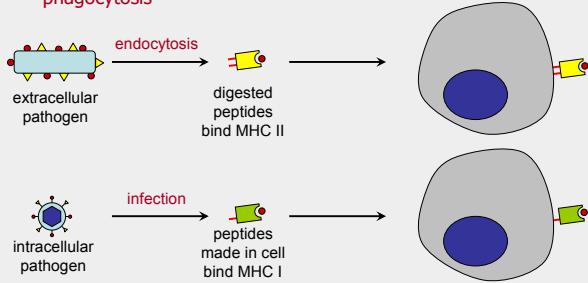


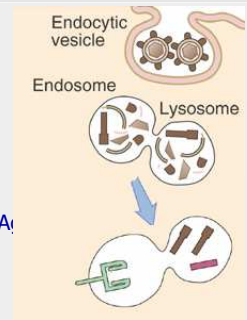
### Antigen processing

- Ag must be processed to peptides
- MHC II must bind peptides from phagocytosis but not cellular peptides
- MHC I must bind cellular peptides but not peptides from phagocytosis



### Extracellular Ag – MHC II

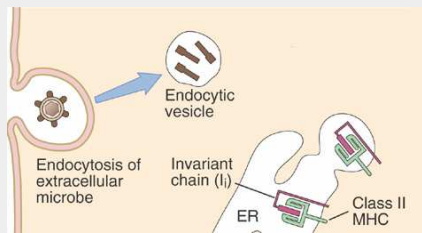
- Uptake of extracellular Ag:
- Endocytosis by macrophages or dendritic cells
    - Mannose receptor
    - Complement receptor
    - Non-specific phagocytosis
  - Pinocytosis of small, soluble Ag
  - Endocytosis of Ag bound to B cell Ag receptor
- Vesicle with MHC II fuses with endosome
- MHC II can bind digested peptides



### Extracellular Ag – MHC II

If MHC II can bind almost any peptide, why doesn't it bind cellular peptides in the ER, Golgi, vesicles, etc.?

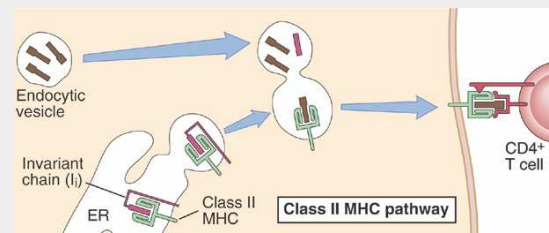
- $\alpha$  and  $\beta$  chains assemble with invariant chain ( $I_i$ ) in ER
  - no stable  $\alpha + \beta$  in absence of  $I_i$
  - blocks peptide-binding cleft



### Extracellular Ag – MHC II

How does MHC II become available to bind peptides from the endosome?

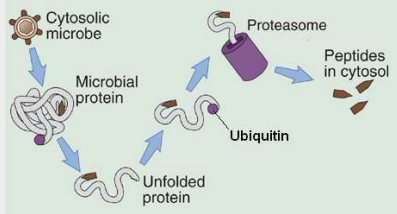
- Proteases cleave  $I_i$ , leave CLIP
- DM protease in endosome removes CLIP
- MHC II only stable if a peptide binds



### Intracellular Ag – MHC I

How is the Ag processed to peptides?

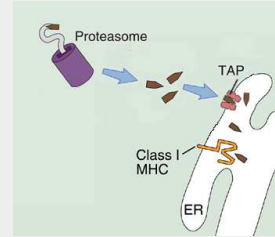
- Ubiquitin binds unfolded proteins
- Targeted to proteasome



### Intracellular Ag – MHC I

How does MHC I encounter the peptides?

- TAP transporter in ER membrane



### Intracellular Ag – MHC I

How does MHC I encounter the peptides?

- TAP transporter in ER membrane
- Again, MHC I is stable only if bound to a peptide

