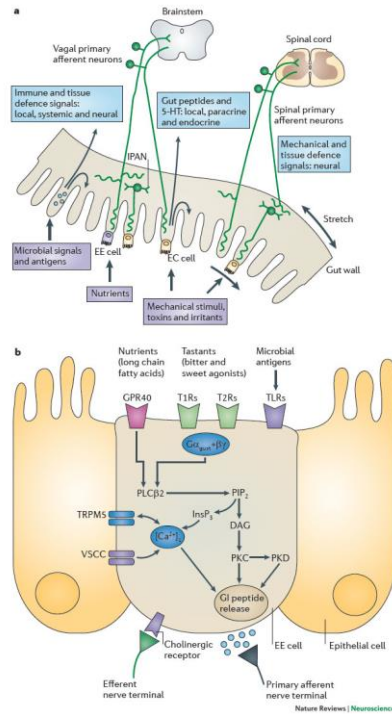
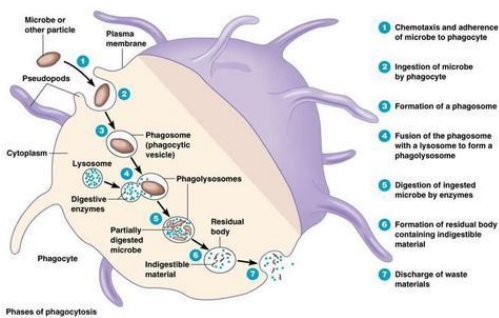
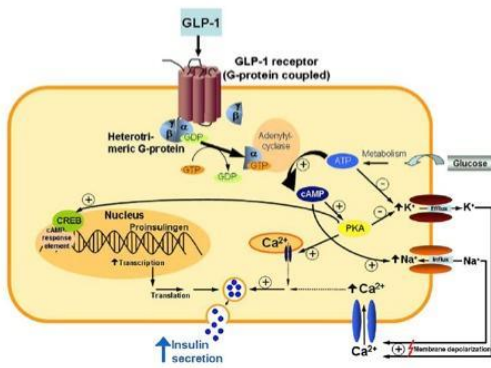
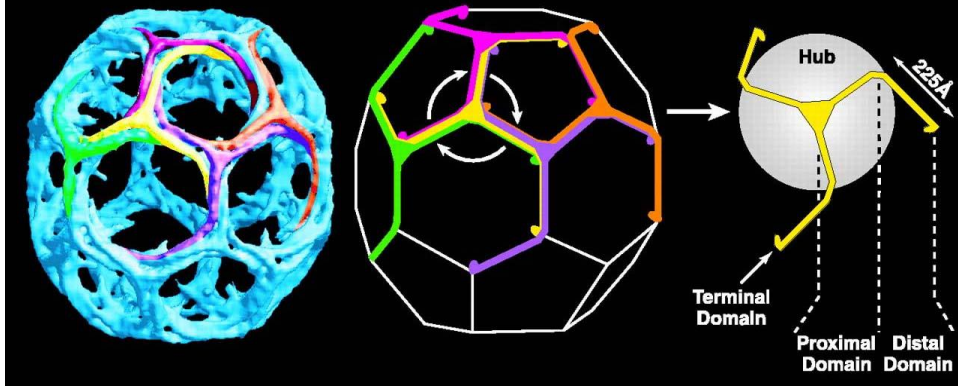


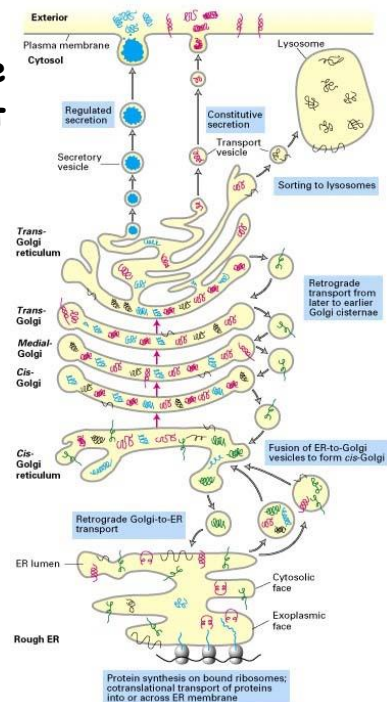
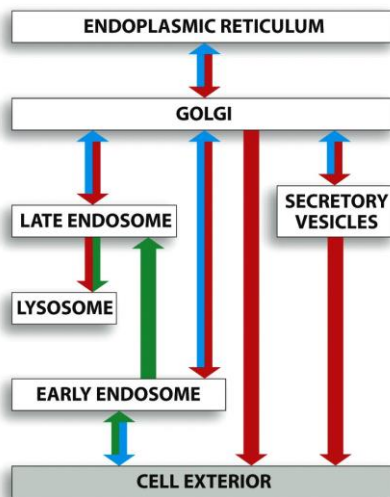
INTRACELLULAR VESICULAR TRAFFIC



- THE MOLECULAR MECHANISMS OF MEMBRANE TRANSPORT AND THE MAINTENANCE OF COMPARTMENT DIVERSITY
- TRANSPORT FROM THE ER THROUGH THE GOLGI APPARATUS
- TRANSPORT FROM THE TRANS GOLGI NETWORK TO LYSSOMES
- TRANSPORT INTO THE CELL FROM THE PLASMA MEMBRANE: ENDOCYTOSIS
- TRANSPORT FROM THE TRANS GOLGI NETWORK TO THE CELL EXTERIOR: EXOCYTOSIS

3

Molecular mechanisms of membrane transport and the maintenance of compartment diversity



Vesicles traffic: budding formation and membrane fusion

- Transport vesicles → coated vesicles
- Coated vesicles →
 - Select appropriate molecules for transport
 - Shapes the vesicles → relatively uniform size and shape
- Three types of **well characterized** coated vesicles, distinguished by their coat proteins:
 - CLATHRIN-coated
 - COP I-coated
 - COP II-coated
- Other coated vesicles i.e. retromer

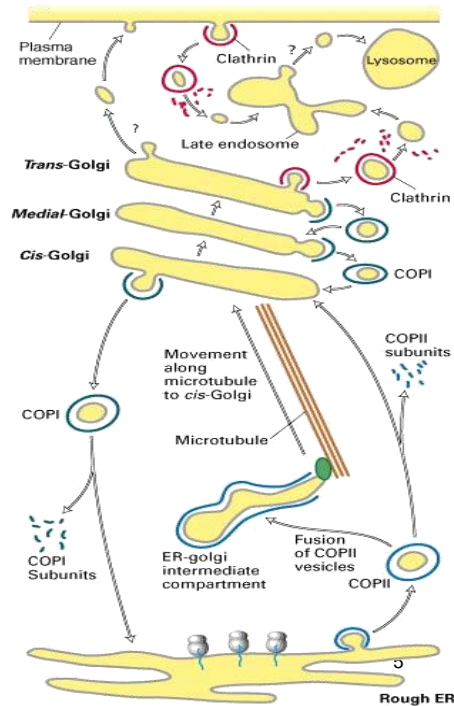


TABLE 14-2 Known Sorting Signals That Direct Proteins to Specific Transport Vesicles

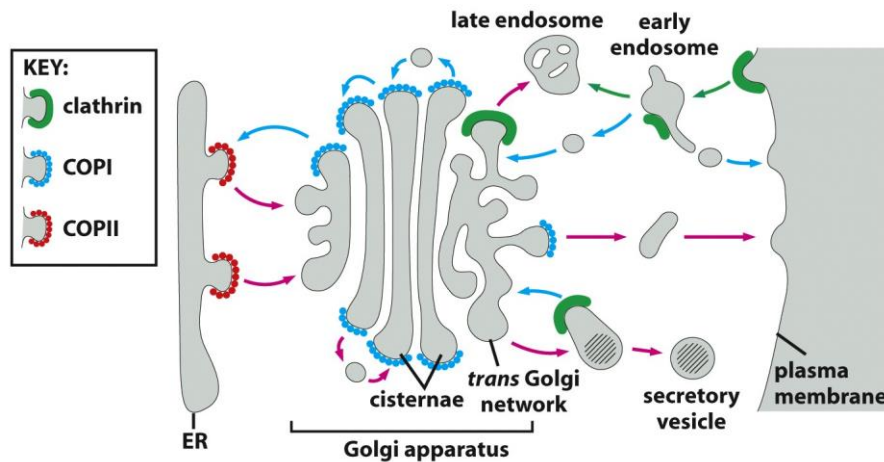
Signal Sequence*	Proteins with Signal	Signal Receptor	Vesicles That Incorporate Signal-Bearing Protein
LUMINAL SORTING SIGNALS			
Lys-Asp-Glu-Leu (KDEL)	ER-resident soluble proteins	KDEL receptor in <i>cis</i> -Golgi membrane	COPI
Mannose 6-phosphate (M6P)	Soluble lysosomal enzymes after processing in <i>cis</i> -Golgi	M6P receptor in <i>trans</i> -Golgi membrane	Clathrin/AP1
	Secreted lysosomal enzymes	M6P receptor in plasma membrane	Clathrin/AP2
CYTOPLASMIC SORTING SIGNALS			
Lys-Lys-X-X (KKXX)	ER-resident membrane proteins	COPI α and β subunits	COPI
Di-arginine (X-Arg-Arg-X)	ER-resident membrane proteins	COPI α and β subunits	COPI
Di-acidic (e.g., Asp-X-Glu)	Cargo membrane proteins in ER	COPII Sec24 subunit	COPII
Asn-Pro-X-Tyr (NPXY)	LDL receptor in plasma membrane	AP2 complex	Clathrin/AP2
Tyr-X-X- Φ (YXX Φ)	Membrane proteins in <i>trans</i> -Golgi	AP1 (μ 1 subunit)	Clathrin/AP1
	Plasma membrane proteins	AP2 (μ 2 subunit)	Clathrin/AP2
Leu-Leu (LL)	Plasma membrane proteins	AP2 complexes	Clathrin/AP2

*X = any amino acid; Φ = hydrophobic amino acid. Single-letter amino acid abbreviations are in parentheses.

TABLE 14-1 Coated Vesicles Involved in Protein Trafficking			
Vesicle Type	Transport Step Mediated	Coat Proteins	Associated GTPase
COPII	ER to <i>cis</i> -Golgi	Sec23/Sec24 and Sec13/Sec31 complexes, Sec16	Sar1
COPI	<i>cis</i> -Golgi to ER Later to earlier Golgi cisternae	Coatomers containing seven different COP subunits	ARF
Clathrin and adapter proteins*	<i>trans</i> -Golgi to endosome	Clathrin + AP1 complexes	ARF
	<i>trans</i> -Golgi to endosome	Clathrin + GGA	ARF
	Plasma membrane to endosome	Clathrin + AP2 complexes	ARF
	Golgi to lysosome, melanosome, or platelet vesicles	AP3 complexes	ARF

*Each type of AP complex consists of four different subunits. It is not known whether the coat of AP3 vesicles contains clathrin.

7



- CLATHRIN-coated vesicles
 - Mediate transport from Golgi and from plasma membrane
- COP-I and COP-II coated vesicles
 - Mediate transport from ER and from Golgi

8

- Assembly of a clathrin coat → drives vesicle formation
- Component of clathrin coat:
 - Clathrin
 - Adaptor protein → bind to cargo receptor

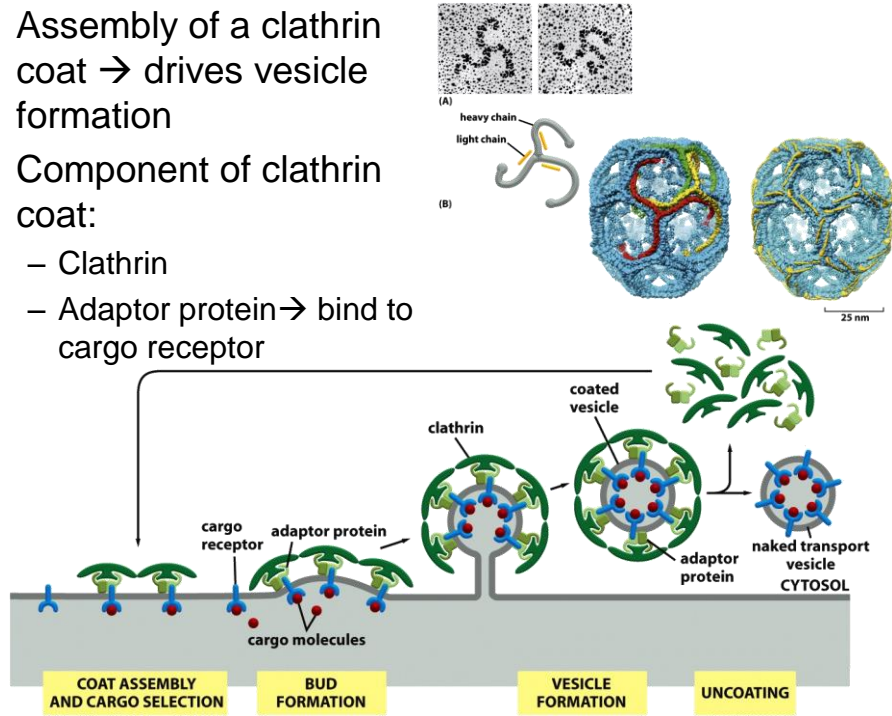
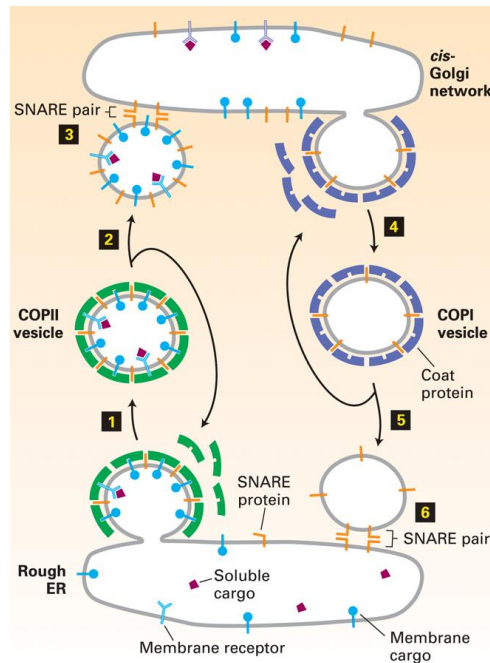
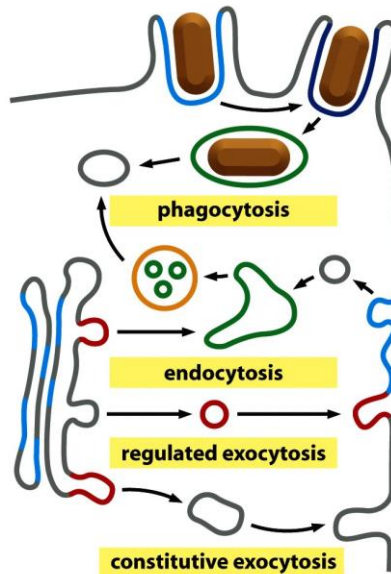
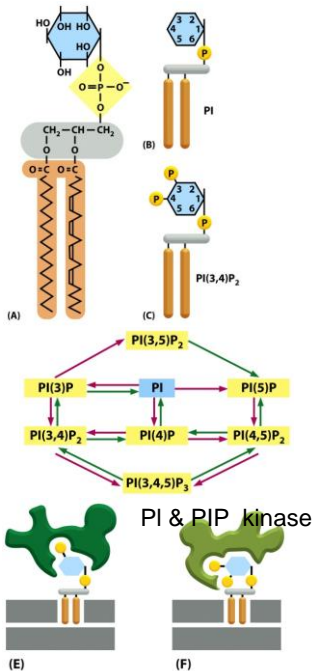
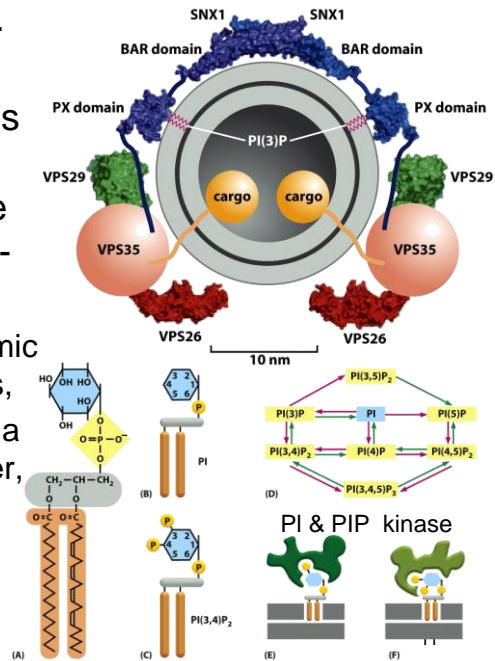


Figure 14.11 Vesicle-mediated protein trafficking between the ER and *cis*-Golgi.



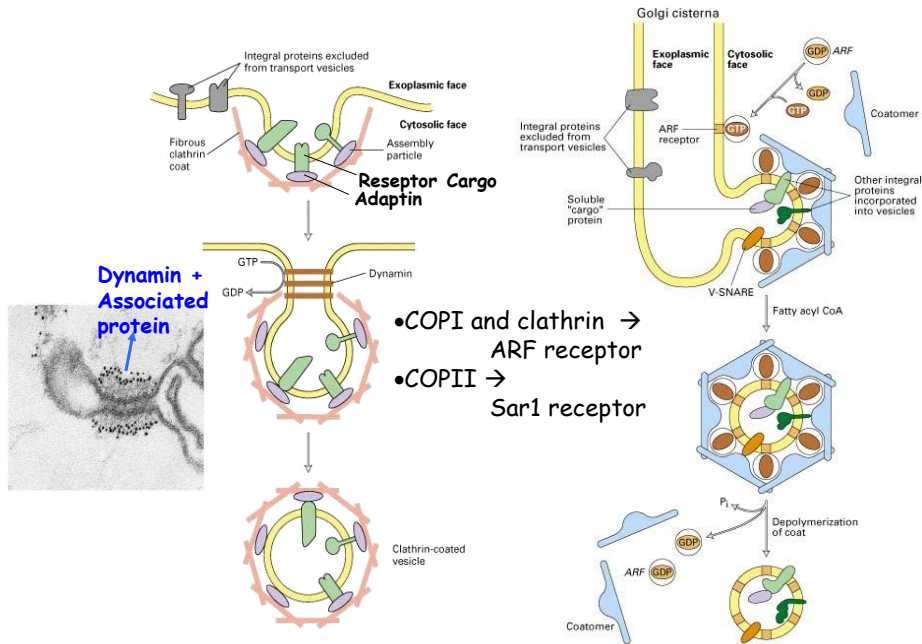
- Other coated vesicles i.e. retromer
- assembles on endosomes → Golgi apparatus i.e. containing acid hydrolase receptors i.e. mannose-6-phosphate receptor,
 - it can bind to the cytoplasmic tails of the cargo receptors,
 - it can interact directly with a curved phospholipid bilayer, and
 - it can bind to a specific phosphorylated phosphatidylinositol lipid



KEY:
 PI(3)P
 PI(4)P
 PI(4,5)P₂
 PI(3,5)P₂
 PI(3,4,5)P₃

Figure 15-10a, b, c *molecular biology of the cell* (© Garland Science 2008)

Monomeric GTPase control coat assembly



Vesicle targeting and specificity

- Selectivity and specificity of vesicle targeting →
 1. SNARE proteins and
 2. Rabs protein → GTPase

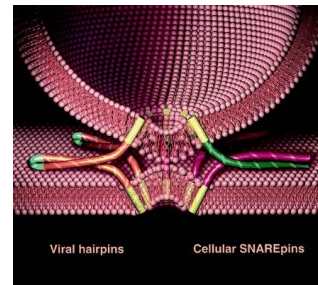
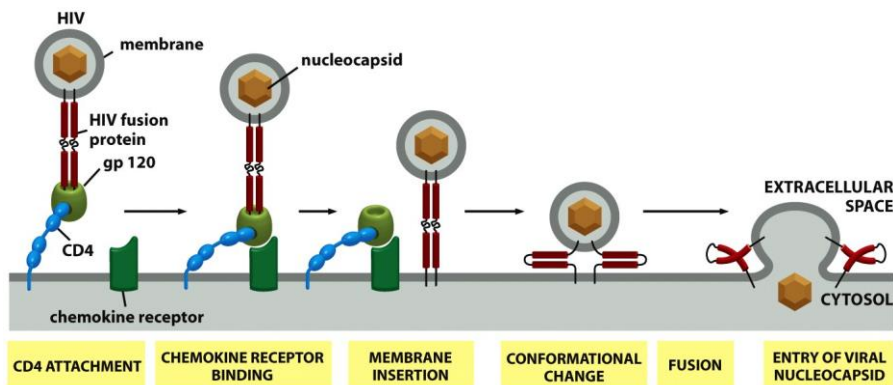
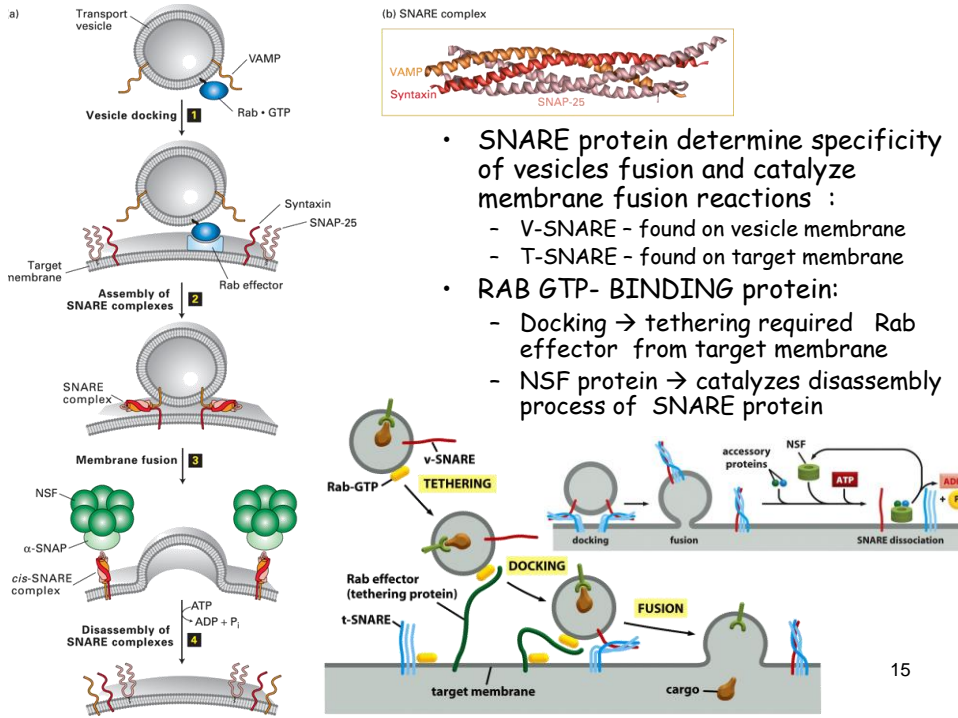


Table 13-1 Subcellular Locations of Some Rab Proteins

PROTEIN	ORGANELLE
Rab1	ER and Golgi complex
Rab2	<i>cis</i> Golgi network
Rab3A	synaptic vesicles, secretory granules
Rab4/Rab11	recycling endosomes
Rab5A	plasma membrane, clathrin-coated vesicles, early endosomes
Rab5C	early endosomes
Rab6	medial and <i>trans</i> Golgi cisternae
Rab7	late endosomes
Rab8	early endosomes
Rab9	late endosomes, <i>trans</i> Golgi network

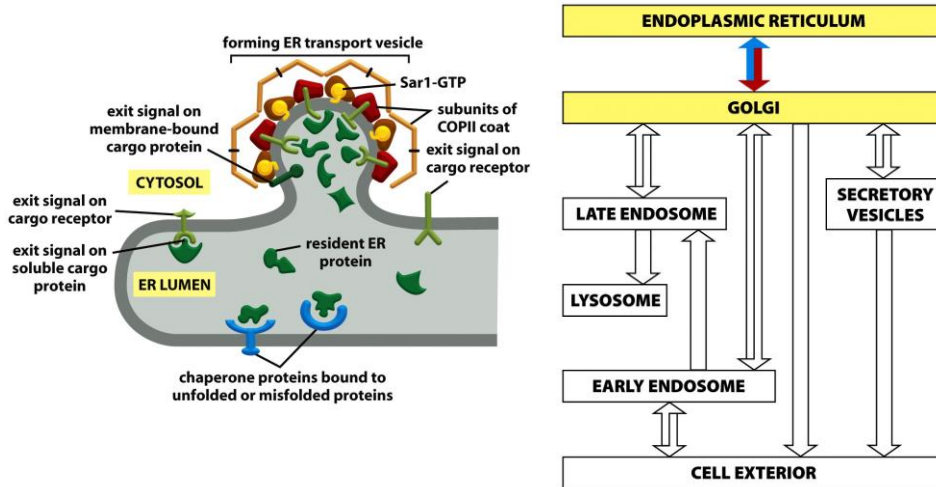


The entry of enveloped viruses into cells

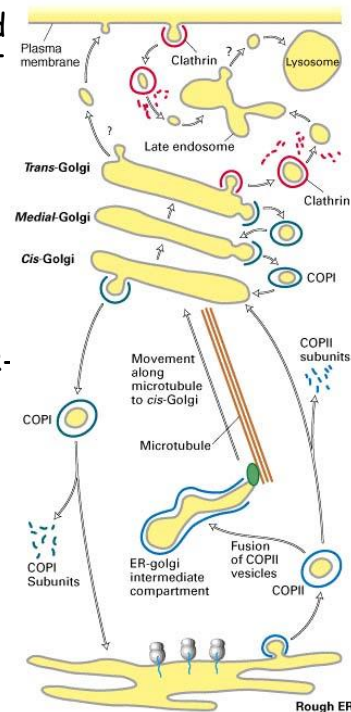
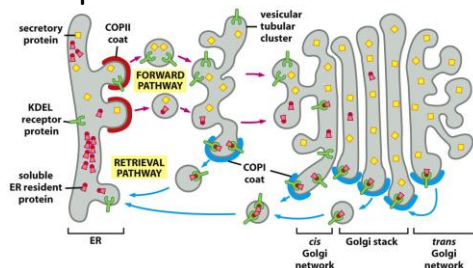
Figure 13-19b *Molecular Biology of the Cell* (© Garland Science 2008)

Transport from ER through Golgi

- Transport mediated by COPII

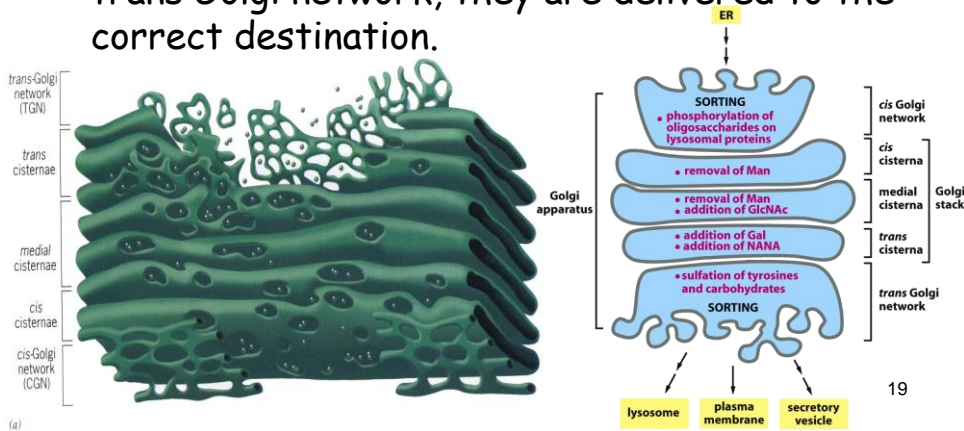


- Only properly folded and assembled proteins can leave ER and transport to Golgi
- Vesicles from ER will be fused with Golgi
- Vesicles transportation → mediated by microtubule
- Protein transport (in vesicles) to Golgi → followed by vesicles formation - transported back to ER- (retrograde) → mediated by KDEL receptor

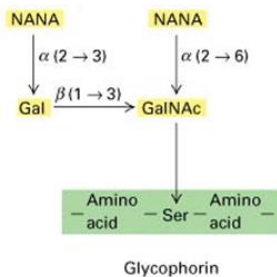
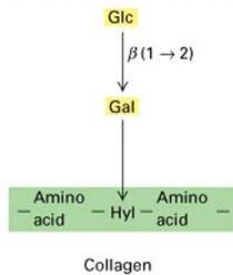


Golgi Apparatus

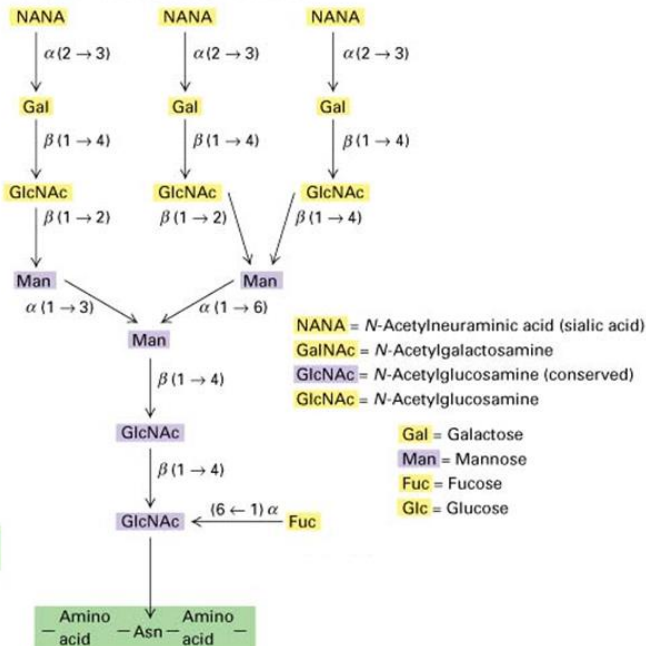
- Glycosylation process of protein
 - Modifies the N-linked oligosaccharides and adds O-linked oligosaccharides.
- Sorts proteins so that when they exit the trans Golgi network, they are delivered to the correct destination.



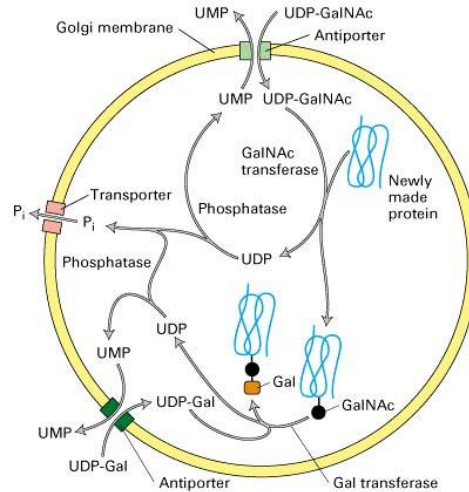
(a) O-linked oligosaccharides



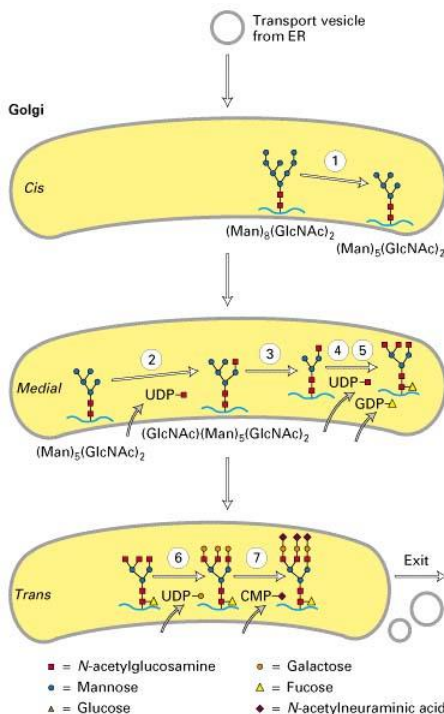
(b) N-linked complex oligosaccharides



- Oligosaccharides transport for glycosylation in Golgi
- Glycosylation is mediated by nucleotide-linked sugars



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Modification the N-linked oligosaccharides

Cis Golgi network (TCN)
- Protein sorting

Cis cisterna
- Removal 3 mannosia residues

Medial
- Three GlcNAc residues are added
- removal two mannosia residues

Trans cisterna
-Gal are added
-NANA are added
-Fucosa is added

Trans Golgi network (TGN)
-Protein Sorting →
○lysosome/
○membrane /
○Secretory vesicles

Transport from Trans Golgi Network to Lysosome ^(a)

Lysosome

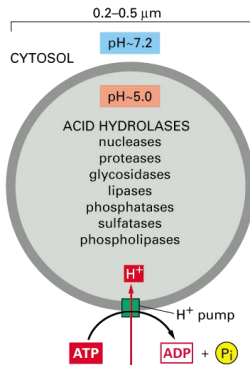
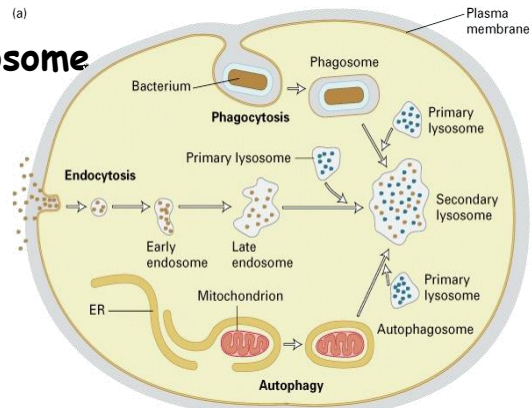


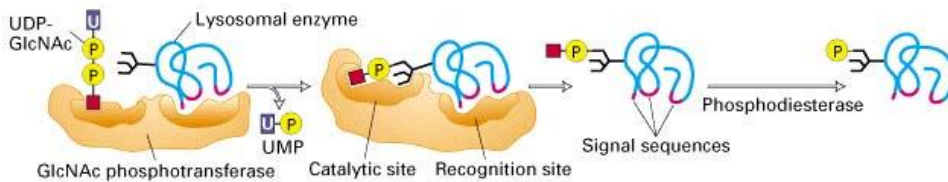
Figure 13-31. Molecular Biology of the Cell, 4th Edition.

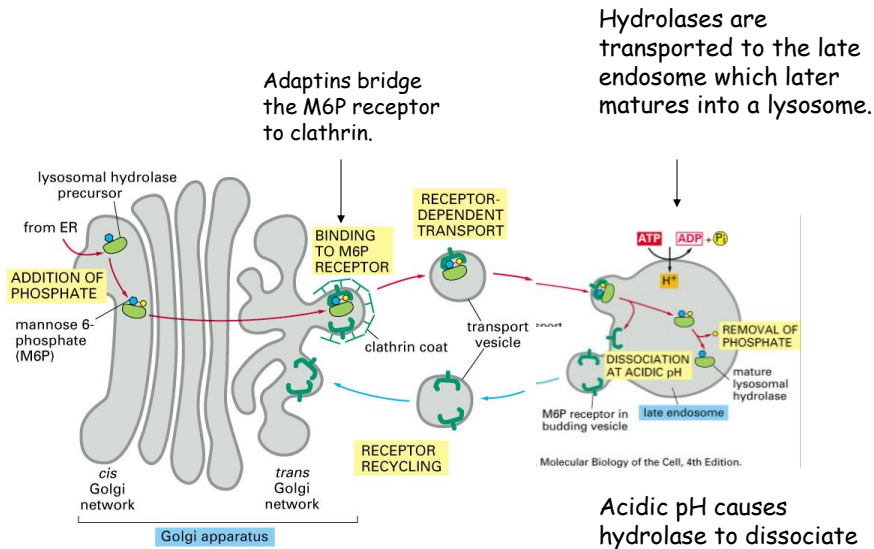


The macromolecules that are degraded in the lysosome arrive by endocytosis, phagocytosis, or autophagy

- pH ~ 5.0 \rightarrow need H^+ -pump
- Plant cells and fungi \rightarrow Vacuole \rightarrow nutrition and waste storage ²³

- The acid hydrolases in the lysosome are sorted in the TGN based on the chemical marker mannose 6-phosphate



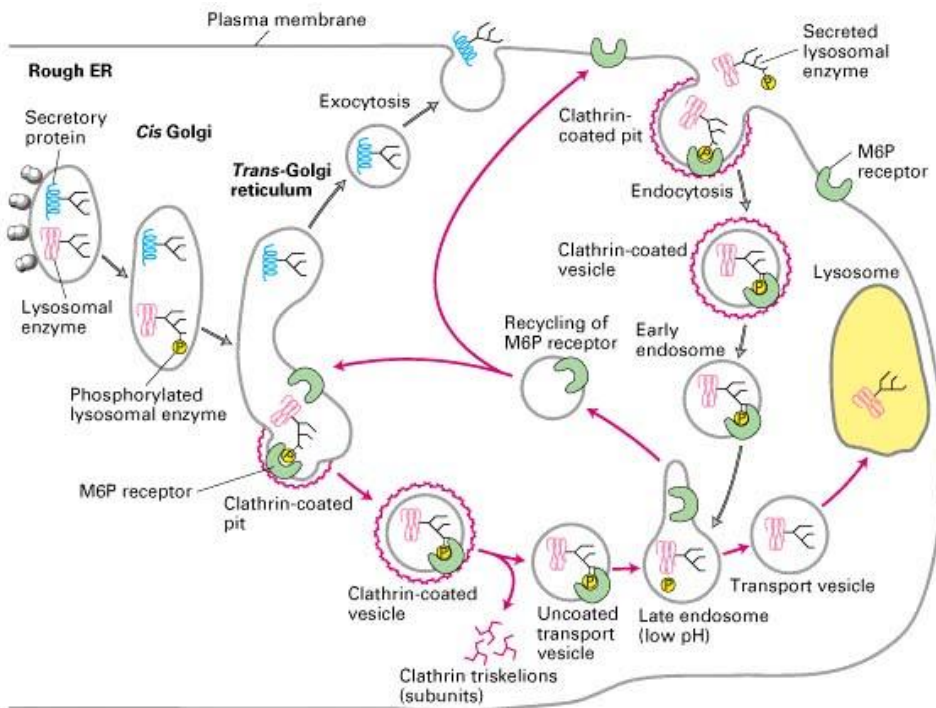


Adaptins bridge the M6P receptor to clathrin.

Hydrolases are transported to the late endosome which later matures into a lysosome.

Acidic pH causes hydrolase to dissociate from the receptor.

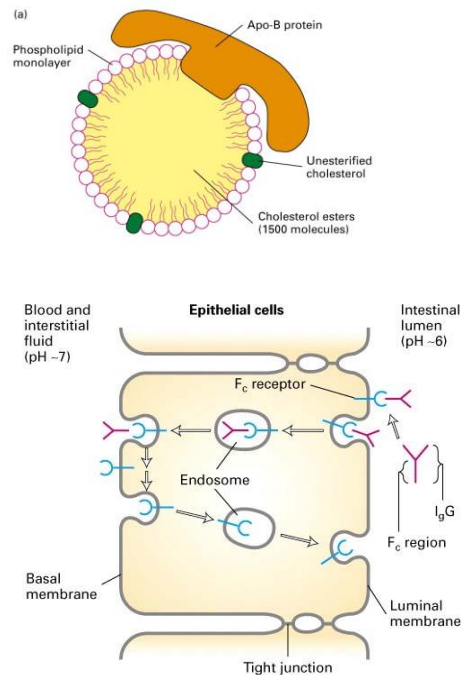
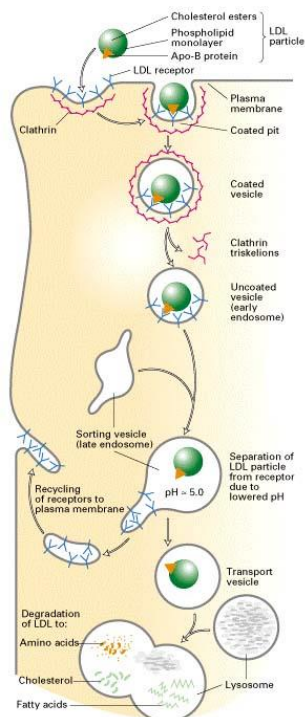
Figure 13-37 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

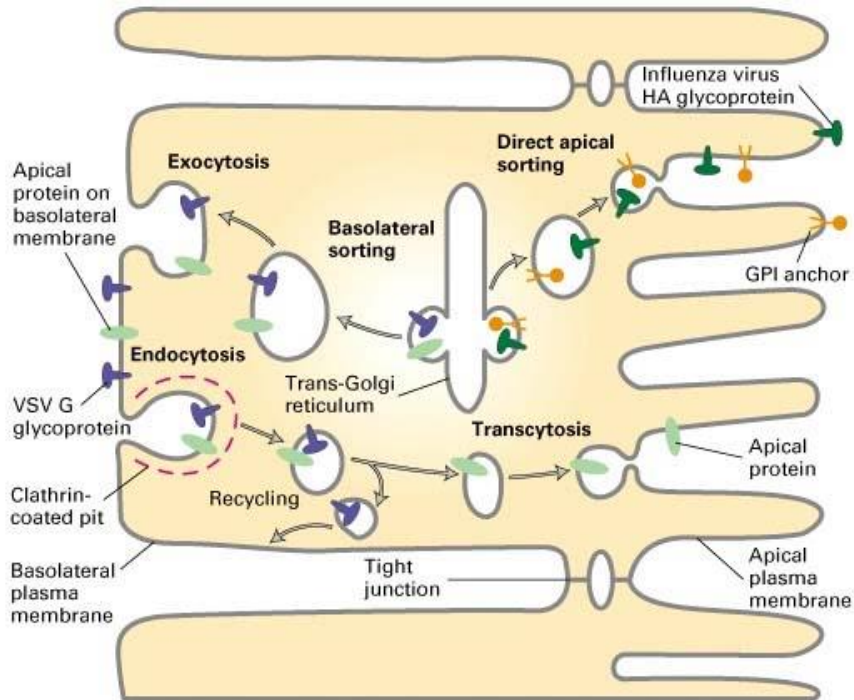


Endocytosis

- Macromolecules uptake
- Phagocytosis → particles
- Pinocytosis → soluble substances
- Two types of endocytosis:
 1. **bulk-phase endocytosis** : unspecific, continuous endocytosis
 2. **receptor-mediated endocytosis** : specific, depend on specific receptor on the cell membrane

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Exocytosis

- 2 secretory activity:
 - constitutive: regular secretory activity
 - Regulative : stimulation is needed for secretion

