Major Histocompatibility Complex

PART- 5

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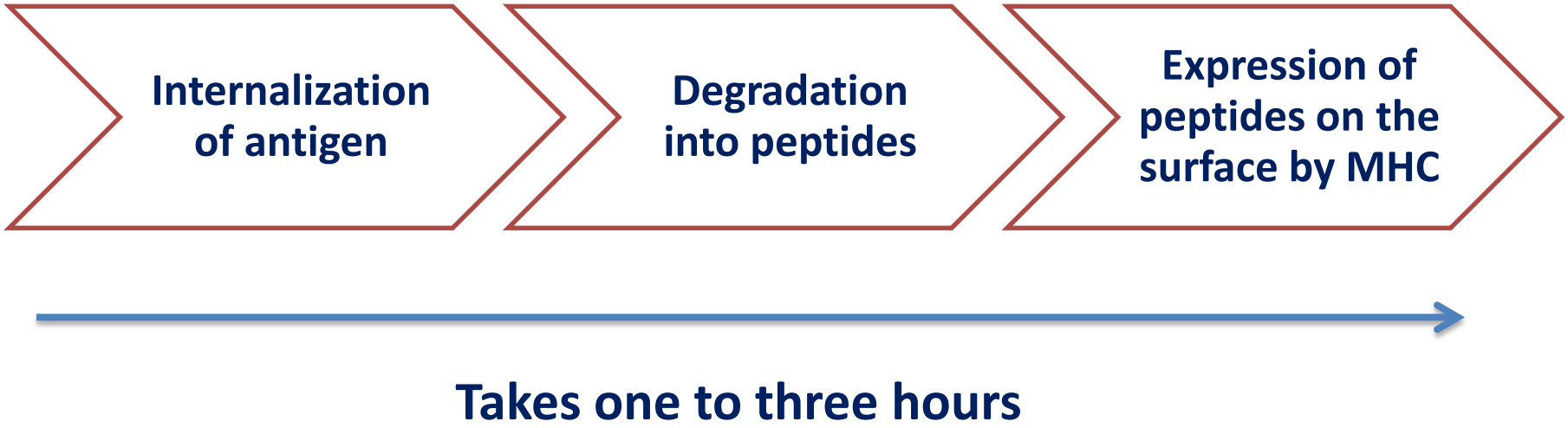
Pathways for processing antigen cont…

Exogenous pathway

- Antigen presenting cells internalized exterior antigen by phagocytosis.
- Endocytic processing pathway- degraded antigen into peptides.
- Expression of peptides on the surface of APCs by class II MHC molecules


Internalization of antigen
Degradation into peptides
Expression of peptides on the surface by MHC
Takes one to three hours

MHC class II- containing compartment (MIIC)
(Unique form of late Endosome)

- **Help in**
  - Final protein degradation
  - Antigenic Peptide loading into class II MHC molecule
- **Within the compartments of the endocytic pathway**
  - Antigen break down into 13-18 amino acid residue.
  - Antigenic peptides bind with Class II MHC molecule in late endosome.

Antigen Presenting Cells express both Class I and Class II MHC molecules

?

Can class II MHC molecule bind with the antigenic peptide designed for class I molecule?

NO

Let us discuss how?

- **When class II MHC molecule synthesized inside the lumen of endoplasmic reticulum**
  - **Class II αβ chain associated with a specific protein called-Invariant chain (Ii, CD 74)**

Invariant chain (Ii, CD 74)

- **Conserved**
- **Non-MHC encoded protein**
- **Interact with class II MHC molecule**
- **Helps in**
  - Prevent binding cleft of class II MHC molecule from other antigenic peptides inside the RER lumen.
  - Proper folding of class II α and β chain.
  - Exit of class II α and β chain from RER.
  - Routing of class II MHC molecule in endocytic processing pathway.

- **Invariant chain (Ii, CD 74) gradually degraded by proteolytic activity in the successive compartment.**

CLIP (For Class II-associated invariant chain peptide)

- **Short fragment of invariant chain**
- **Remains attached to class II MHC molecule**
- **Help in, preventing the premature binding of antigenic peptide to the class II MHC molecule binding cleft.**

HLA-DM

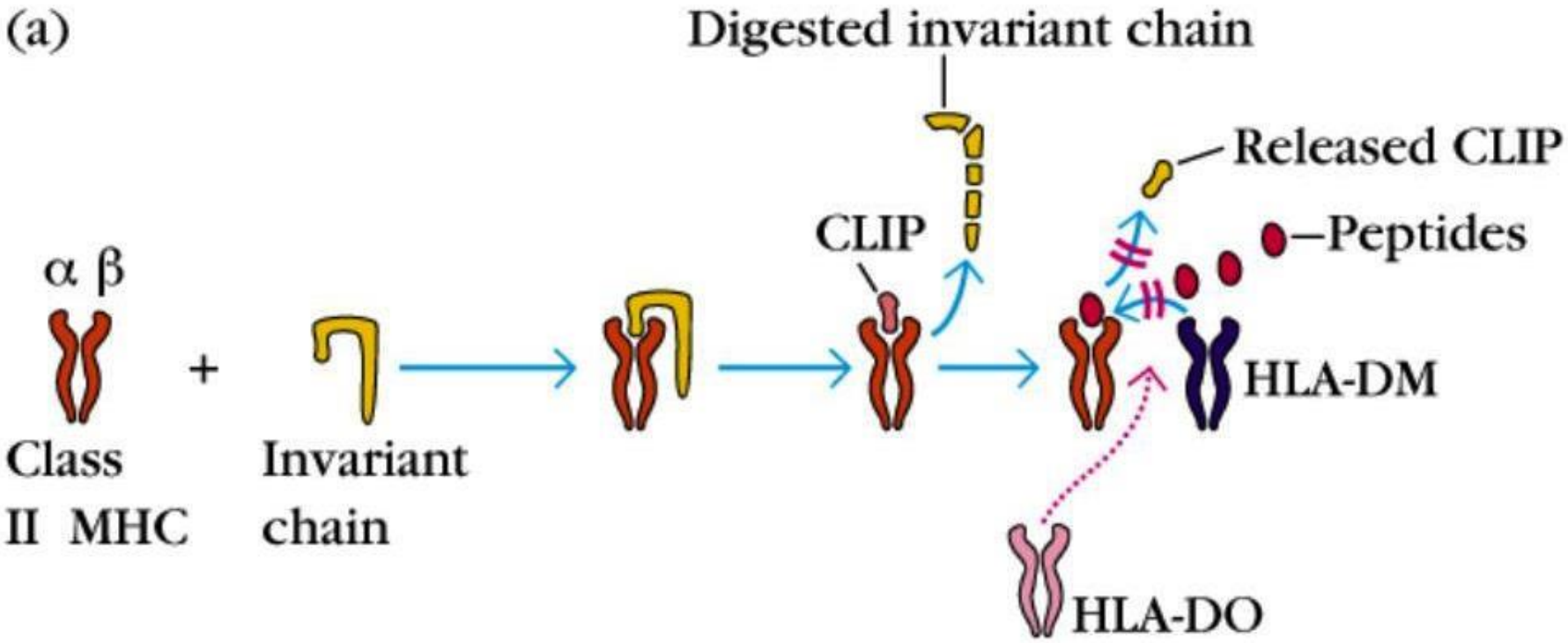
- Required to catalyse the exchange of CLIP with antigenic peptides.
- In Human, Position of DM α and DMβ genes near TAP & LMP gene in the MHC complex.
- Non-polymorphic
- Normally, not expressed at the plasma membrane.
- Mostly found within endosomal compartment.
- Help in removing or editing peptides and CLIP

- **High affinity antigenic peptide bind with the class II MHC molecule.**
- **HLA-DM molecule unable to compete with class II MHC molecule regarding the binding of antigenic peptide.**
- **Finally, antigenic peptide and class II MHC complex transported to plasma membrane of APCs**

HLA-DO

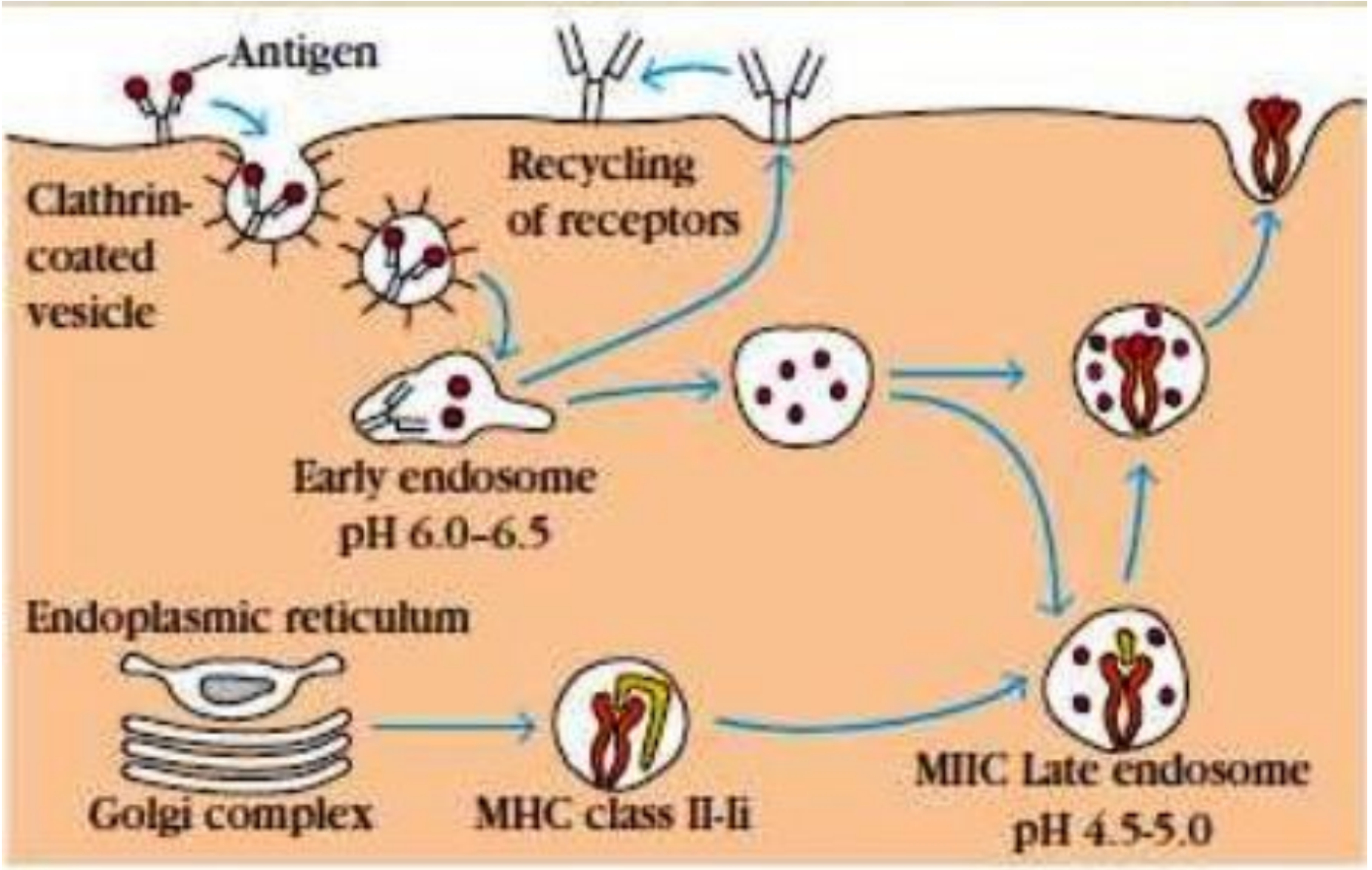
Found to act as a negative regulator of antigenic binding cleft.

Assembly of class II MHC molecules



Reference: Kuby –Immunology; 7th Edition by Judith A. Owen, Jenni Punt, Sharon A. Stranford and Patricia P. Jones; Chapter-8: The Major Histocompatibility Complex and Antigen Presentation; Page: 290

Generation of antigenic peptides in the exogenous processing pathway



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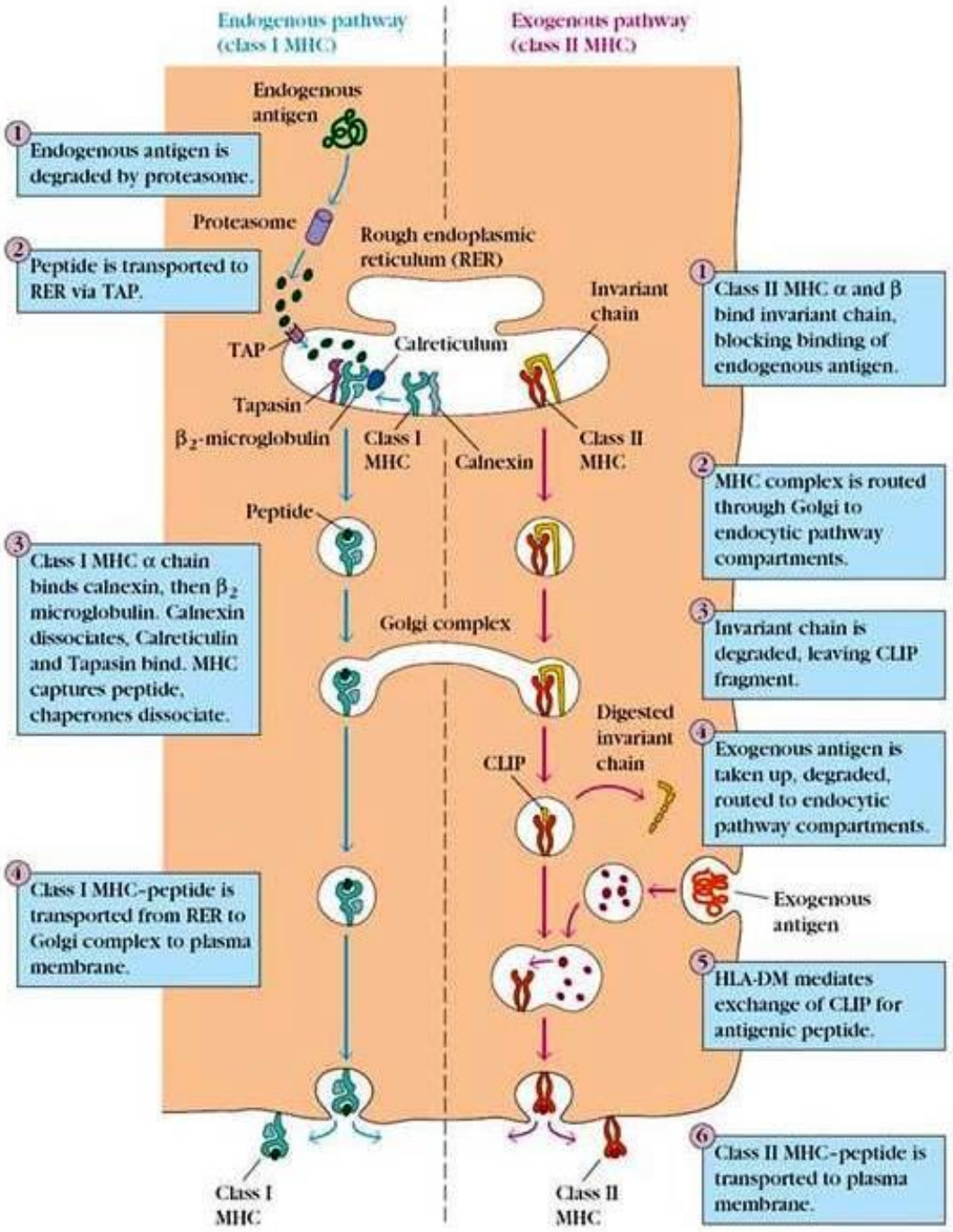
Overview of endogenous and Exogenous pathway



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Thanks