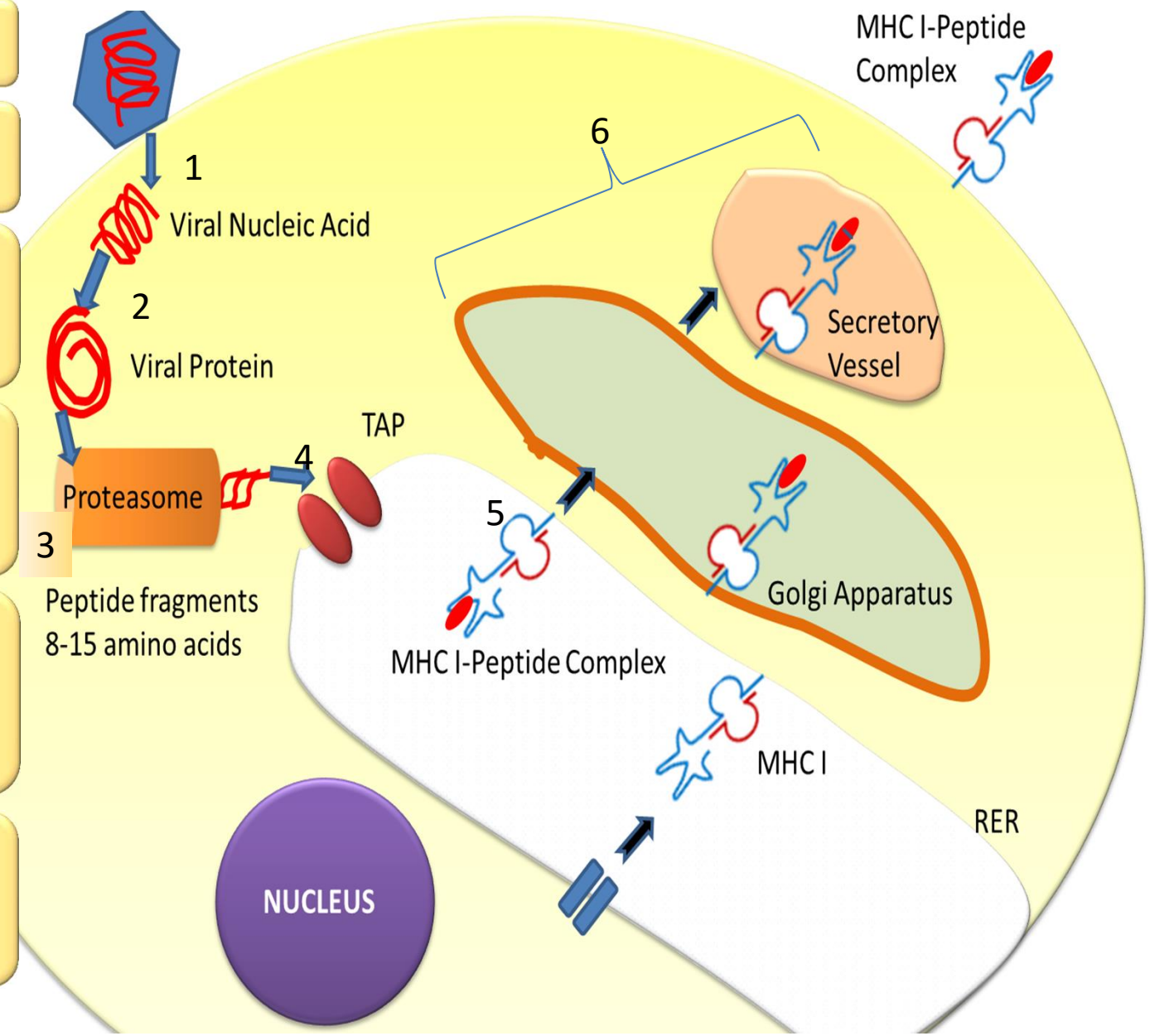
2. Viral Proteins are synthesized in the host cell

3. Viral Proteins are digested in the proteasome and processed in the cytosol

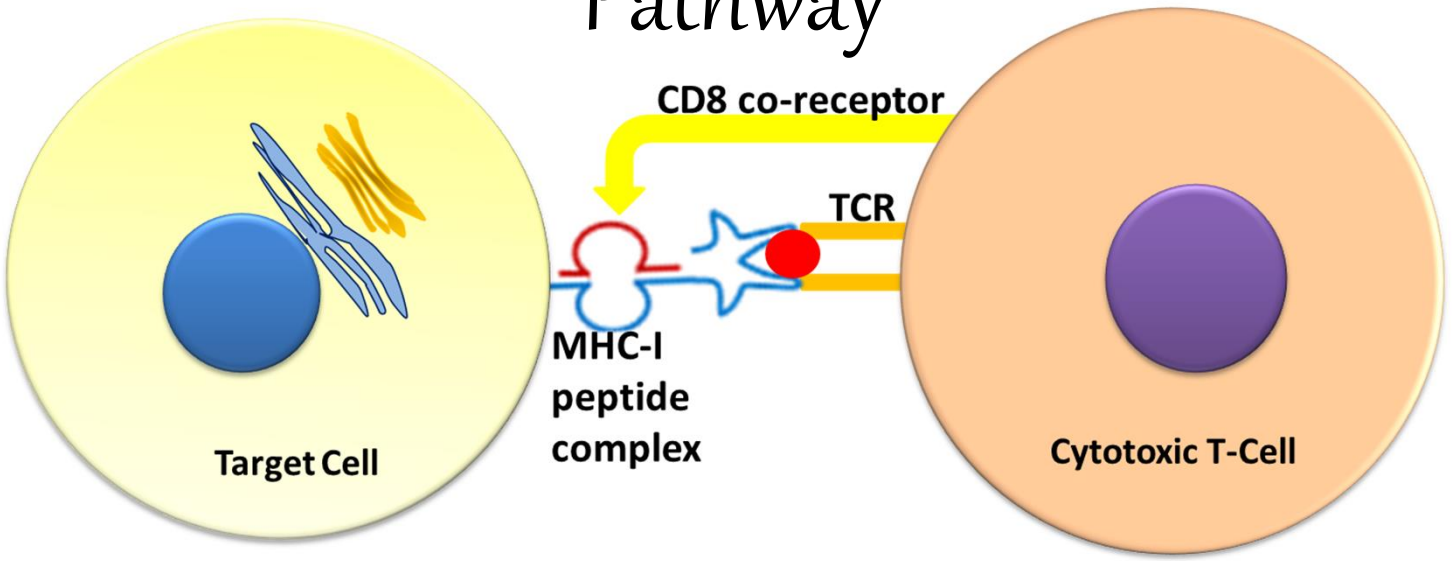
4. TAP Transporters associated with antigen processing) consists of TAP-1 and TAP-2

5. Peptides transported from cytosol to endoplasmic reticulum and bind to newly synthesized MHC-I

6. MHC-I peptide complex moves to the cell surface via Golgi apparatus



MHC 1 Antigen Presentation and Presentation Pathway



- ✓ Target cell normally presents self antigens with MHC-1
- ✓ Under infection by an intracellular pathogen presents processed antigen with MHC-1

- ✓ Cytotoxic T-Cells bearing TCR along with CD8+ co-receptor.
- ✓ It recognizes the processed peptide presented in the antigen binding cleft of the MCH-1

PROCESSING AND PRESENTATION OF EXTRACELLULAR OR EXOGENOUS ANTIGENS

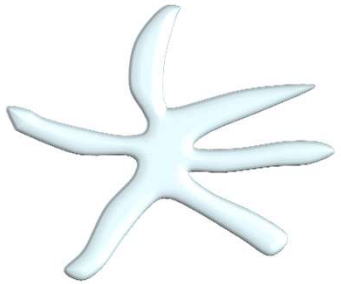
PROCESSING AND PRESENTATION OF EXTRACELLULAR ANTIGEN

- ✓ Exogenous proteins are presented by MHC-II.
- ✓ Antigens after phagocytosis/ macropinocytosis/ endocytosis, move to late endosome and after further processing are presented with MHC-II.
- ✓ Cytoplasmic/nuclear antigens after autophagy are processed and presented with MHC-II molecules.

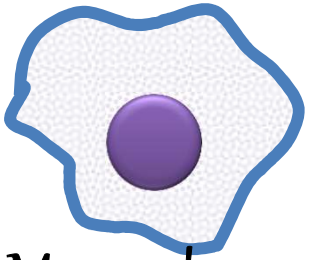
ANTIGEN PRESENTING CELLS (APCS)

Present peptides derived from extracellular or exogenous antigens

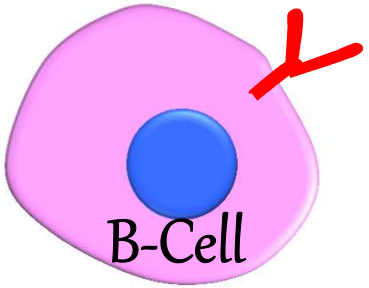
TYPICAL APCs



Dendritic Cell



Macrophage



B-Cell

- ✓ Phagocytic.
- ✓ Found in T-Cell zone of Lymph node.
- ✓ Express MHC II constitutively and have antigen processing pathway.
- ✓ Express co-stimulatory molecules once activated.

- ✓ Internalize antigens through B-Cell Receptor.
- ✓ Express MHC II constitutively and have antigen processing.
- ✓ Express co-stimulatory molecules once activated.

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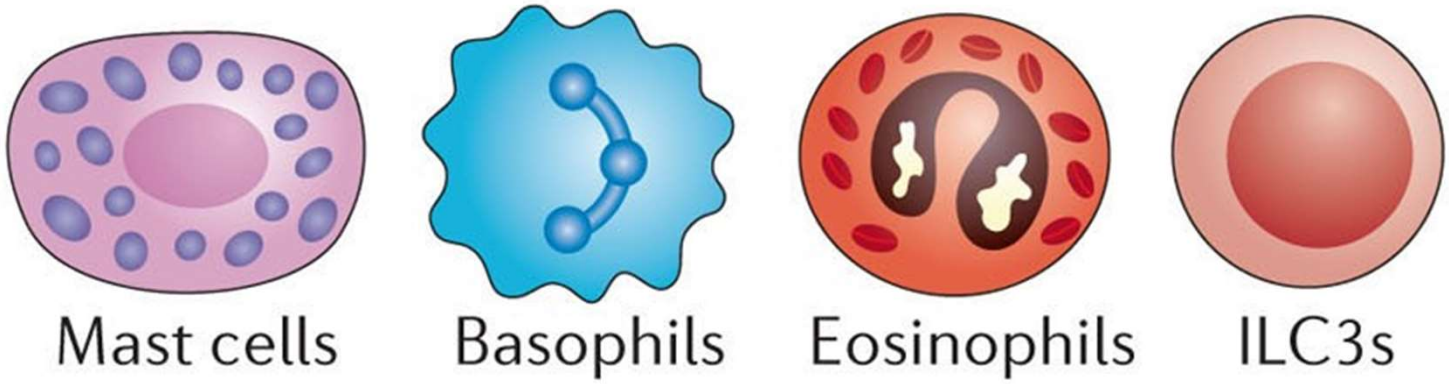
Antigen Presenting Cells (APCs)

ATYPICAL APCs



- ✓ Have inducible MHC-II
- ✓ Antigen presentation limited to specific immune environments.
- ✓ No t confimed whether they can activate T-Helper Cells.

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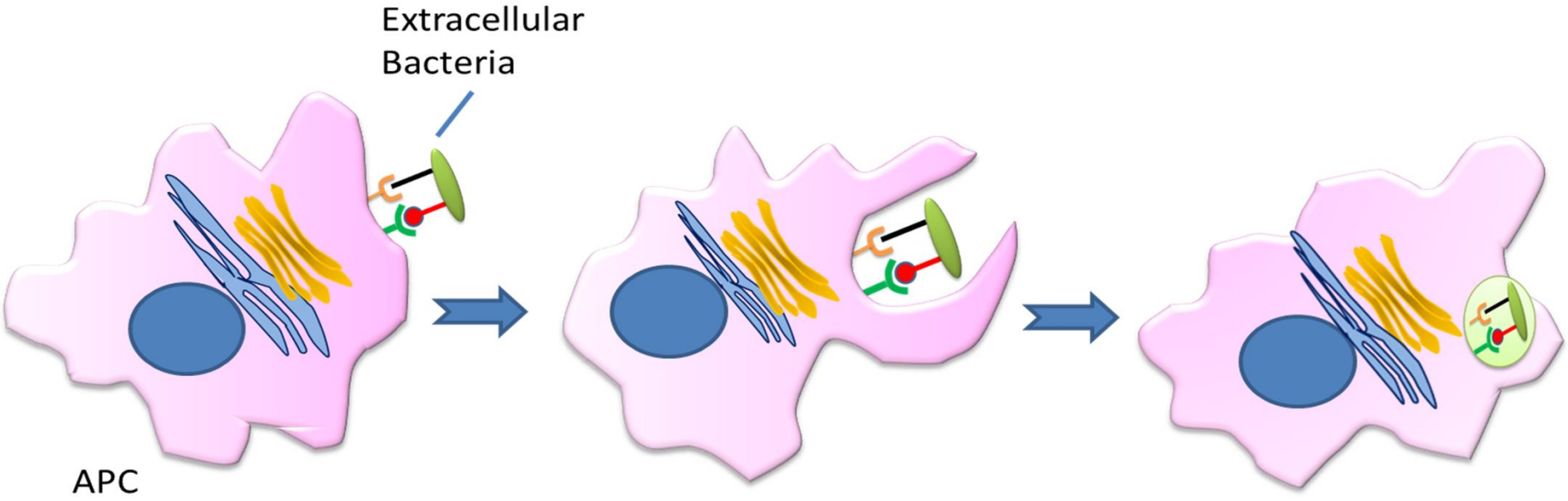
PHAGOCYTOSIS OF EXTRACELLULAR BACTERIA BY APC

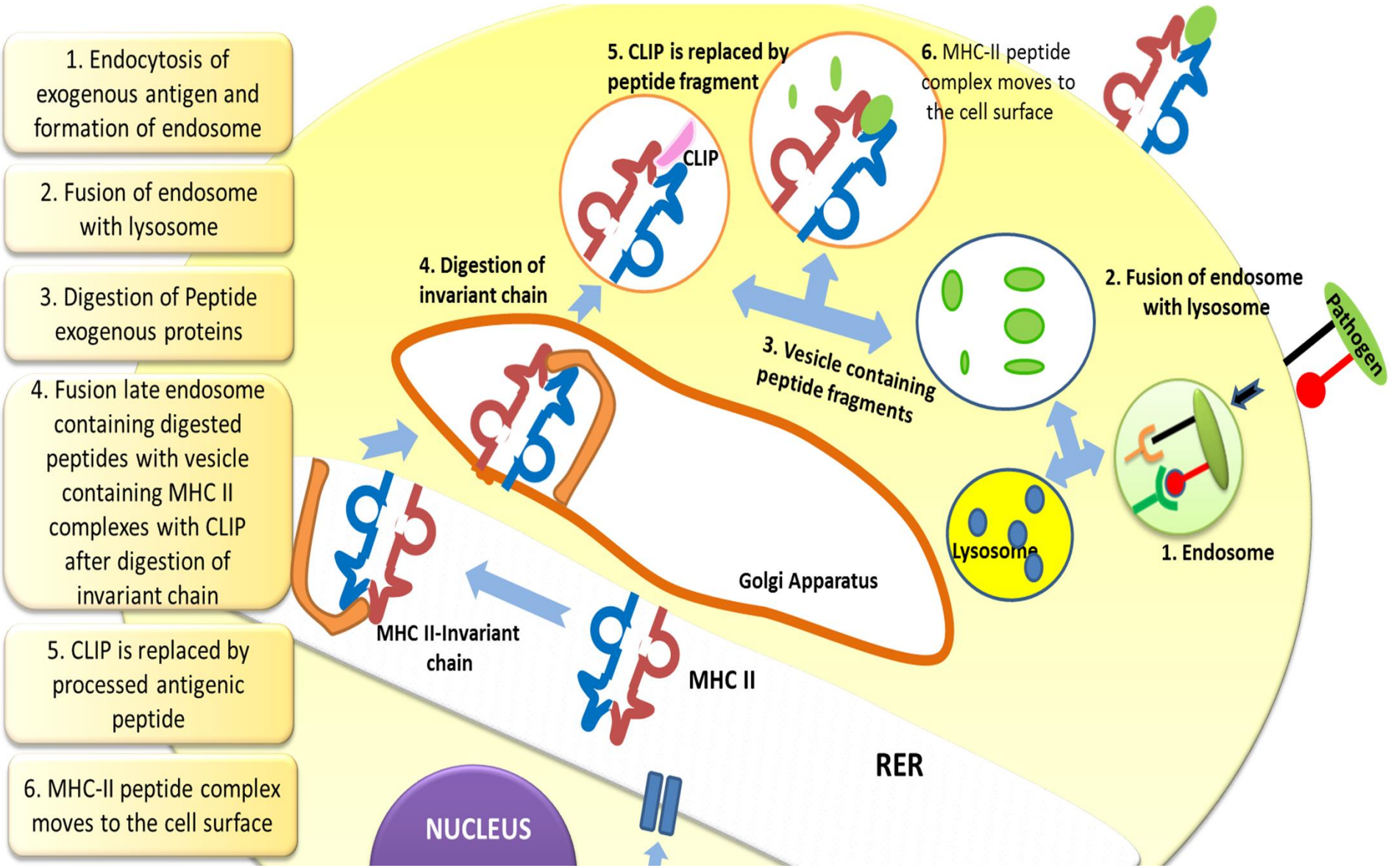


- ✓ Extracellular Pathogen is recognized
- ✓ Phagocytosed
- ✓ Endocytosed

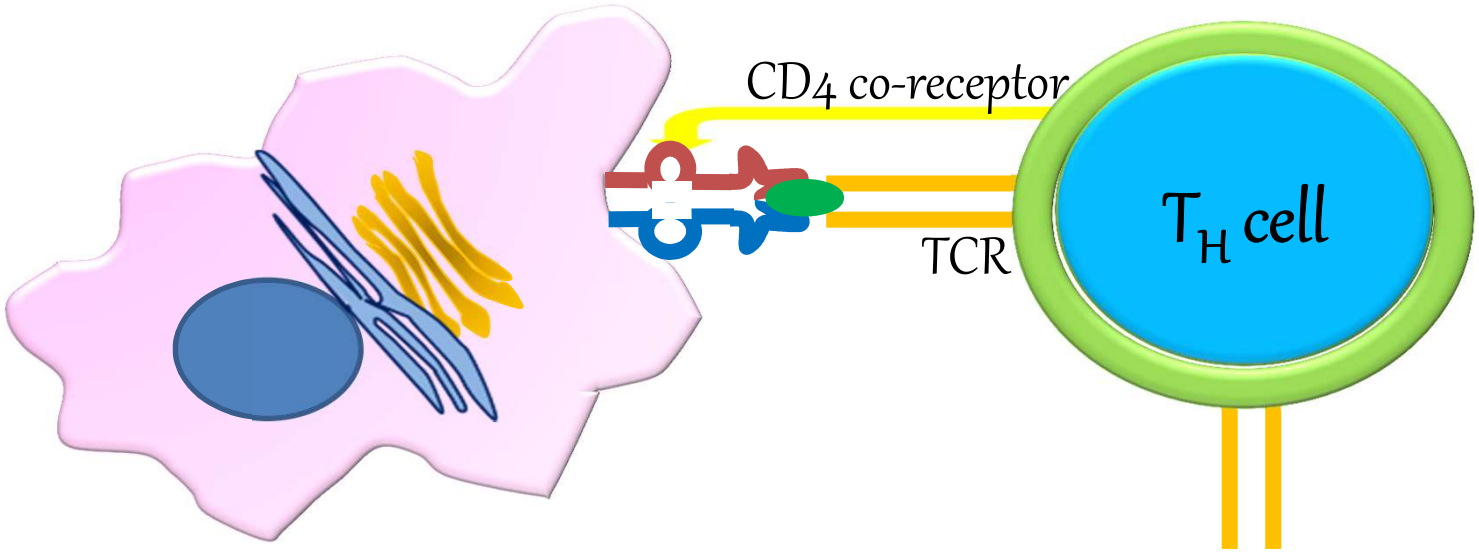
ANTIGENIC PEPTIDE BINDING TO MHC-II

- ✓ MHC-II associate with Invariant Chain (**I chain**) and move to mature endosomes via TGN or from the cell surface after recycling.
- ✓ Within endosomes, **I chain** is sequentially proteolyzed to residual I chain fragment, **CLIP** (class II-associated invariant chain peptide).
- ✓ Subsequent removal of **CLIP** ; MHC-II loaded with antigenic peptides.
- ✓ Antigens delivered to late endosomes by phagocytosis, pinocytosis, endocytosis, and autophagy, are
- ✓ Processed by **cathepsins** and the **thiol oxidoreductase** ,GILT.
- ✓ The MHC-II-peptide complexes are subsequently transported to the cell surface .

MHC-II Antigen Presentation Pathway



RECOGNITION OF PEPTIDE : MHC COMPLEX BY T-HELPER CELL



- ✓ APC cells display the processed peptide in the Antigen Binding Cleft of the MHC-II

- ✓ T Helper Cells recognize the Antigen displayed in the MHC-II with the TCR and co-receptor CD4.

REFERENCES

- Antigen Presentation, In Immunology Guidebook, 2004.
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THANK YOU

To be continued...