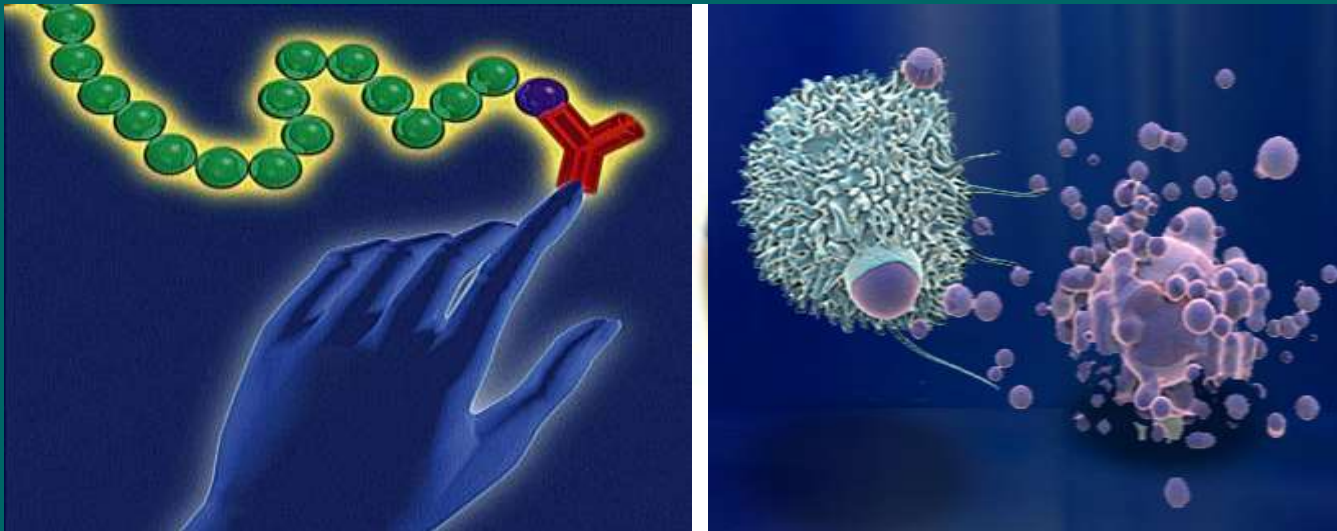


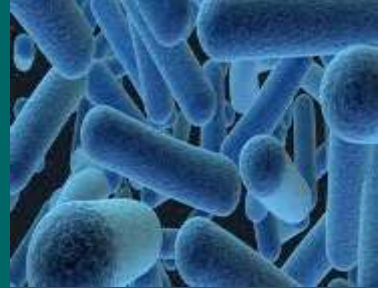
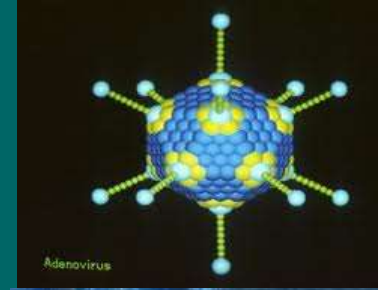
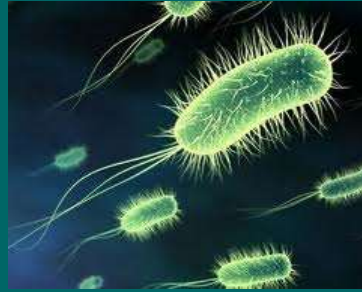


# ANTIGEN PROCESSING AND PRESENTATION



**J. Dandapat**  
**Dept. of Biotechnology**  
**Utkal University**  
**Bhubaneswar**

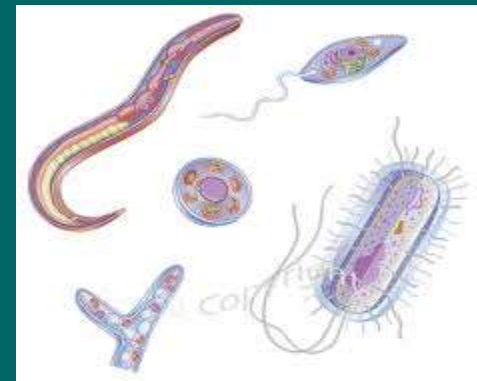
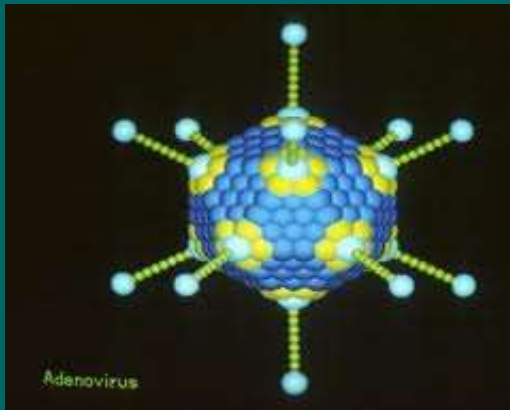
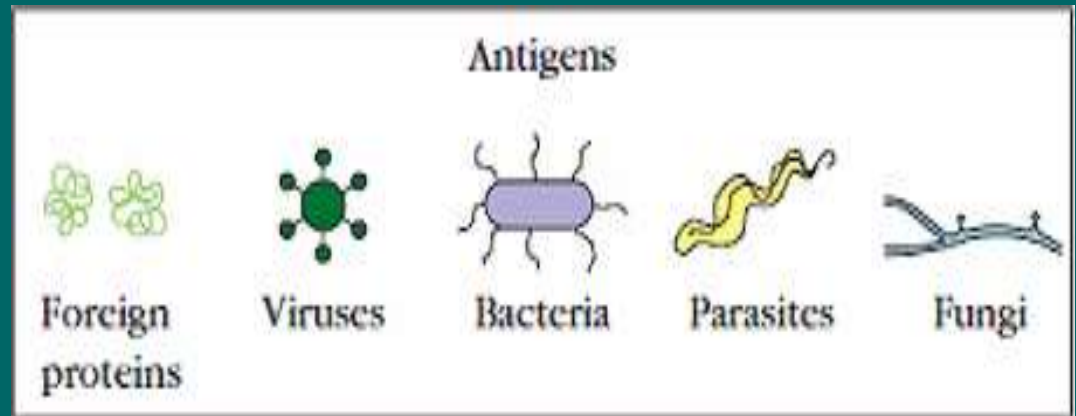
# Man is floating in the ocean of microbes



Every single moment we are in the state of war

# DIVERSE NATURE OF ANTIGEN

- ANTIGEN
- IMMUNOGEN
- HAPTEN





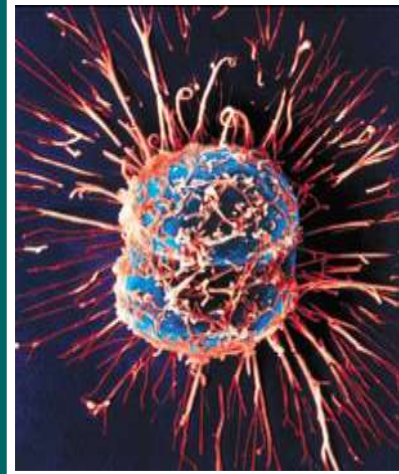
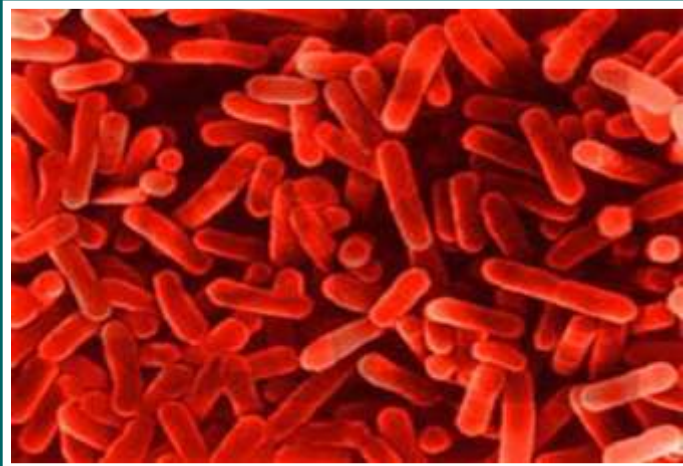
# OUR IMMUNE SYSTEM: NEIGHBOUR'S ENVY, OWNER'S PRIDE

- Nature has gifted the human body with a built in defense system consisting of varieties of troops, tailor-made ammunition factories (antibodies) and suicide brigades (regiments of lymphocytes).
- The defense organization of human body is so
- efficient, so well structured and so sophisticated it can manage / try to manage every adverse situation.
- That is why the body emerges victories in its battle most of the time and the credit goes to our immune system.





- Immunity: The body's defense against disease causing organisms, malfunctioning cells, and foreign particles





# IMMUNITY

## INNATE IMMUNITY

- Physical and chemical barriers
- Phagocytes  
(Neutrophils & Macrophages)
- Inflammatory process.

## ACQUIRED IMMUNITY

Specific towards particular antigen and enhanced with repeated exposure

### Naturally Acquired Immunity

#### Active Immunity

- Lifelong: Chickenpox
- Temporary: Influenza, Intestinal infections

#### Passive Immunity

Colostrum

### Artificially Acquired Immunity

#### Active Immunity

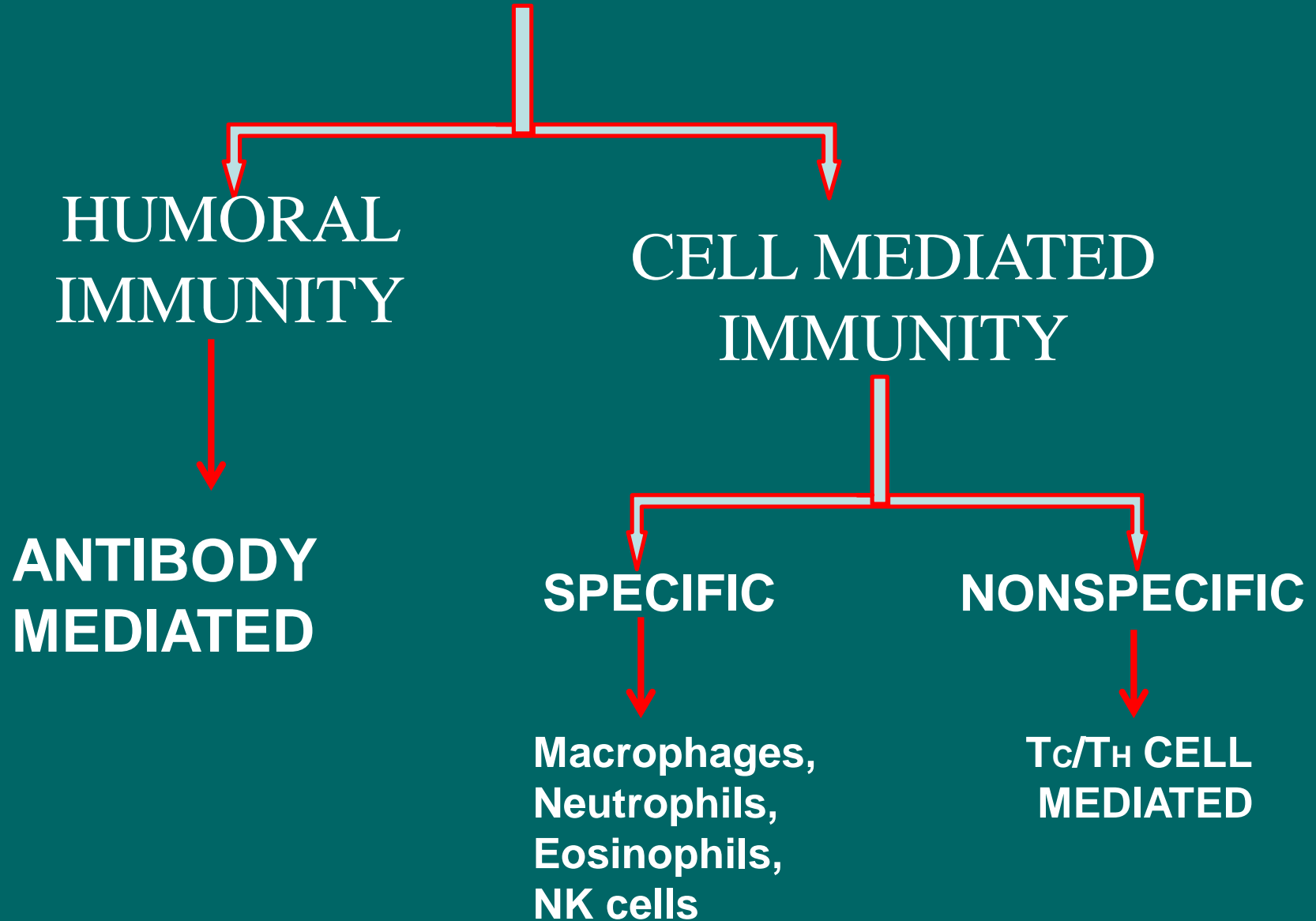
- Life Long: Oral polio vaccine
- Temporary: Tetanus toxoid

#### Passive Immunity

Antiserum:  
Snake antivenom



# ACQUIRED IMMUNITY



# EVENTS

- **Endogenous Ags:** antigens synthesized within cells, including self and nonself protein---class I MHC molecules.
- **Exogenous Ags:** antigens comes outside the cells, including self and nonself protein---class II MHC molecules.
- **Ag capturing**---Endocytosis (internalization), Phagocytosis, Pinocytosis, Receptor-mediated endocytosis.
- **Antigen processing:** the conversion of native proteins to peptides which can combine with MHC molecules.
- **Antigen presentation:** the course of formation and display of peptide-MHC complexes on the surface of APCs and the course of peptide-MHC complexes recognition by T cells.

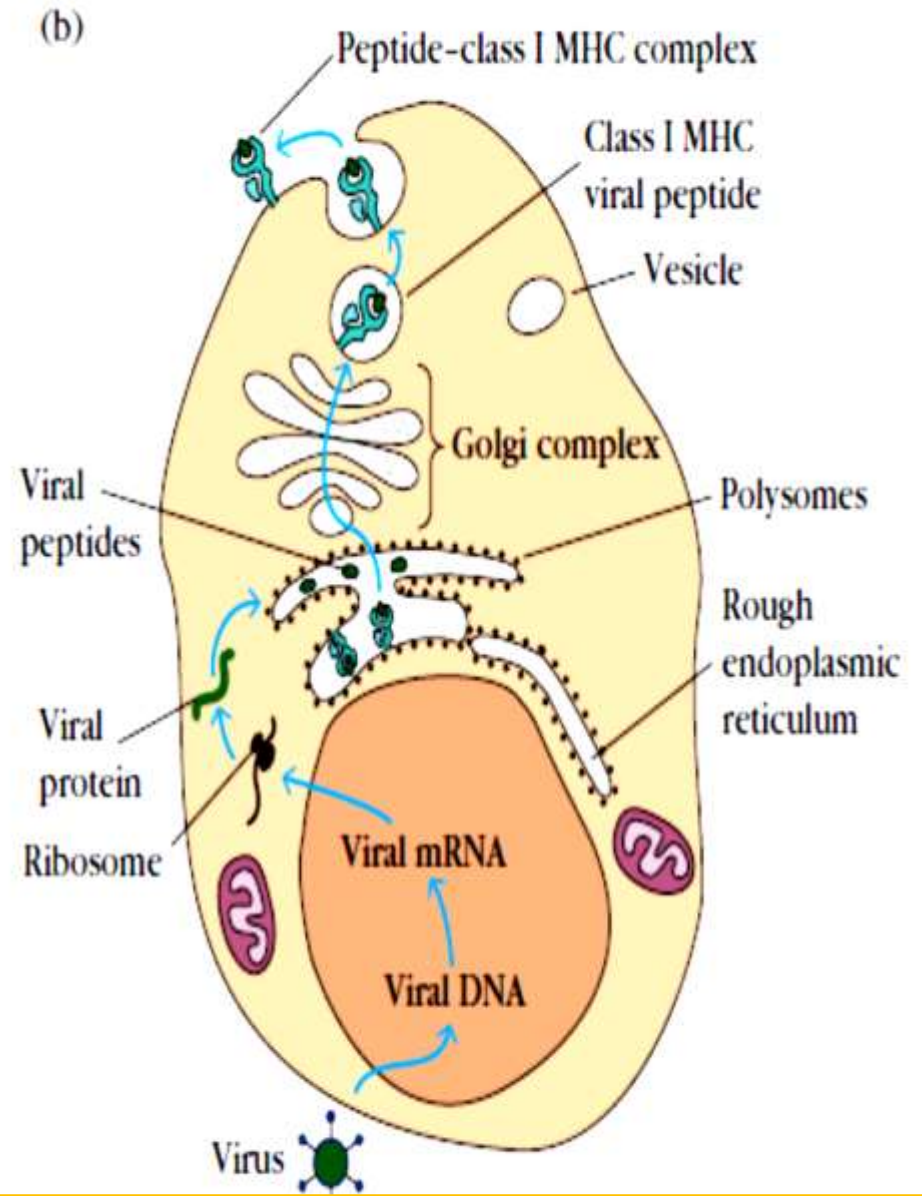
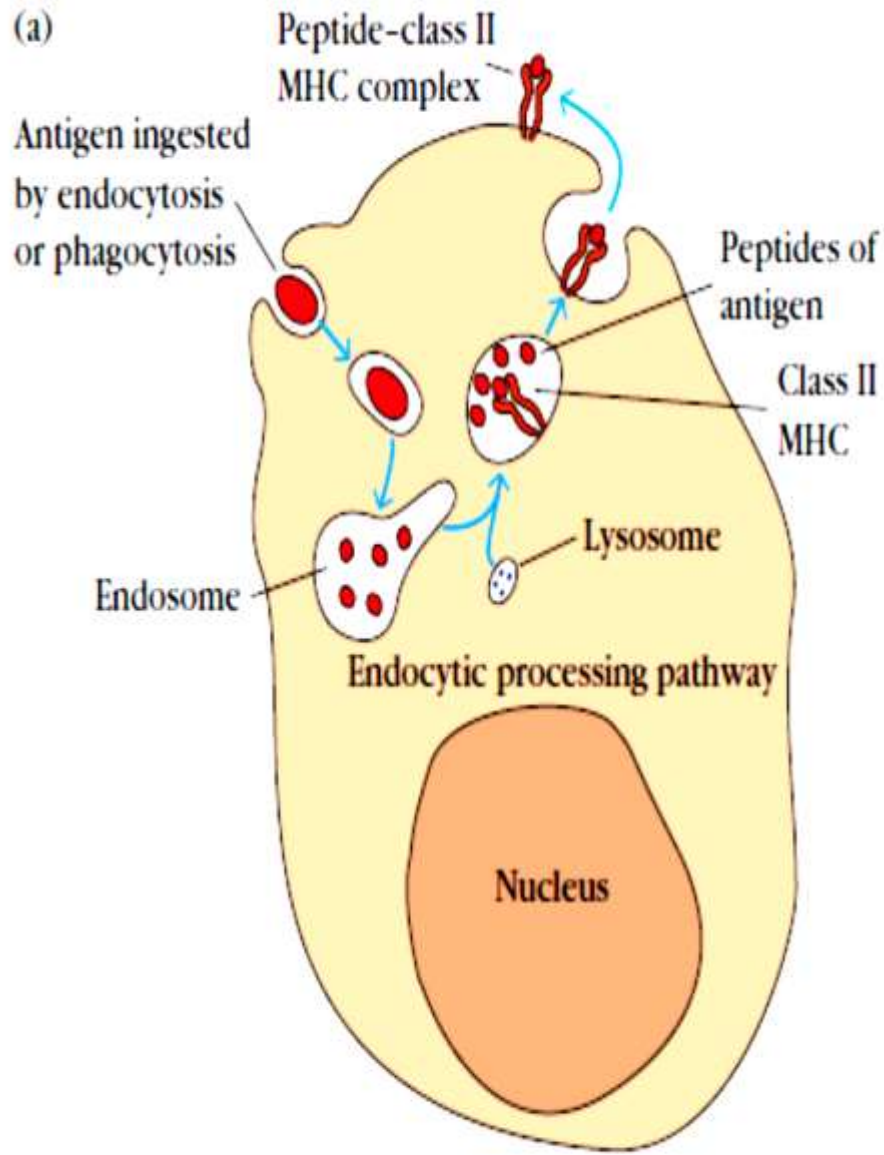


# ANTIGEN PRESENTING CELLS (APC)

- A group of immune cells, whose role is to take up, process and present antigenic peptides to T cells.
  - **Professional APC**
    - Macrophages, dendritic cells, and B cells, which can express MHC class II molecules.
  - **Non-professional APC**
    - Other cell type capable of expressing MHC class II molecules
    - eg. Endothelial cells, EC
    - Fibroblasts
    - Activated T cell

# ANTIGEN PRESENTING CELLS (APC)

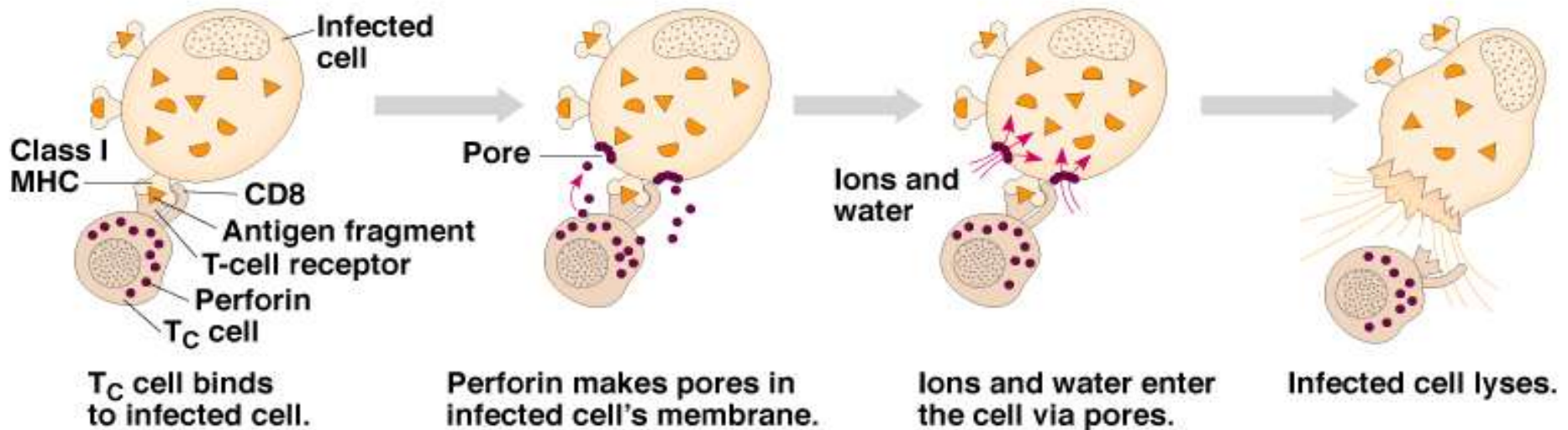
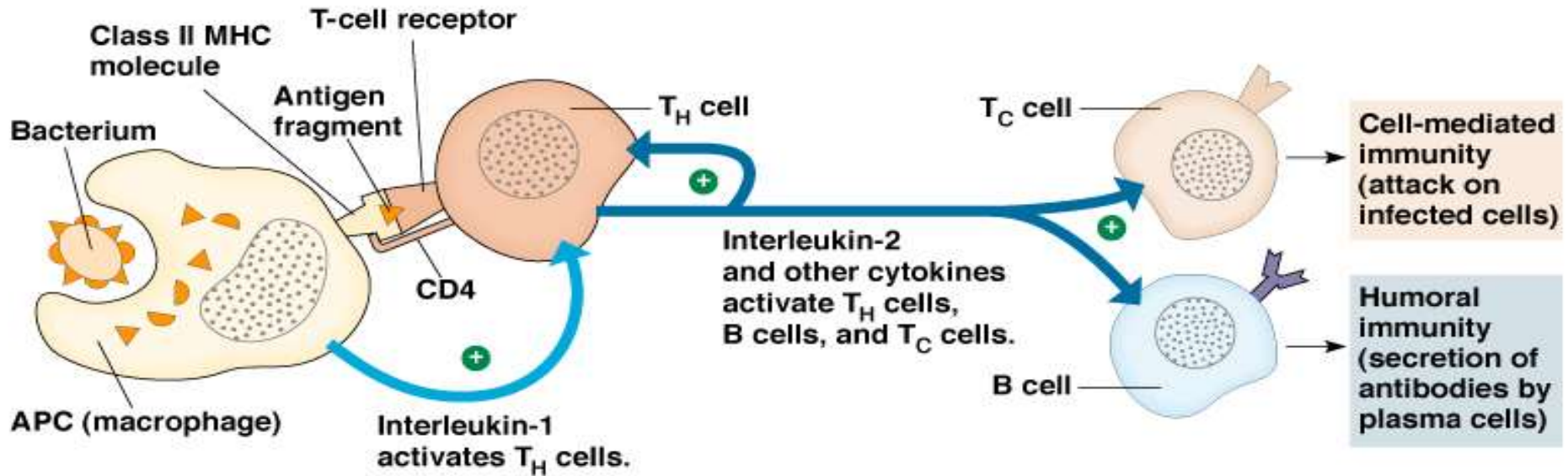
APC	Present to
Macrophage	T cell via MHC antigen
Dendritic cells	T cell via MHC antigen
B cells	T cell via antigen capture by surface antibody and MHC antigen
Activated T cells	T cell via MHC antigen



**PROCESSING OF EXOGENOUS ANTIGEN**

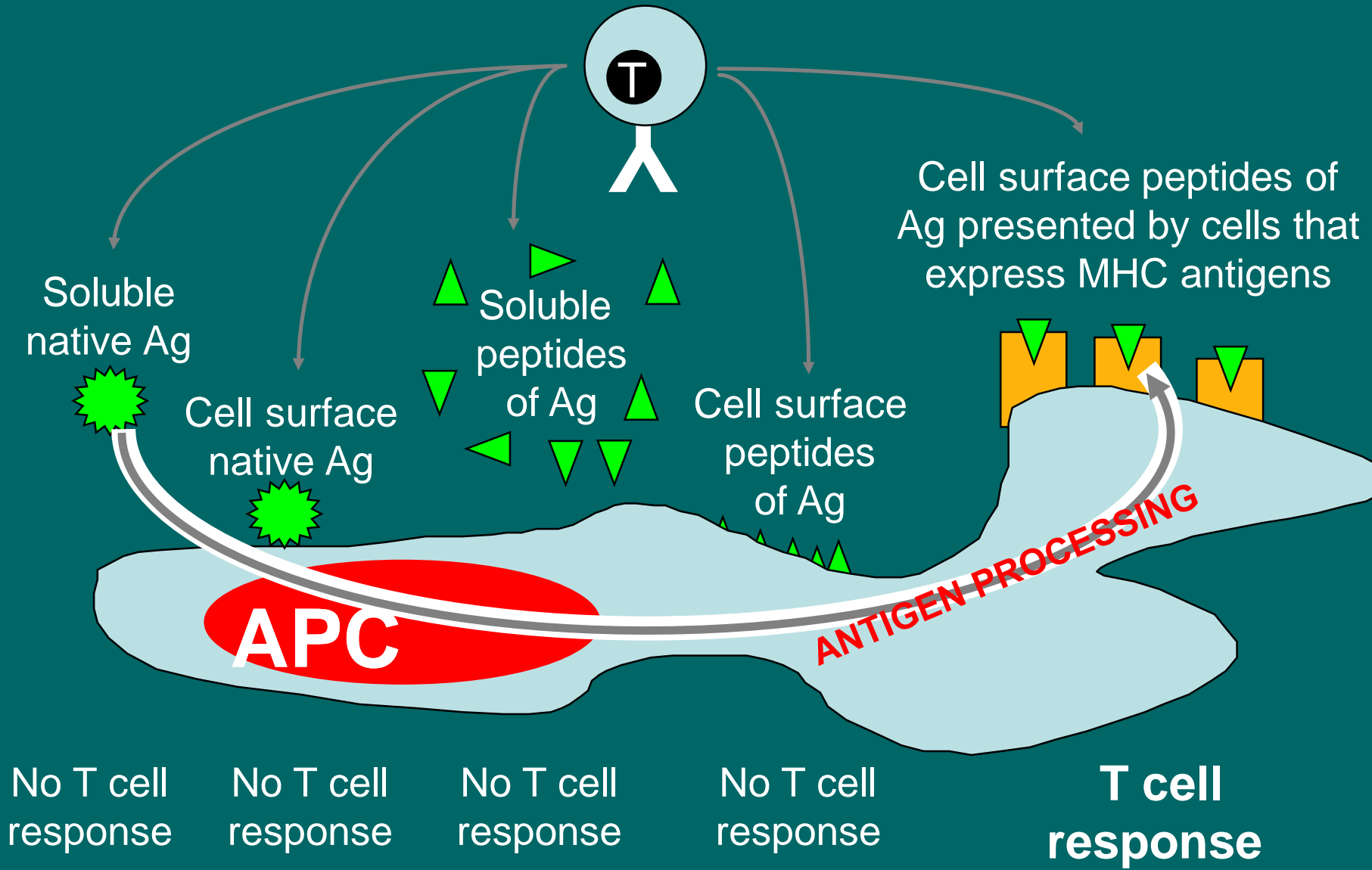
**PROCESSING OF ENDOGENOUS ANTIGEN**

# Central Role of Helper T Cells



(a)

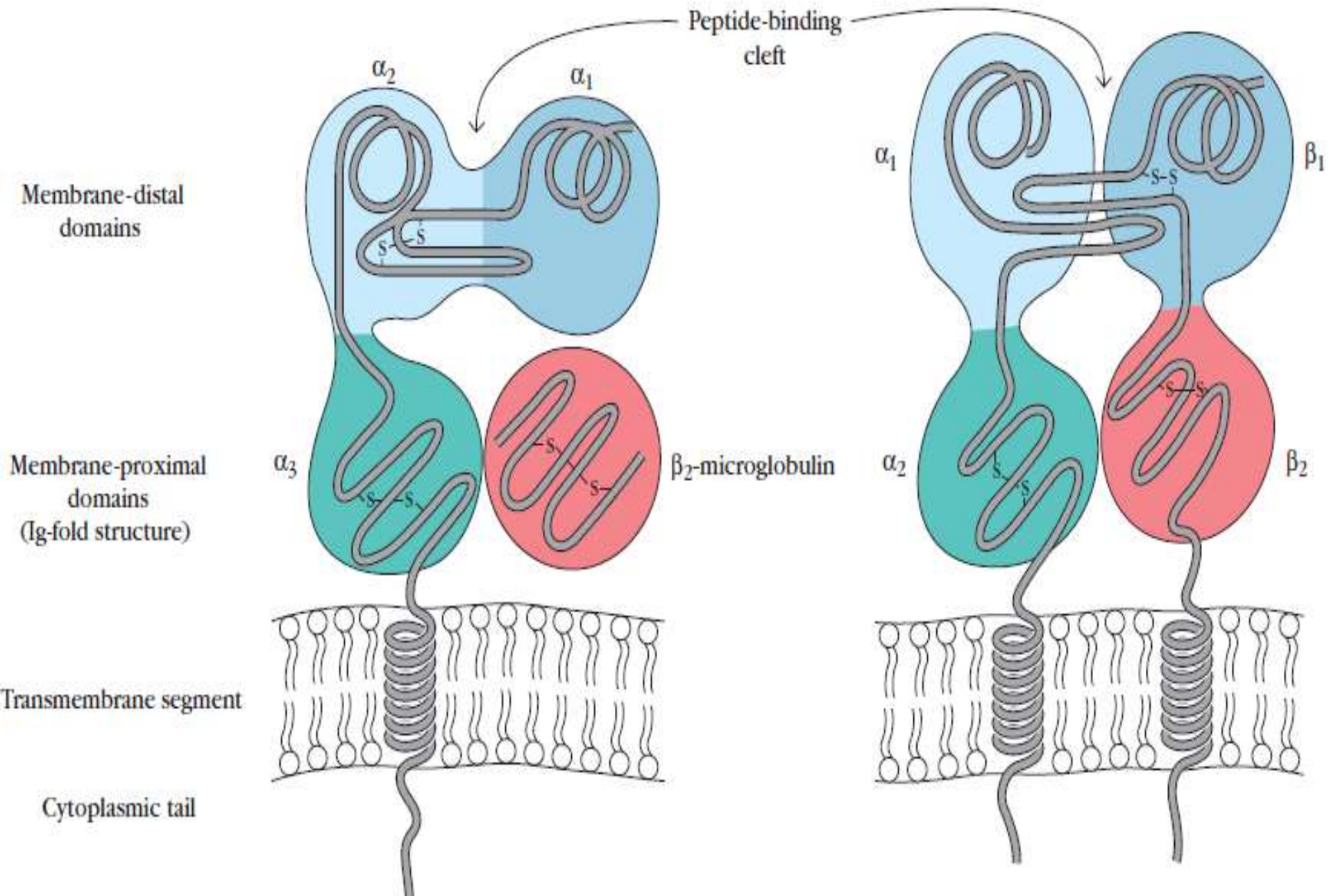
# Antigens must be processed in order to be recognised by T cells





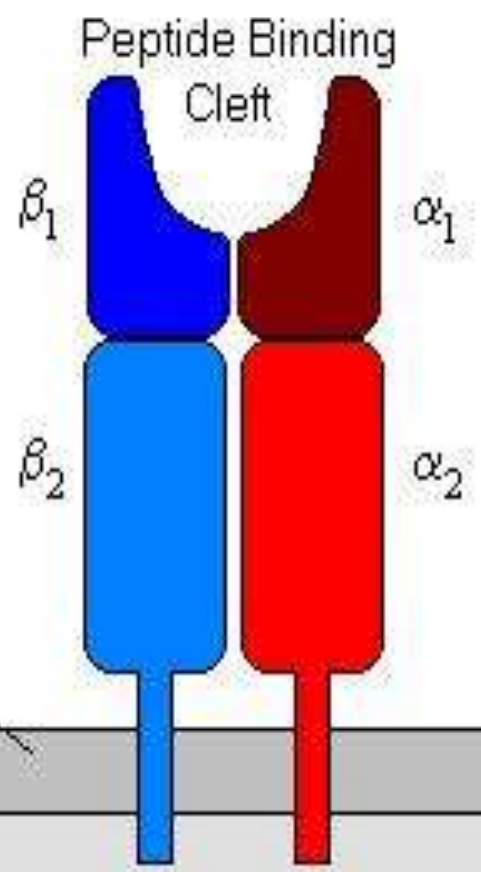
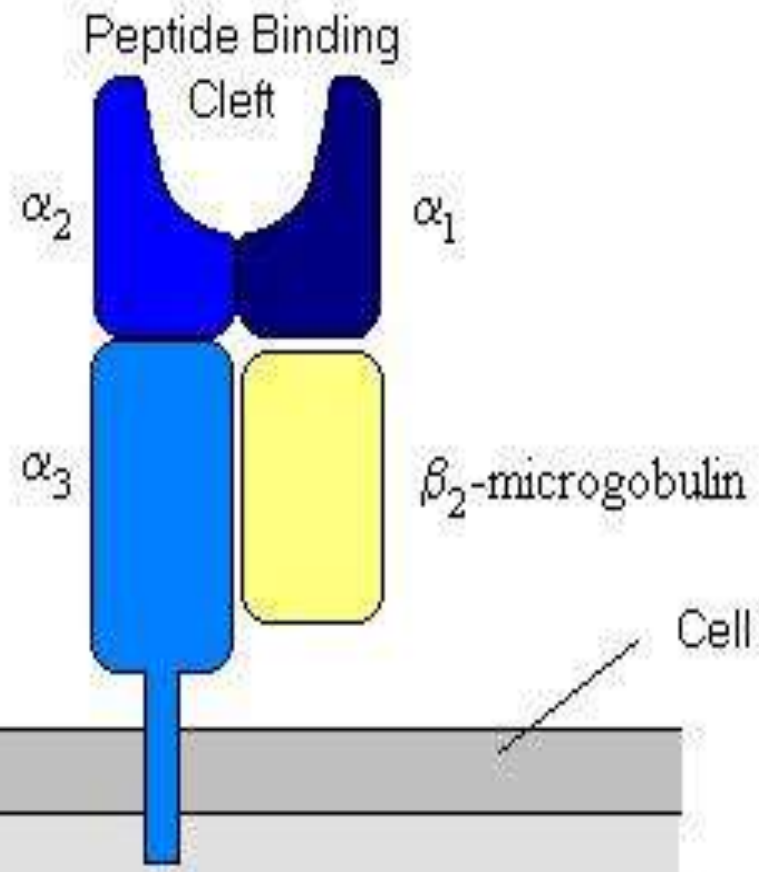
# MHC CLASS-I MOLECULE

# MHC CLASS-II MOLECULE



# MHC Class I

# MHC Class II



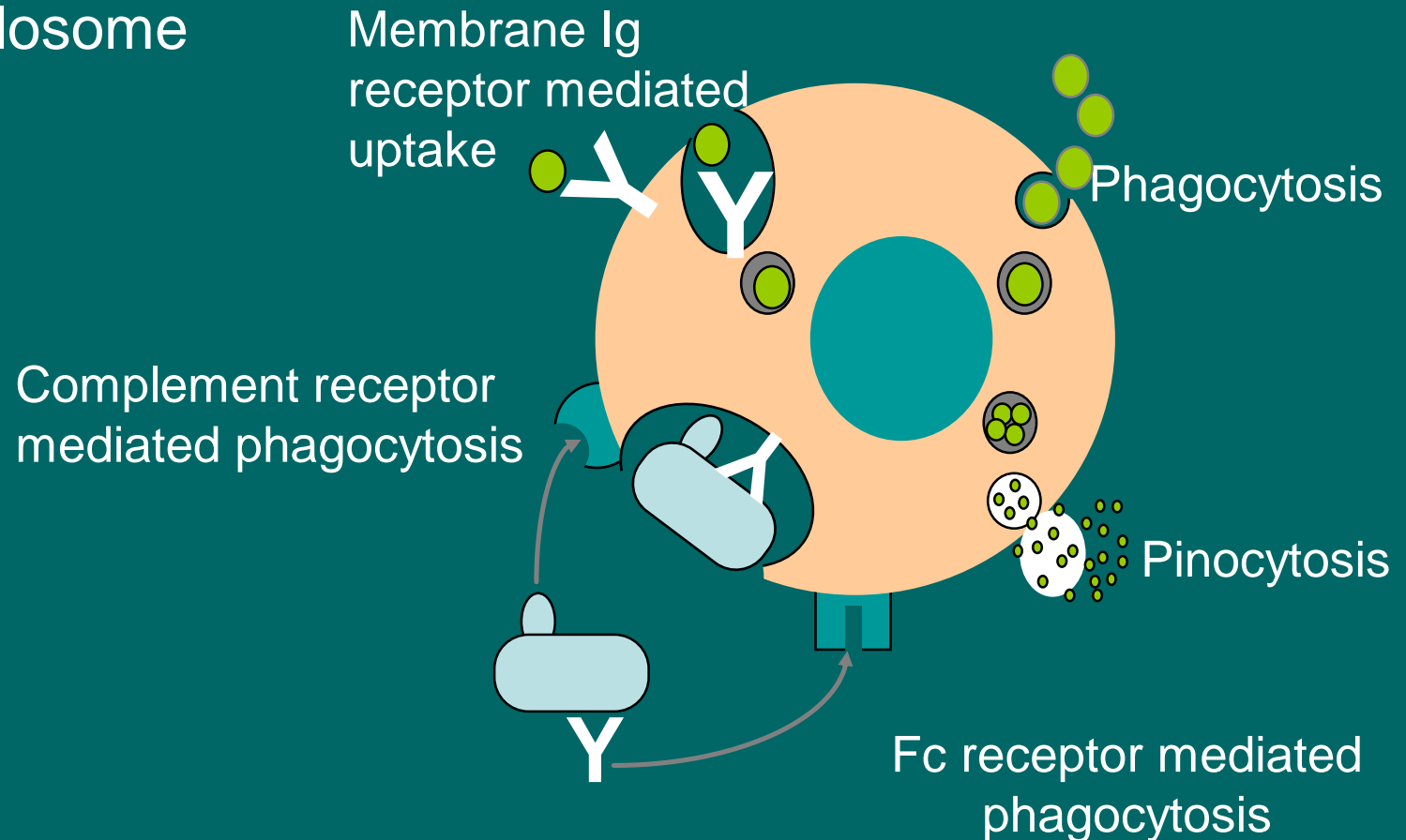
# ***Processing and presentation of exogenous antigen (Class II MHC pathway)***

- 1. Capture of exogenous Ag**
- 2. Processing of Ag**
- 3. Synthesis and transportation of class II MHC molecules**
- 4. Peptide loading of class II MHC molecules**
- 5. Presenting to CD4+T cells**

# Capture of exogenous Ag

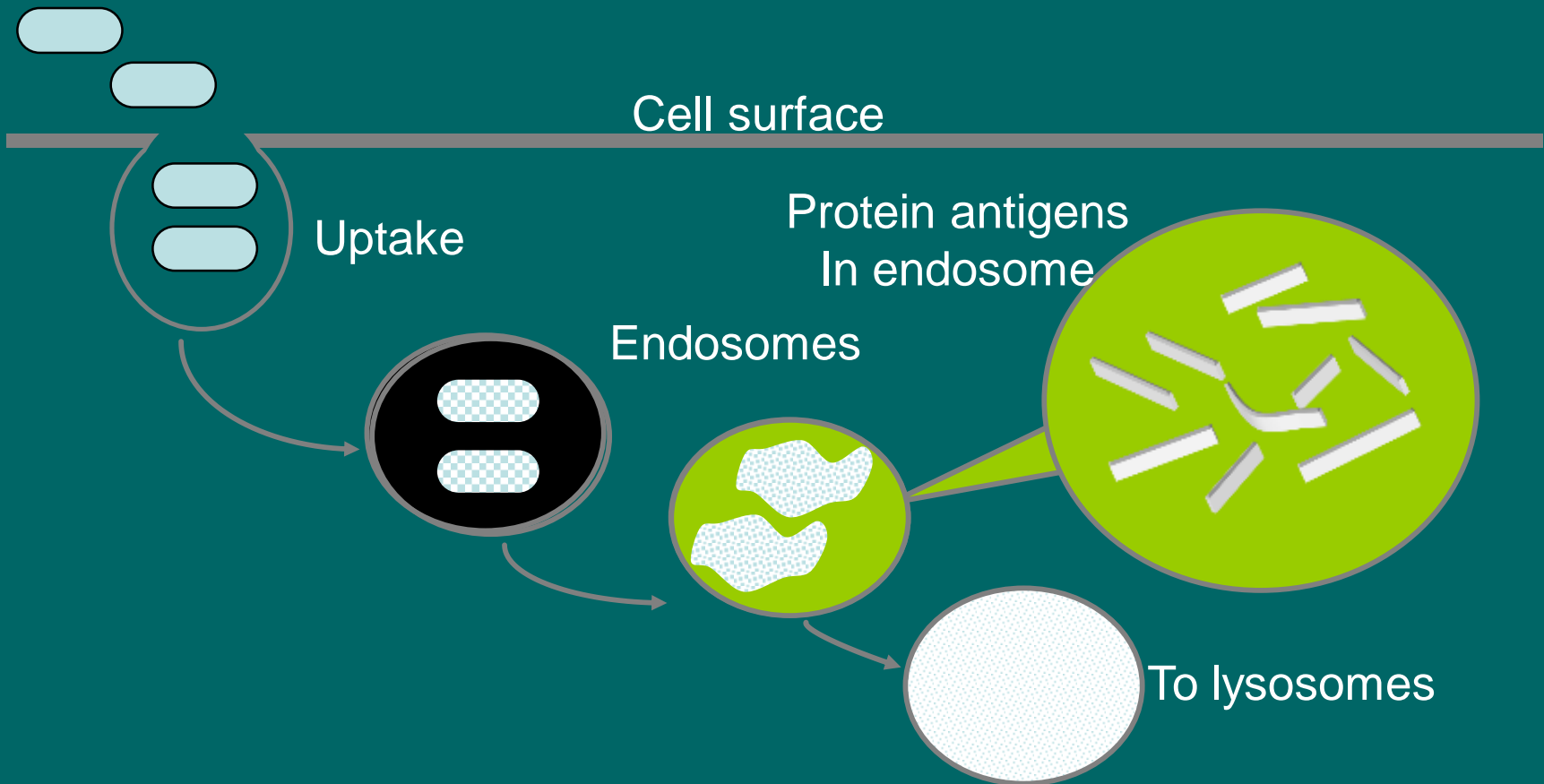
- Endocytosis:
  - Phagocytosis: particles or granules
  - Pinocytosis: soluble antigens
  - Receptor-mediated endocytosis:

- Form endosome



# Processing of exogenous Ag

Ag  $\xrightarrow[\text{endosome + lysosome}]{\text{Cathepsin}}$  antigen peptides(13-18aa)



Cathepsin B, D and L proteases are activated by the decrease in pH



### 3. Synthesis and transportation of class II MHC molecules

#### Synthesis of class II MHC molecules in ER



Ii chain --- class II MHC molecule (I<sub>i</sub>3 α 3 β 3 )

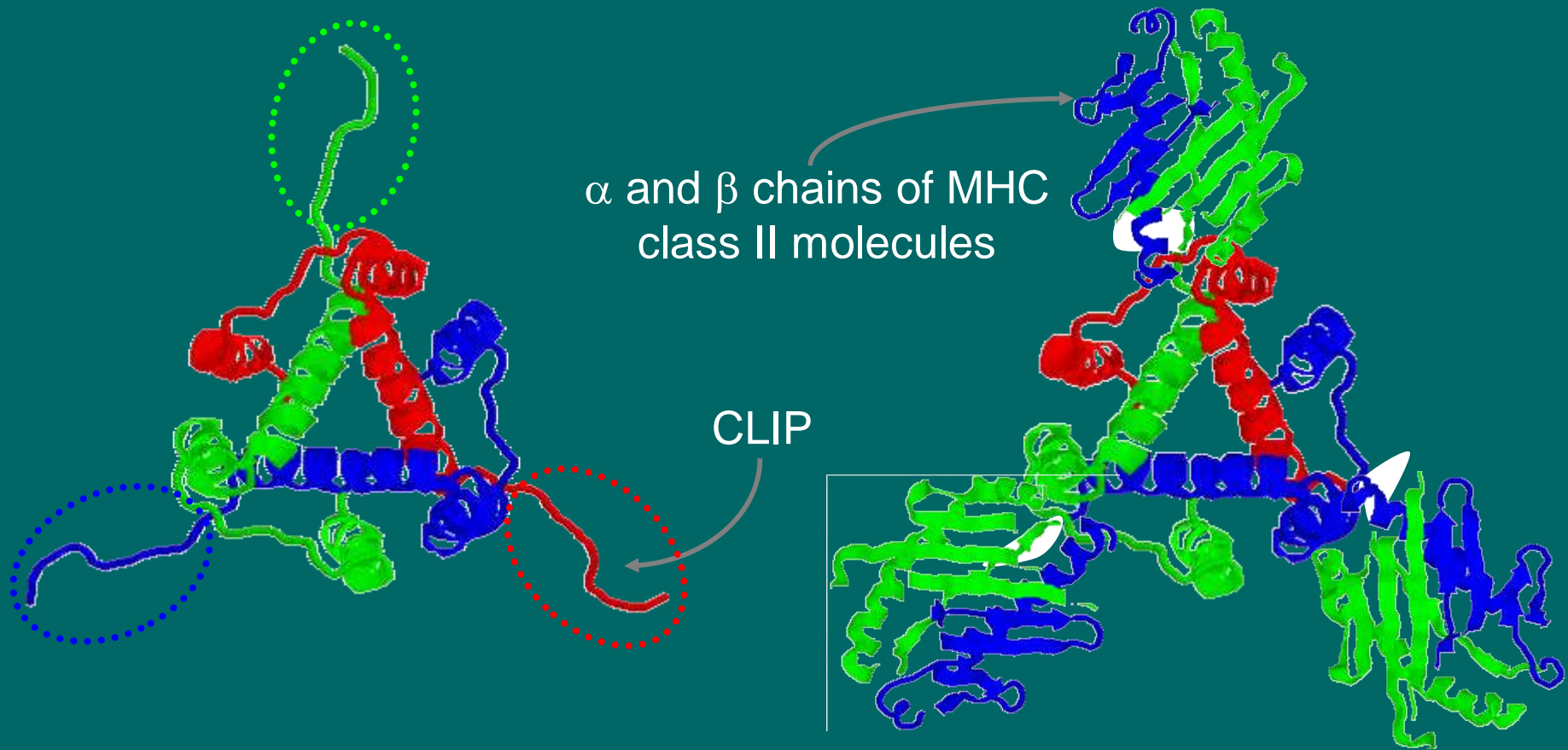
- ① Promote formation of class II MHC dimer
- ② Preventing endogenous peptide from combining with class II MHC molecules within ER
- ③ Leading class II MHC molecules into endosome from ER



Endosome (MHC)

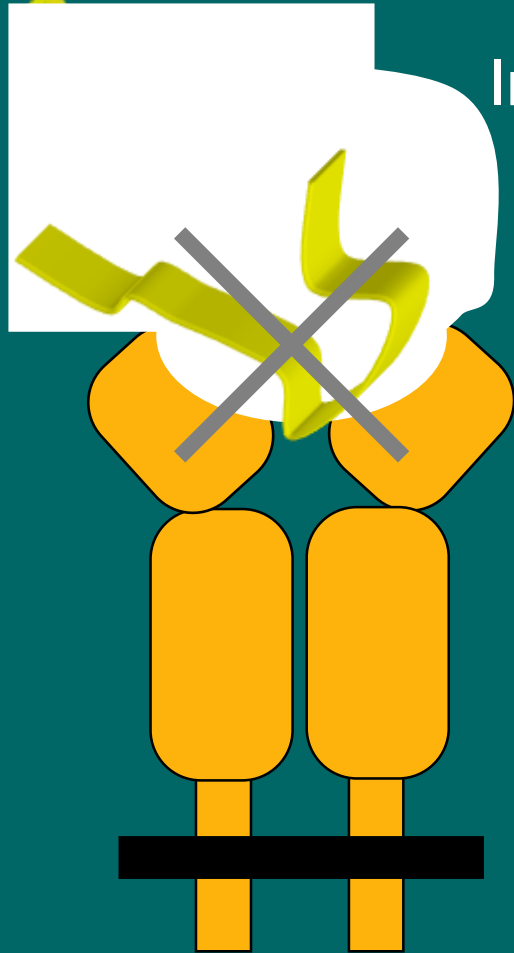
\*Ii chain: Class II-associated invariant chain

# Invariant chain CLIP peptide



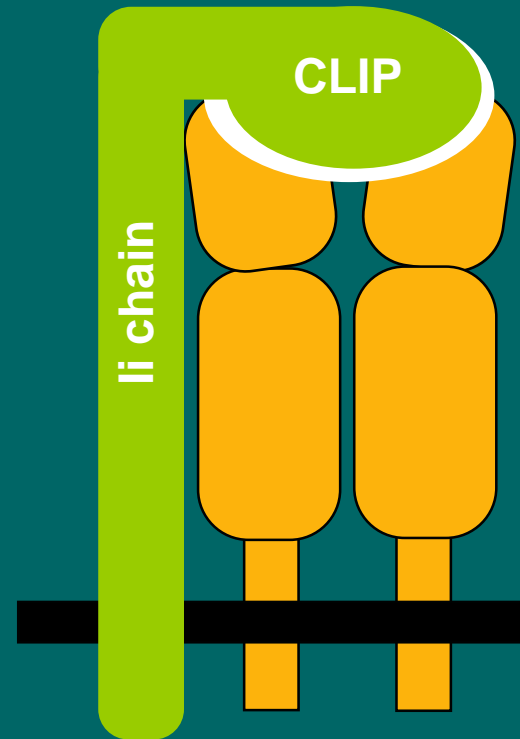
A peptide of the invariant chain blocks the MHC molecule binding site. This peptide is called the Class II associated Invariant chain Peptide (CLIP)

# MHC class II maturation and invariant chain



Need to prevent newly synthesised, unfolded self proteins from binding to immature MHC

In the endoplasmic reticulum



Invariant chain stabilises MHC class II by non-covalently binding to the immature MHC class II molecule and forming a monomeric complex

## 4. Peptide loading of class II MHC molecules

**Ii - class II MHC molecules**

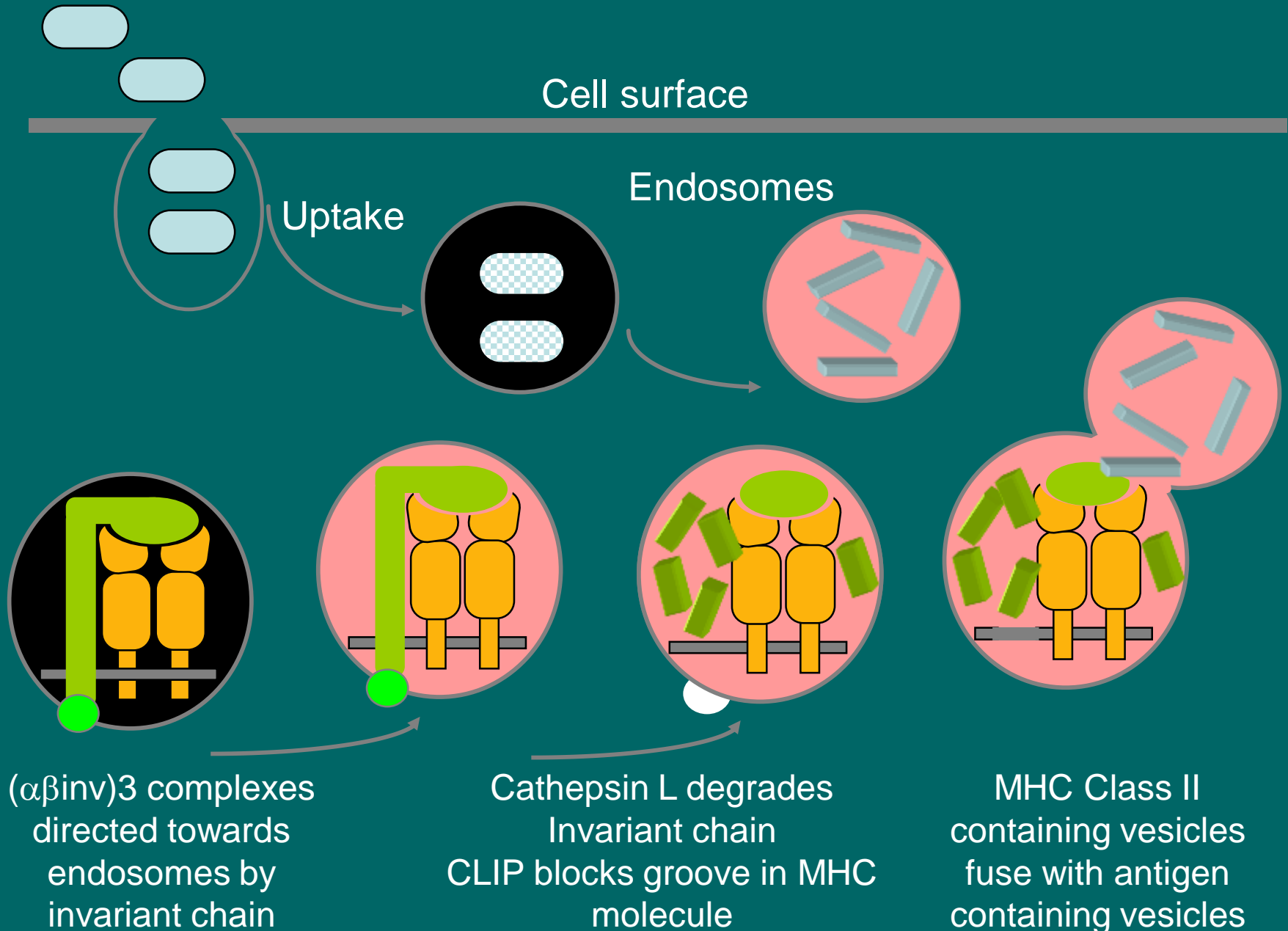
protease      Ii chain cleaving

**CLIP - class II MHC molecules**

HLA-DM      CLIP releasing

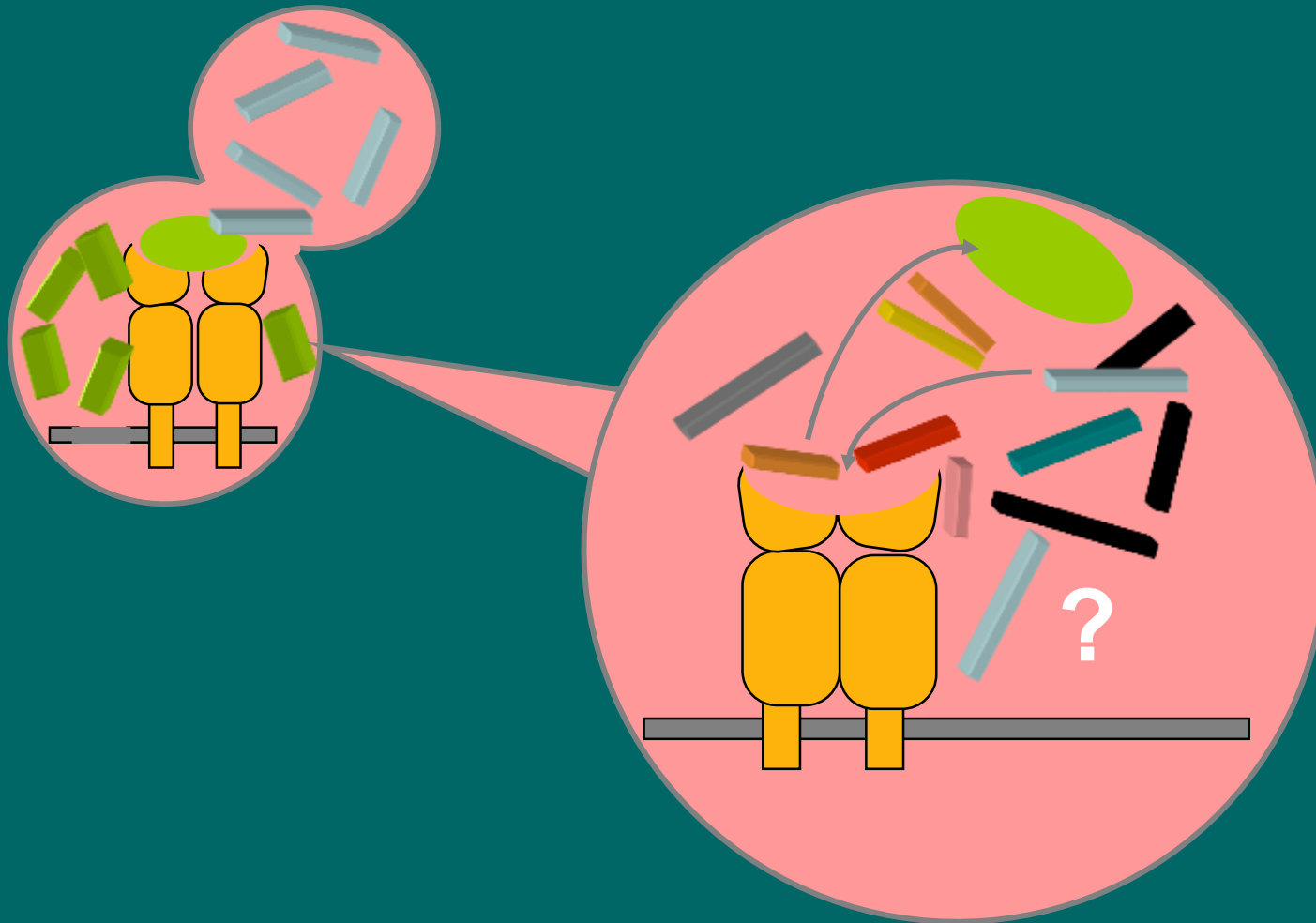
**Antigen peptide - class II MHC complexes**

# Class II associated invariant chain peptide (CLIP)

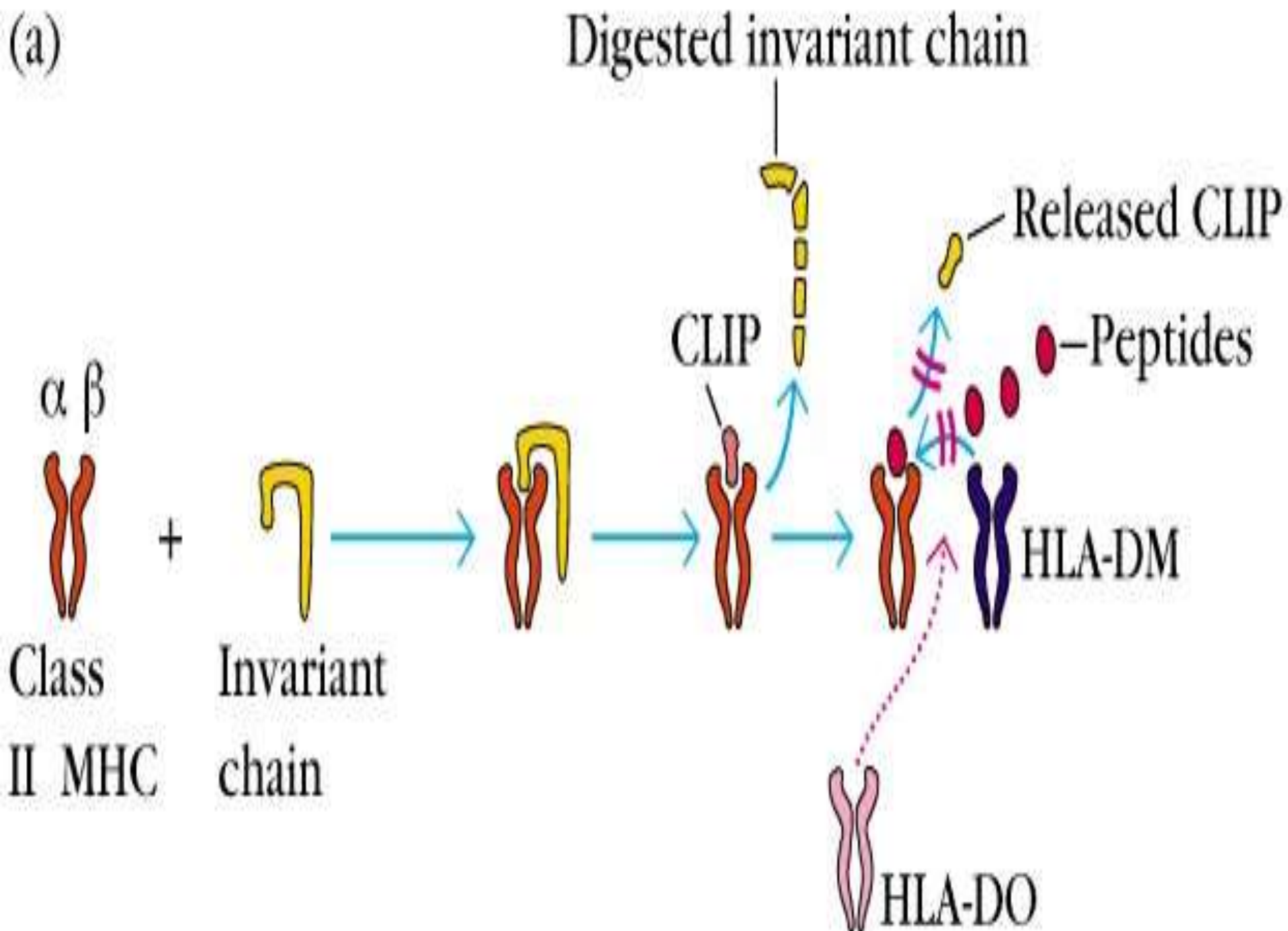




# Removal of CLIP

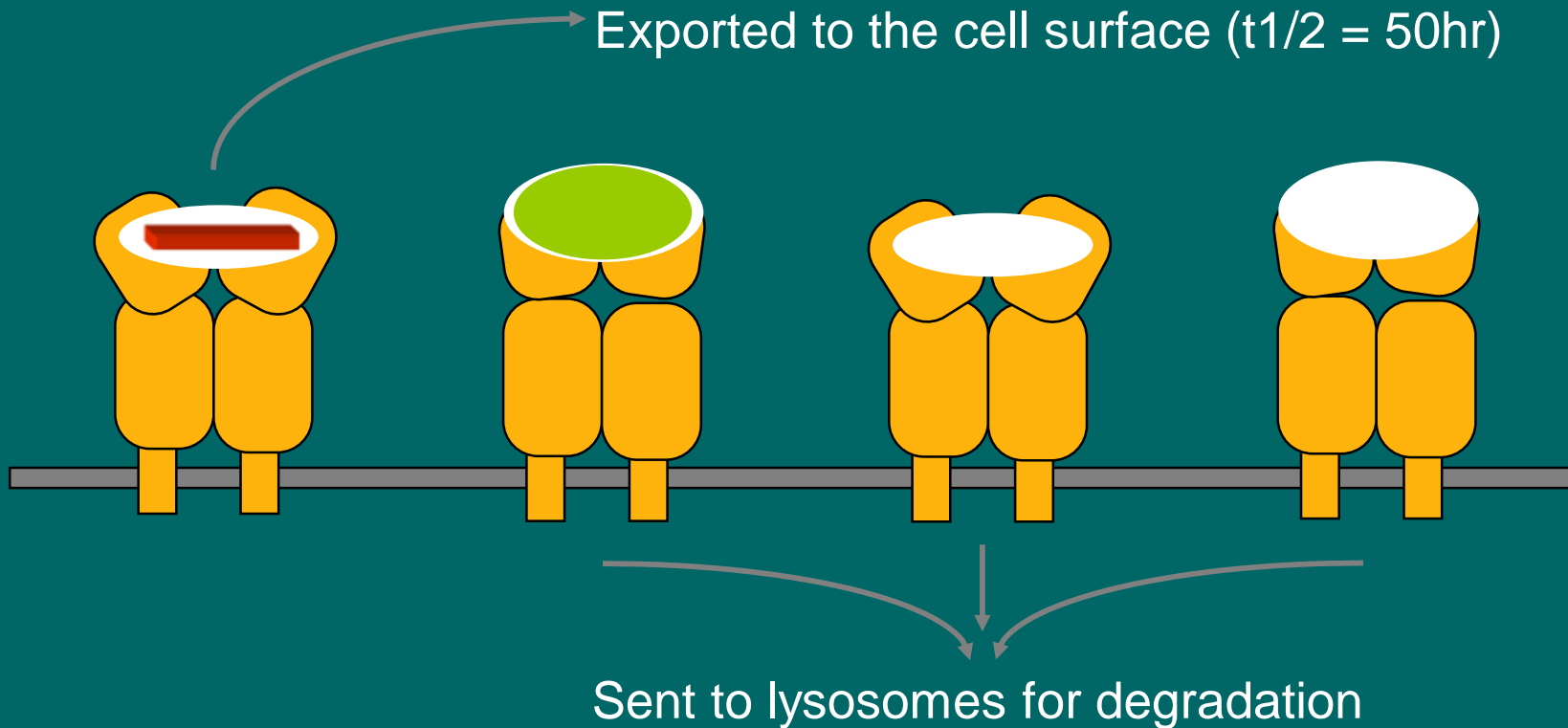


How can the peptide stably bind to a floppy binding site?  
Competition between large number of peptides



# 5. Presenting to CD4<sup>+</sup>T cells

Antigen peptide-class II MHC molecules presented on cell membrane by exocytosis  
Surface expression of class II MHC-peptide complexes



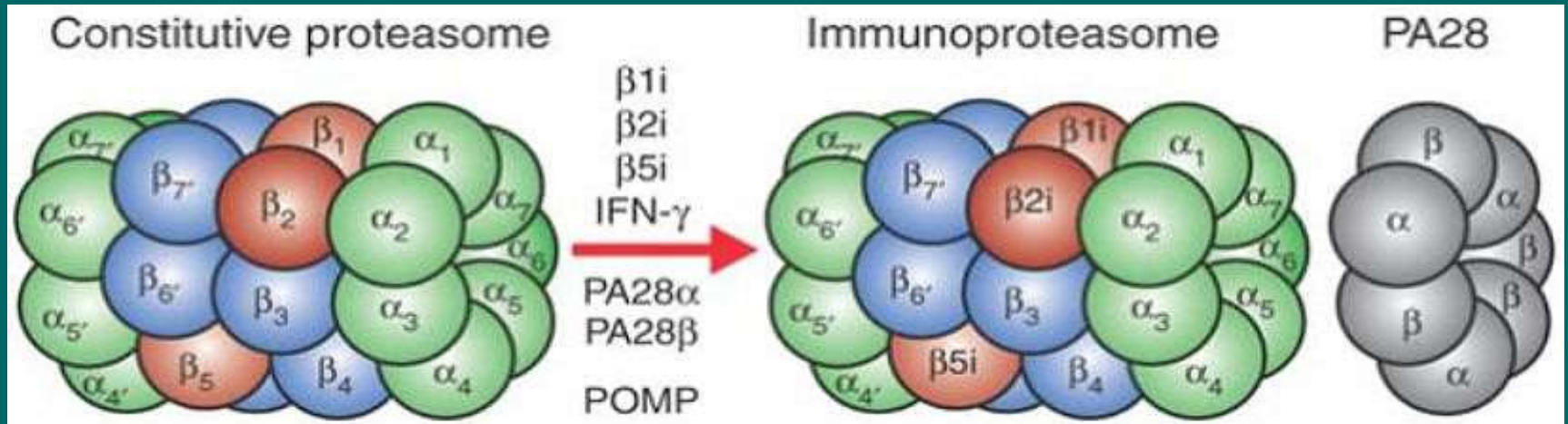
MHC compartment sorts peptide-MHC complexes for surface expression or lysosomal degradation

# ***Processing and presentation of endogenous antigen (class I MHC pathway)***

- 1. Processing of endogenous Ag**
- 2. Transporting of antigen peptide into ER**
- 3. Peptide loading of class I MHC molecules**
- 4. Presenting to CD8+T cells**

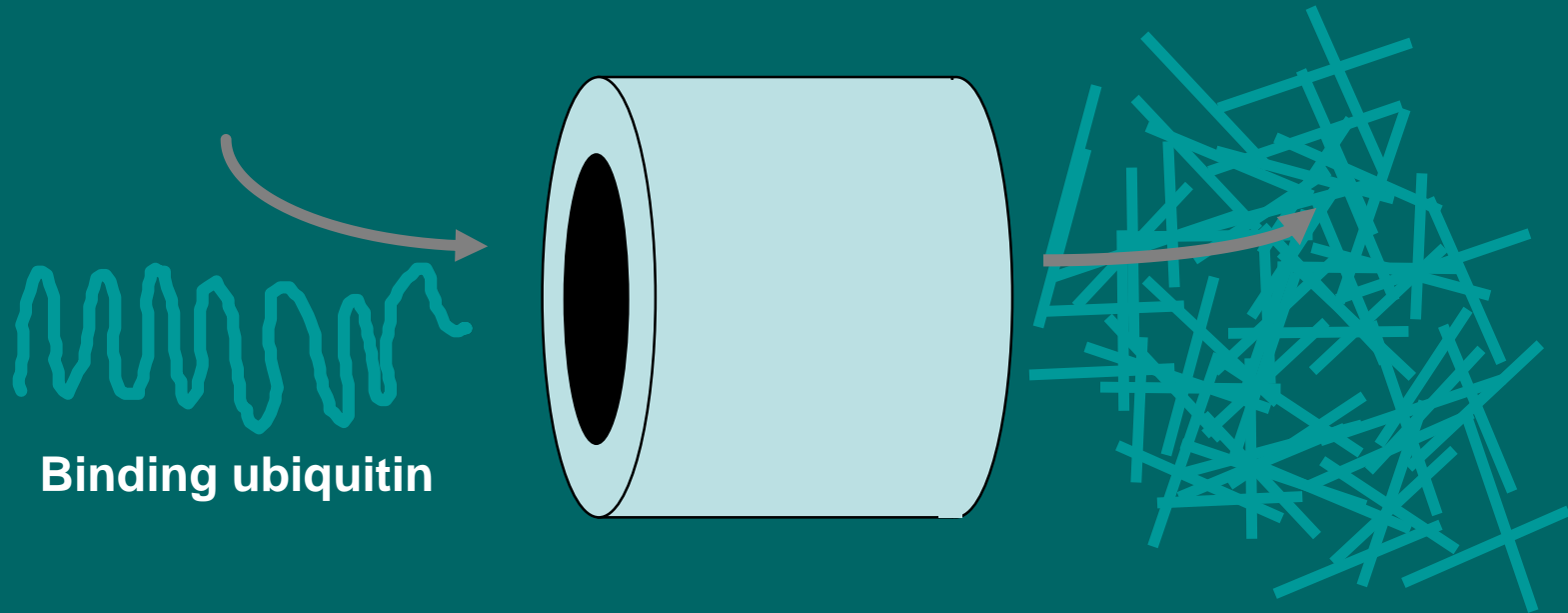
# 1. Processing of endogenous Ag

- **Proteasome : 20S, 26S**
- Low molecular weight polypeptide (LMP) : **LMP2, LMP7, LMP10**
- Ag  $\longrightarrow$  antigen peptides (6-10aa)



# Degradation in the proteasome

Cytoplasmic cellular proteins, including non-self proteins are degraded continuously by a multicatalytic protease



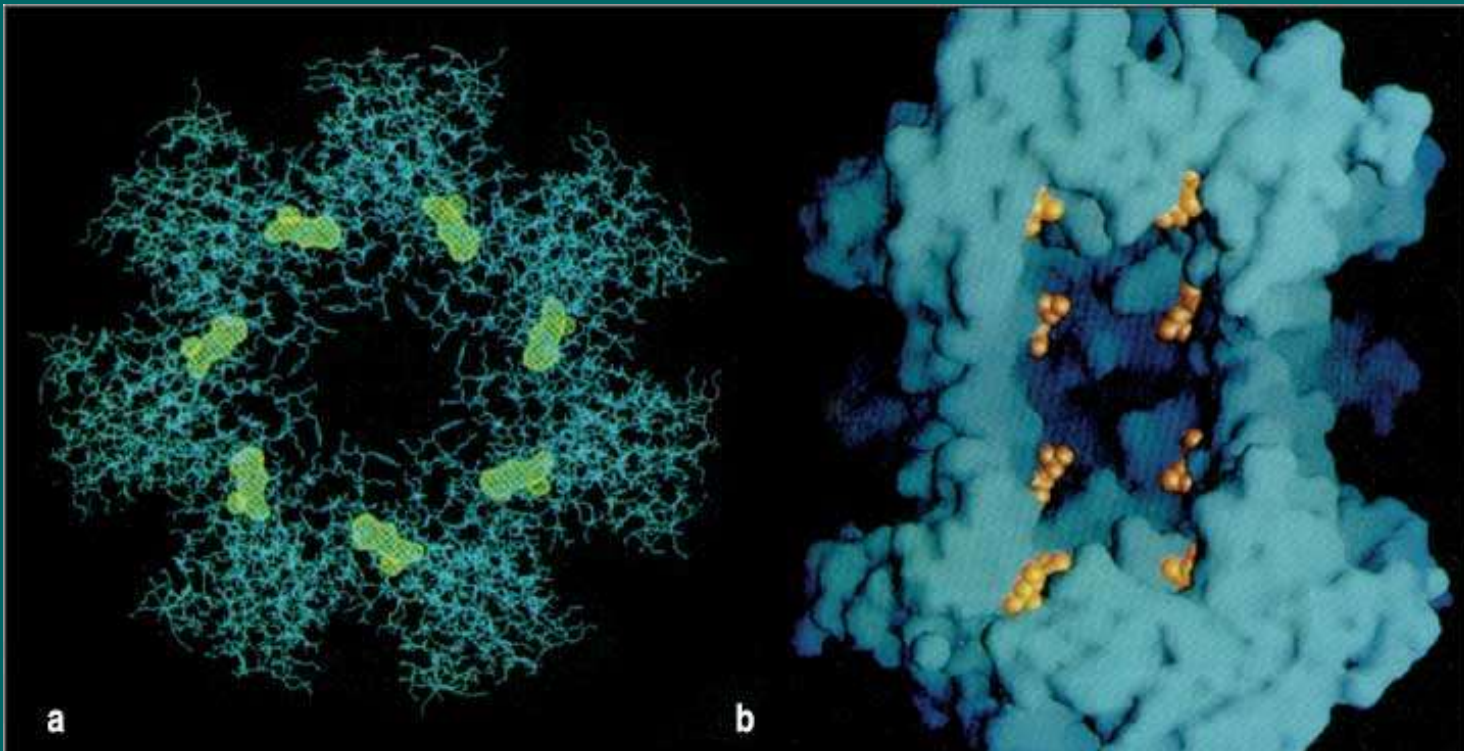
The components of the proteasome include LMP2, LMP7, MECL-1 (LMP10)

\*MECL-1: Multicatalytic endopeptidase complex subunit



# The Proteasome

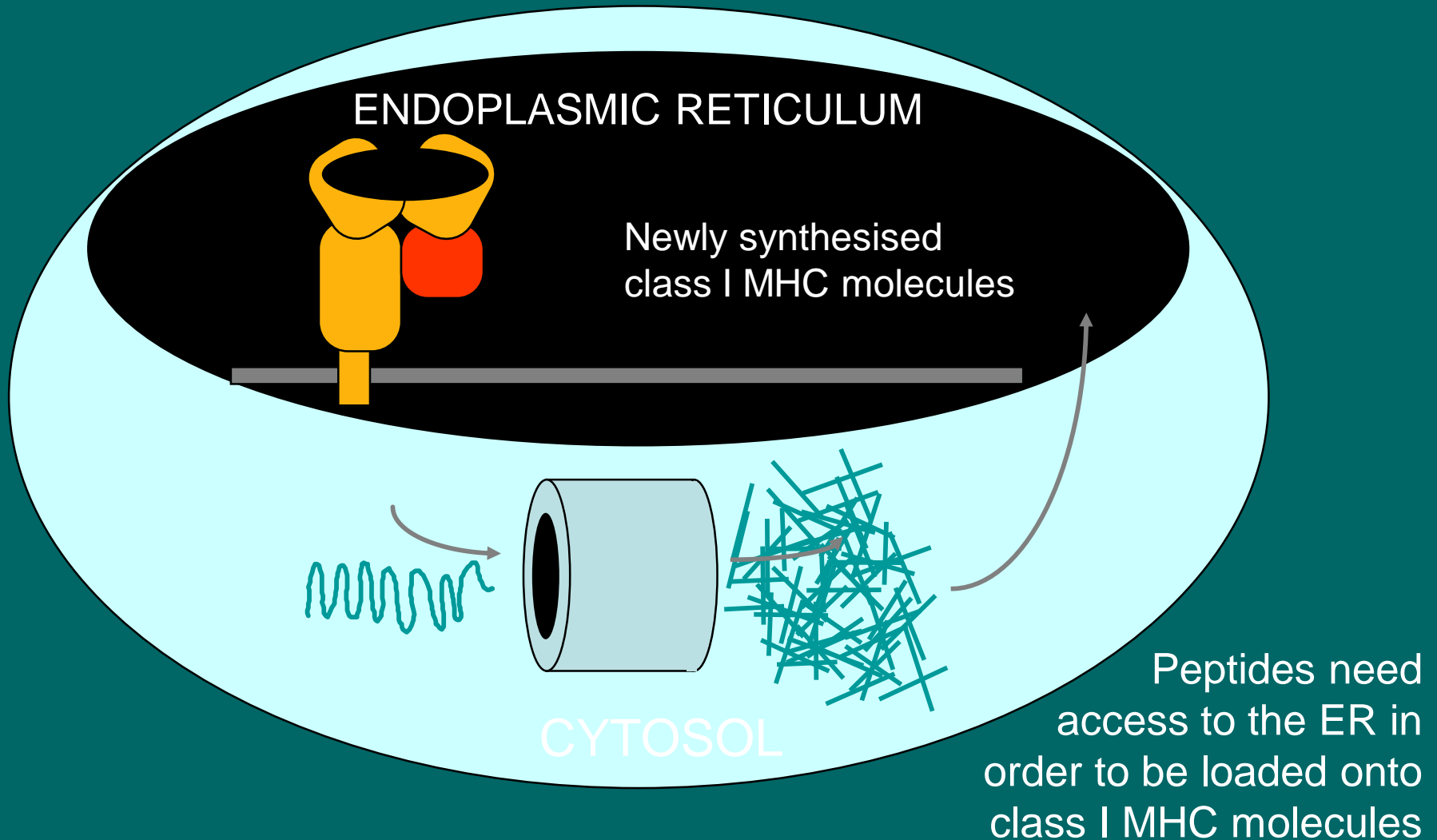
- 28 subunits in four stacked rings
- Proteins pass through catalytic core
- Constitutive vs. immunoproteasome
- Retrograde translocation



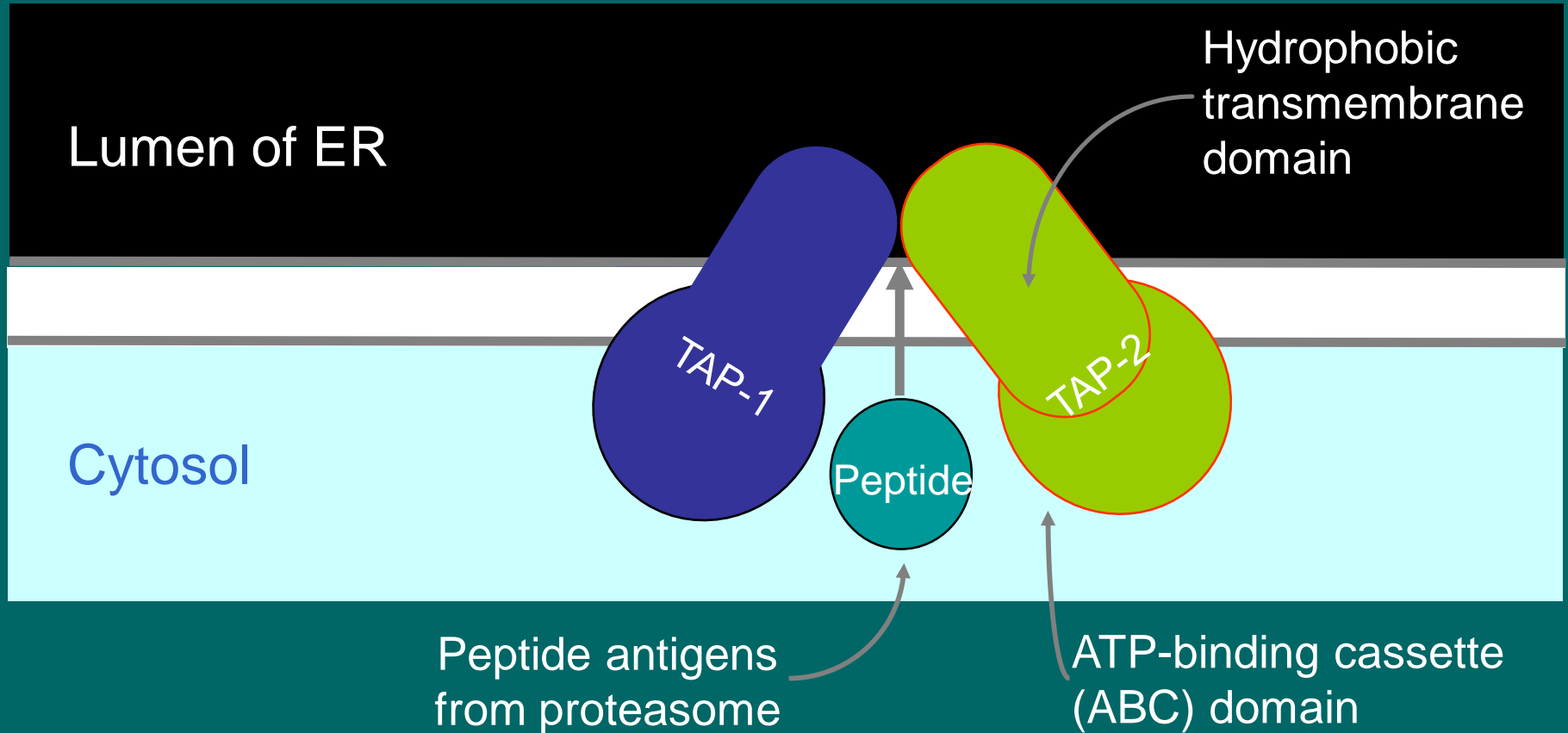
## **2. Transporting of antigen peptide into ER**

**TAP(transporter associated with antigen processing):**  
**Consisting of TAP1 and TAP2**  
**ATP dependent transporter**  
**Selective transporting (8-15aa)**

# Peptide antigens produced in the cytoplasm are physically separated from newly formed class I MHC



# Transporters associated with antigen processing (TAP1 & 2)

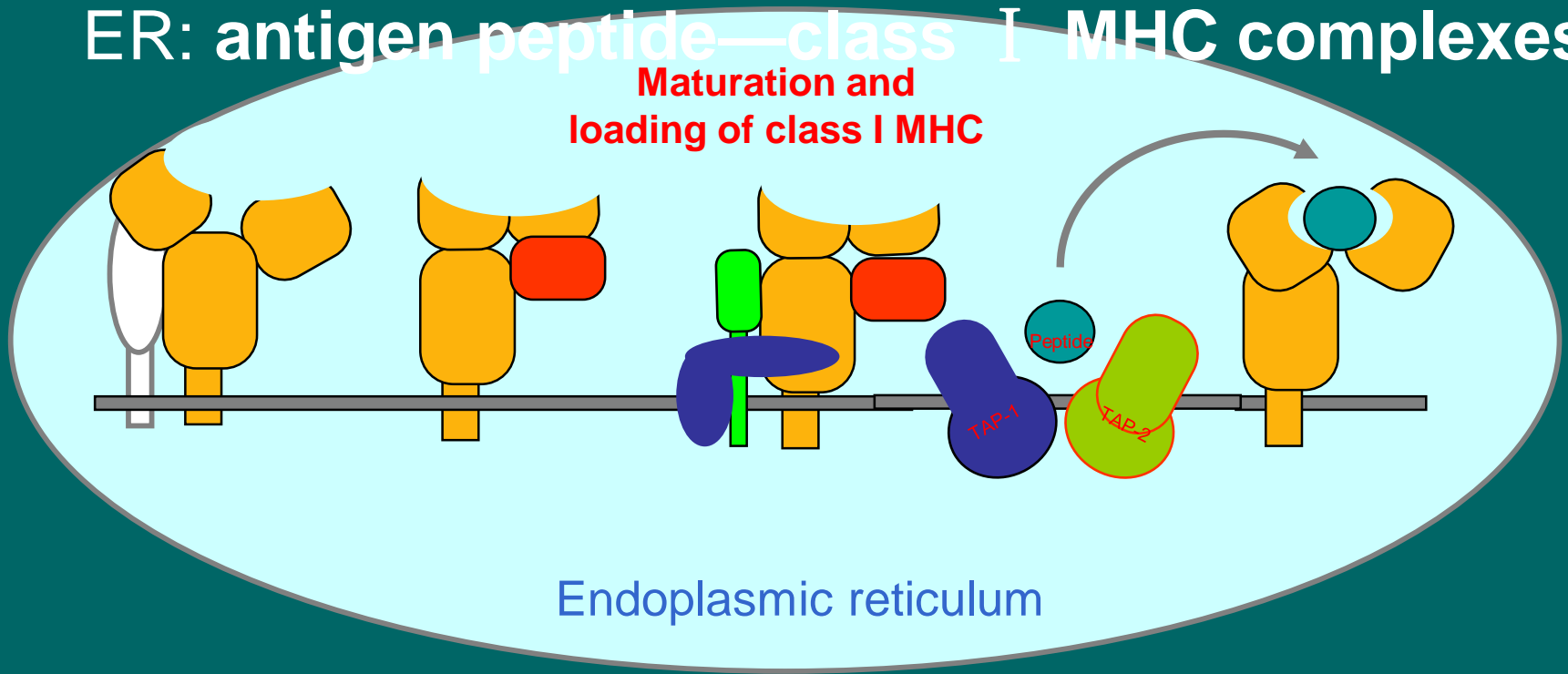


Transporter has preference for >8 amino acid peptides with hydrophobic C termini.

# 3. Peptide loading of class I MHC molecules

ER: antigen peptide—class I MHC complexes

Maturation and loading of class I MHC



Calnexin binds to nascent class I  $\alpha$  chain until  $\beta$ 2-M binds

B2-M binds and stabilises floppy MHC

Tapasin, calreticulin, TAP 1 & 2 form a complex with the floppy MHC

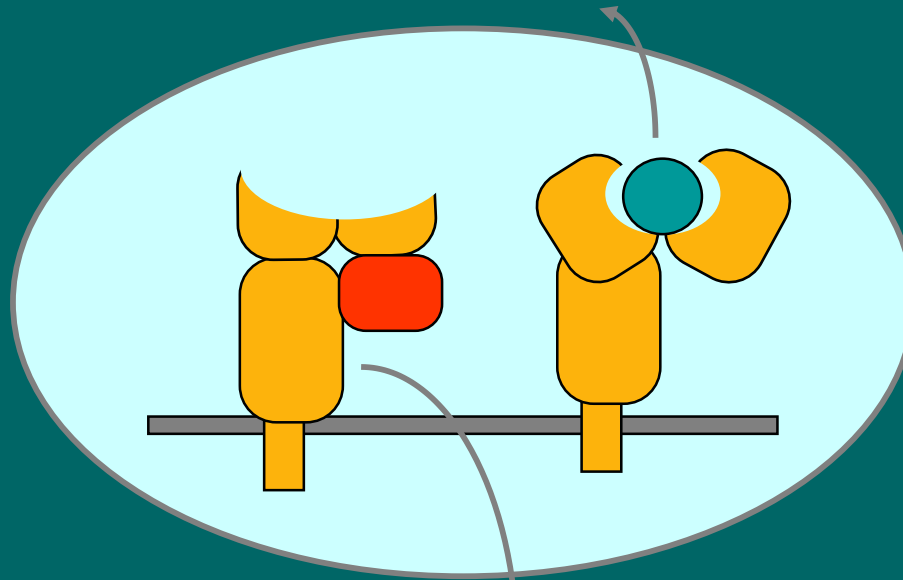
Cytoplasmic peptides are loaded onto the MHC molecule and the structure becomes compact

## 4. Presenting to CD8<sup>+</sup>T cells

Antigen peptide-class I MHC molecules presented on cell membrane by exocytosis

### Fate of class I MHC

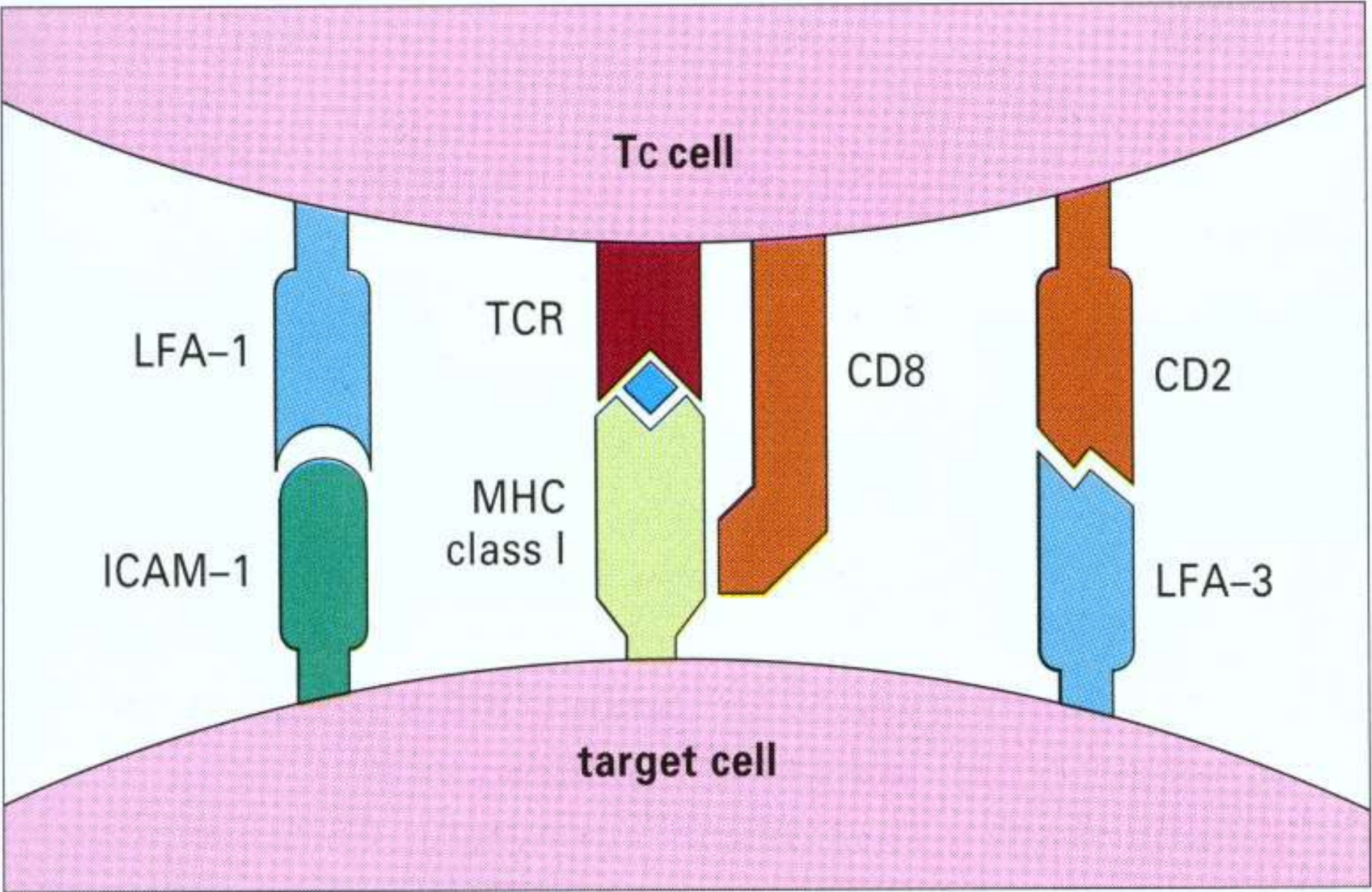
Exported to the cell surface



Sent to lysosomes for degradation



# Interactions between Tc and target cells



**Ag (cytosolic protein)**

**Proteasome**

**proteolytic degradation**

**Ag peptide**

**TAP complex**

**transporting into ER**

**antigen peptide-class I MHC complexes**

**Golgi complex**

**exocytosis**

**Presenting to CD8<sup>+</sup>T cells**

Thank you  
for your attention

