

# Molecular Biology of THE CELL

## Chapter 13: Intracellular Membrane Traffic

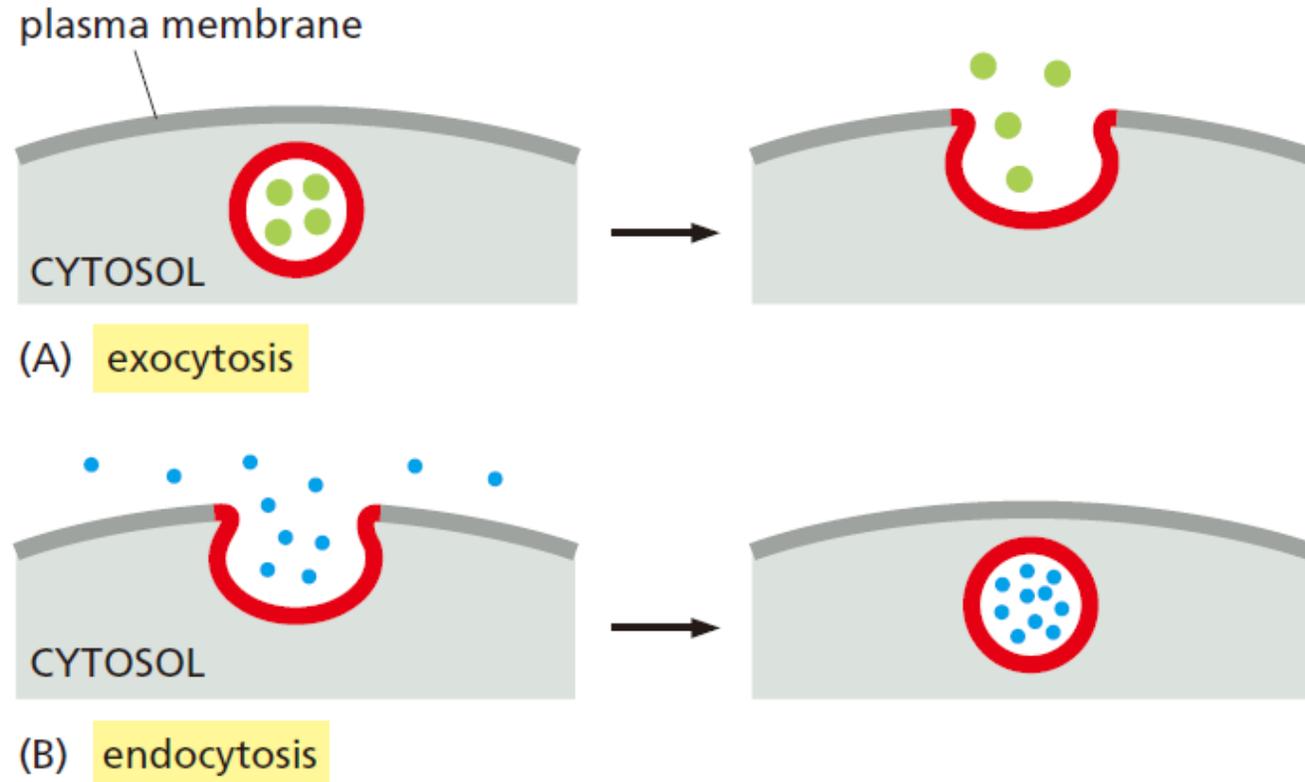
**08.22.2025**

**박용환**

**미생물학교실**

Sixth Edition

# Endo/Exocytosis



균형 이룸

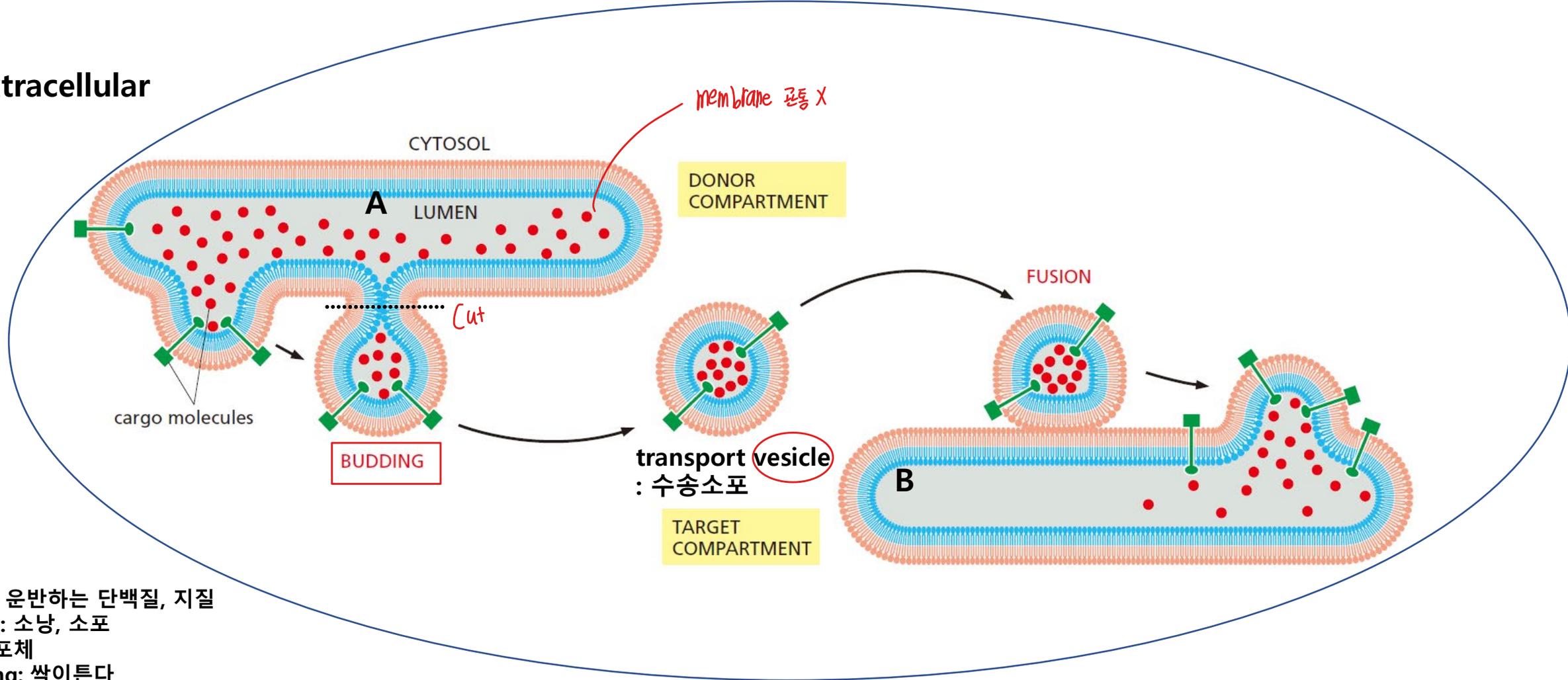
# Vesicle transport

소포체의 lumen은 위상적으로 세포의 바깥과 같다고 합니다. (신기하지 않나요?) ✖

The lumen of the endoplasmic reticulum is **topologically equivalent** to the outside of the cell. (Isn't it interesting?)

*A=B = extra cellular*

Extracellular

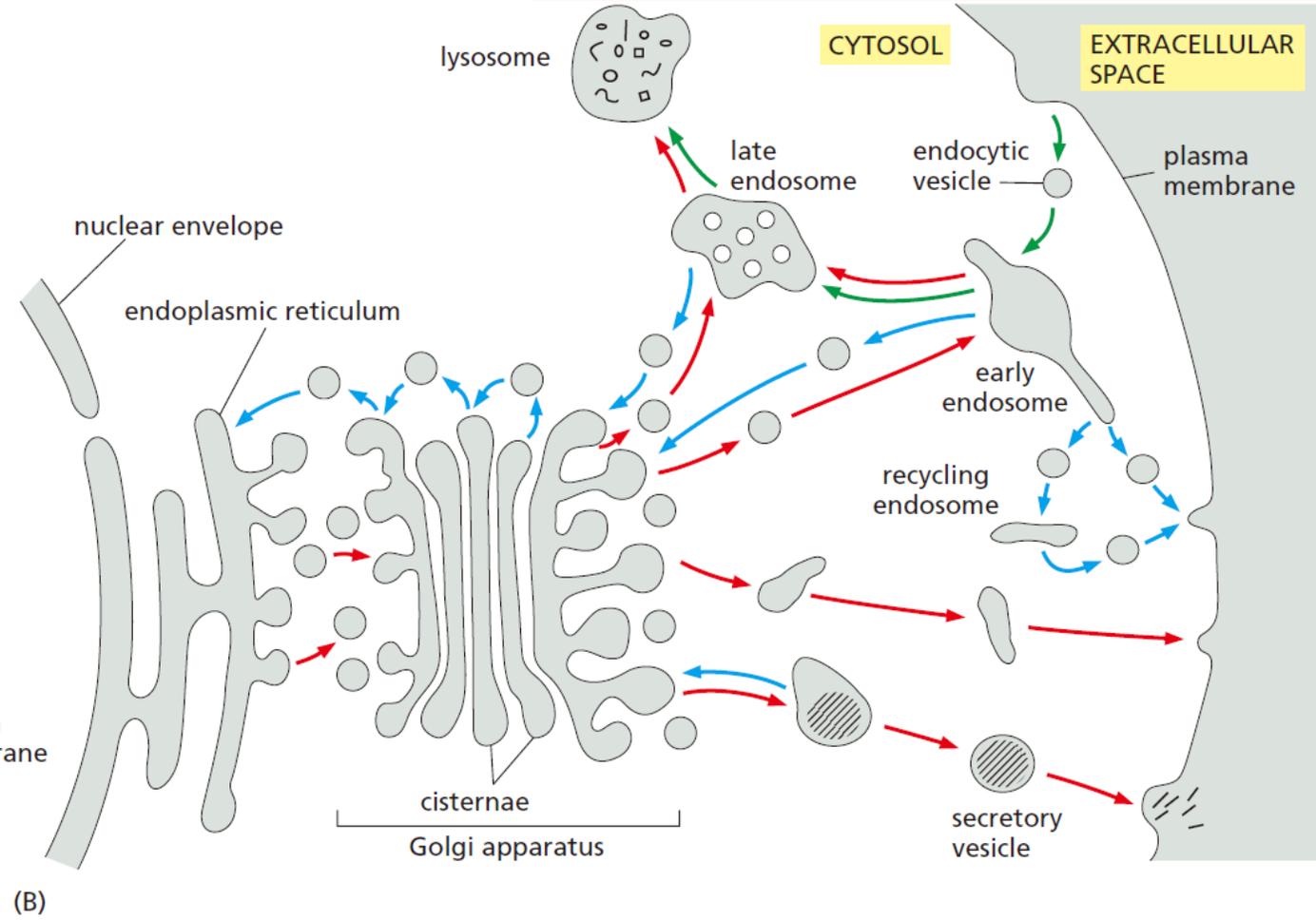
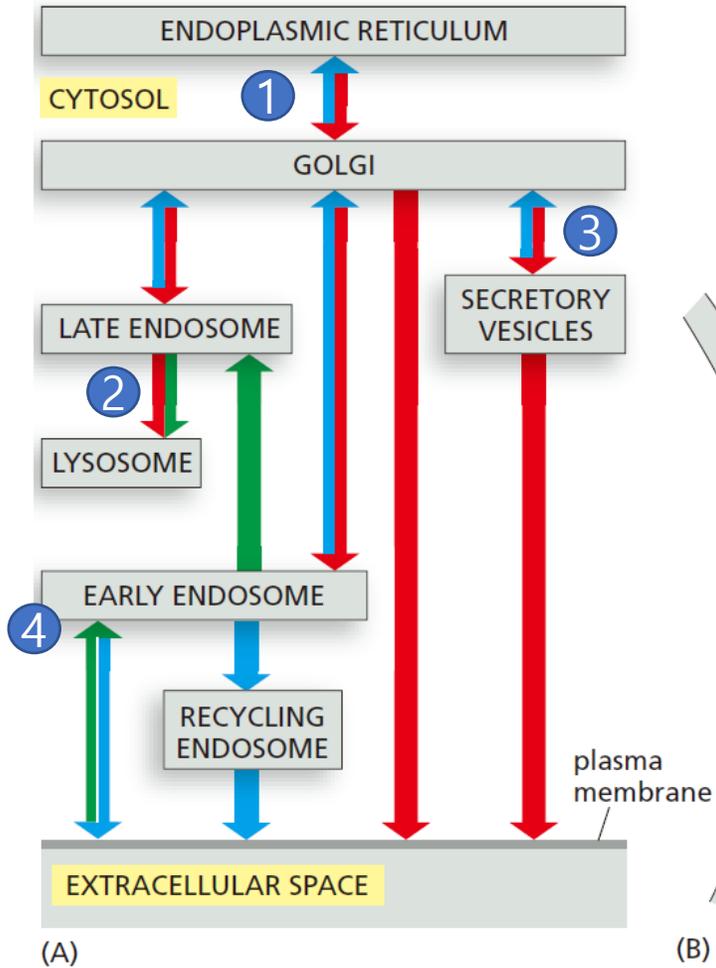


Cargo: 운반하는 단백질, 지질  
Vesicle: 소낭, 소포  
ER: 소포체  
Budding: 싹이튼다

# A "road-map" of the secretory and endocytic pathways& contents

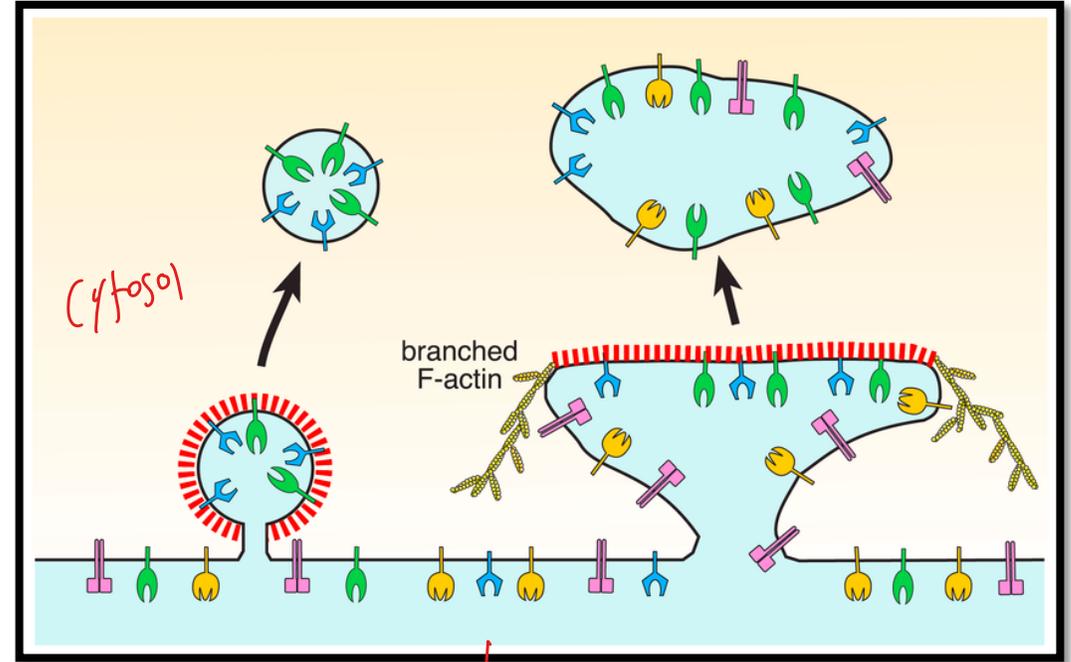
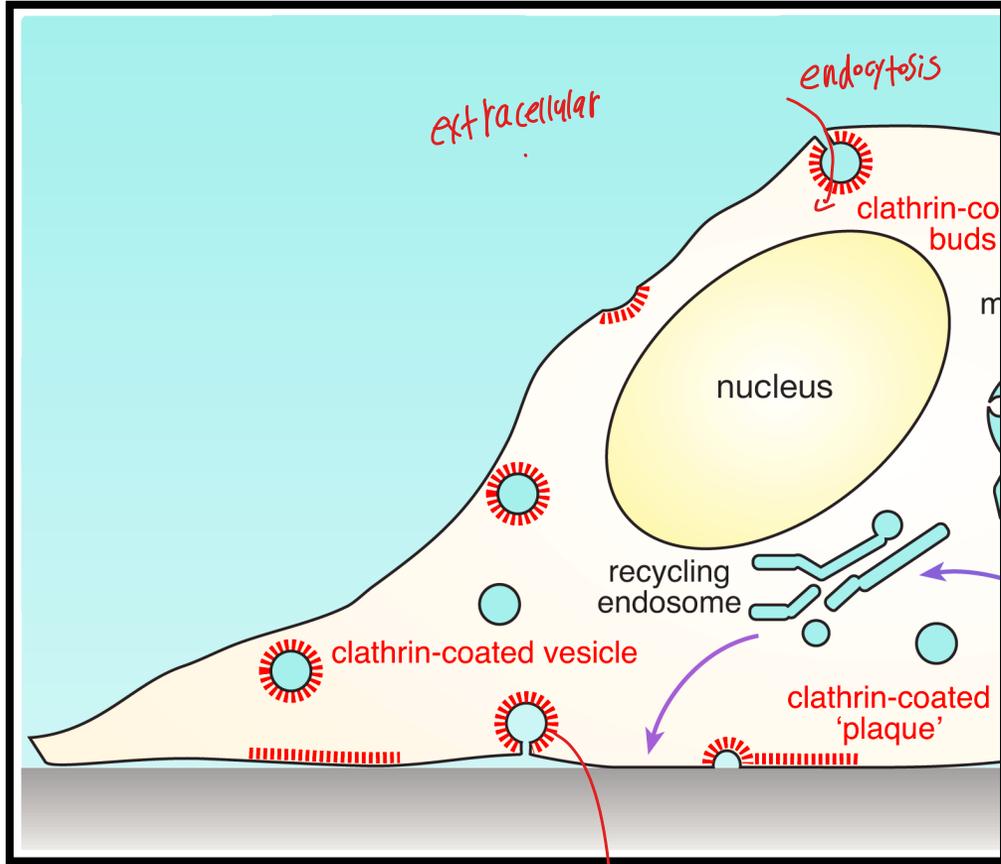
7 Main Point

1. 버딩(출아) 과 fusion (융합)의 기전
2. 각각의 세포 소기관 사이의 기능유지 방법
3. 각각의 세포 소기관의 연결 기전



# The Molecular Mechanisms of Membrane Transport and the Maintenance of Compartmental Diversity

## Coating: 감싼 부분



budding은 여기서만 일어남 / 3가지의 다른 색의 coat protein 있음

extracellular

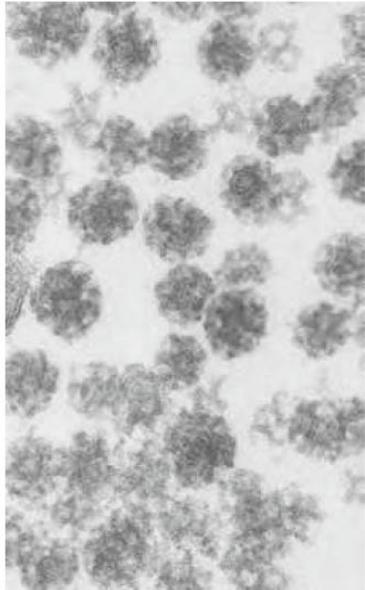
# Various Types of Coated Vesicles

Coat protein complex (COP) I & II

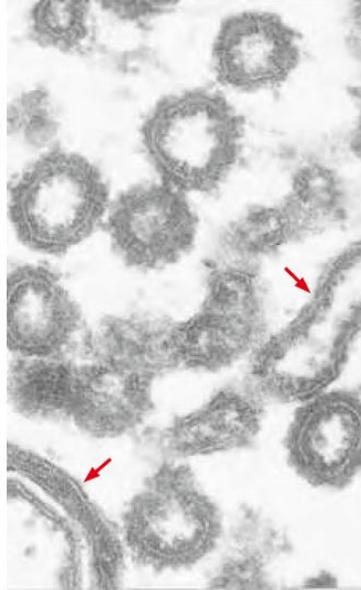
*Cop one*

*Cop two*

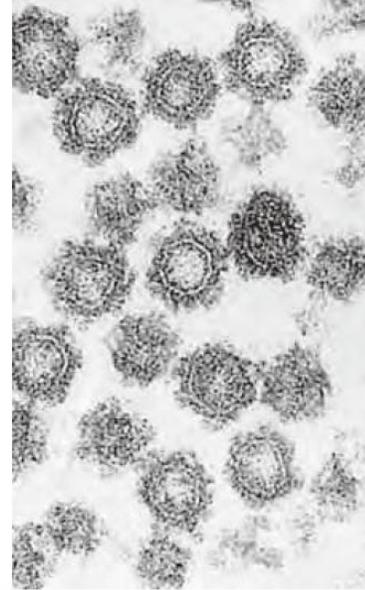
**clathrin-coated, COPI-coated, and COPII-coated**



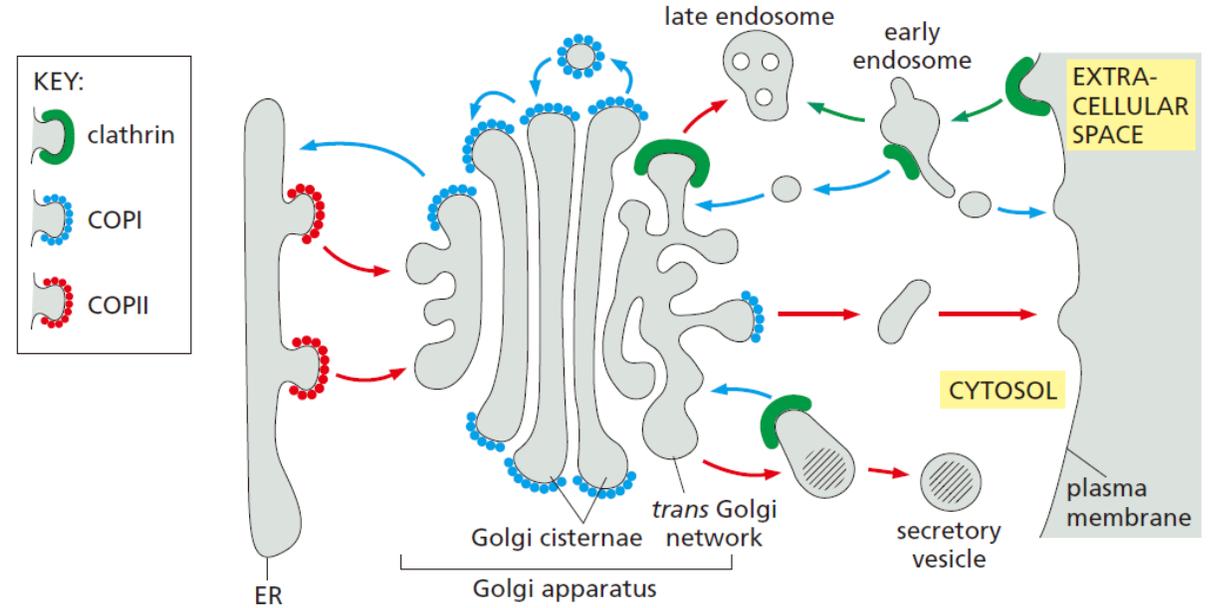
(A) clathrin



(B) COPI



(C) COPII 100 nm

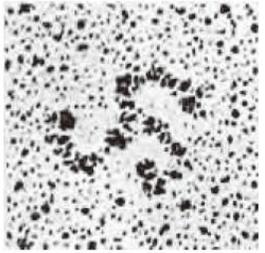


Clathrin : endocytosis

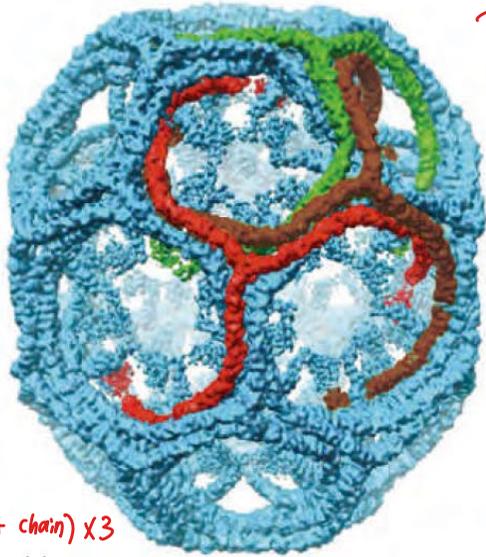
ER에서 export : COPII

Golgi에서 export / 회수 경로 : COPI

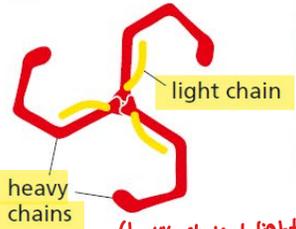
# Clathrin



(A)



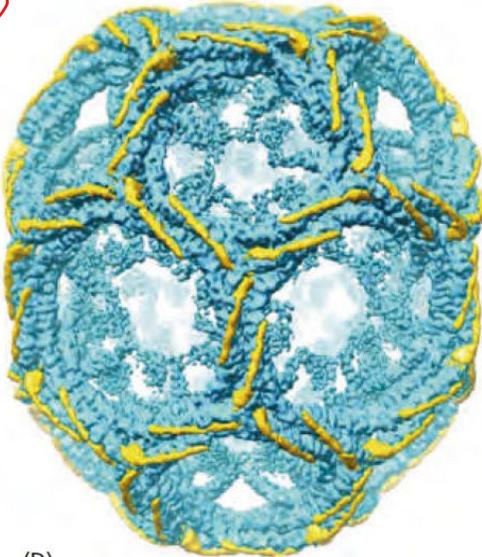
(C)



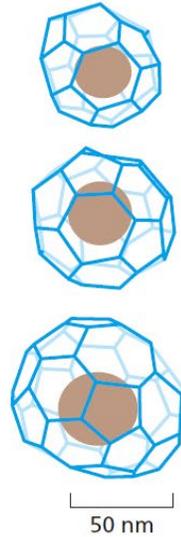
(B)

(heavy chain + light chain) x 3

triskelion이 triskelion을 모아  
구멍 같이 될



(D)

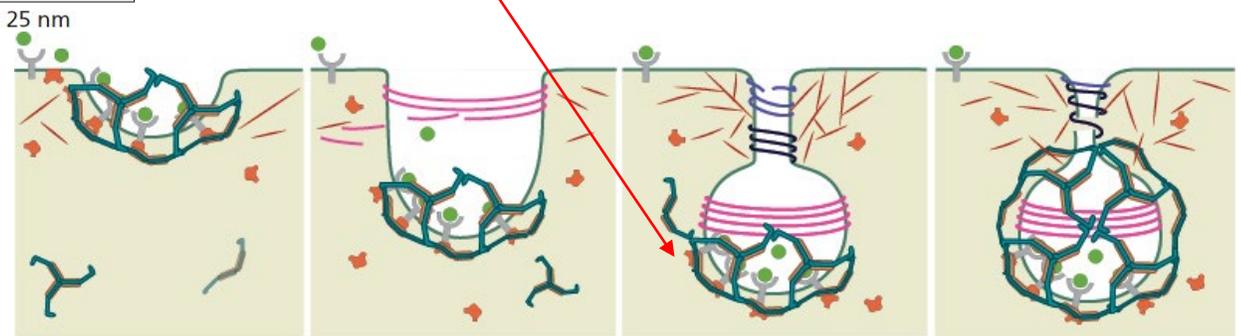


(E)

50 nm

**Triskelion:** a Celtic symbol consisting of three legs or lines radiating from a center

3개의 가지가 같은 중심에서 소용돌이 모양으로 퍼져나간 형태



Binding and recruitment

Invagination

Maturation

Scission

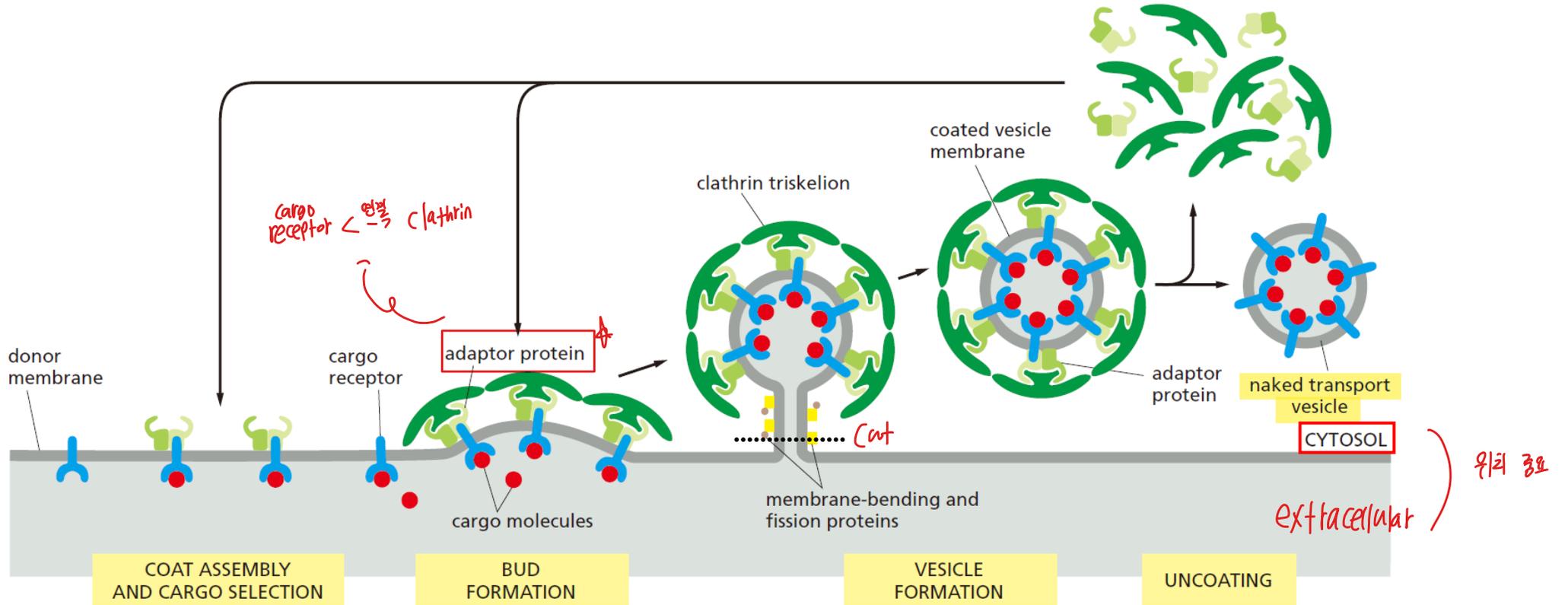
Receptor	AP2	F-BAR domain protein	Dynamin
Ligand	Clathrin	BAR domain protein	Actin filament

<https://www.mechanobio.info/what-is-the-plasma-membrane/what-is-membrane-trafficking/what-is-clathrin-mediated-endocytosis/invagination-and-maturation-of-the-clathrin-coated-vesicle/>

# Molecular mechanism of Clathrin: Assembly & disassembly

Endocytosis : receptor에 결합하는 물질만 가져옴

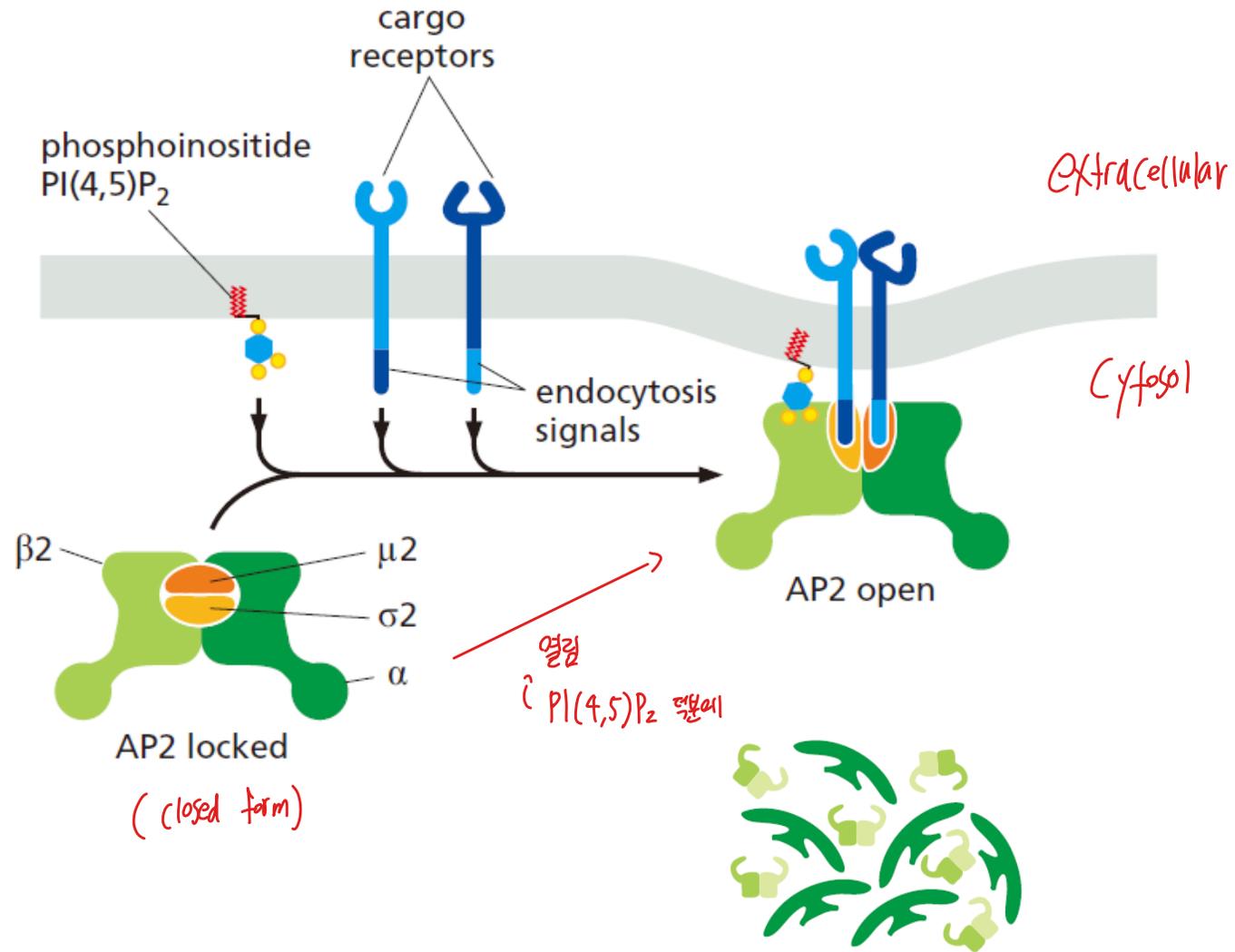
=> receptor가 중요.



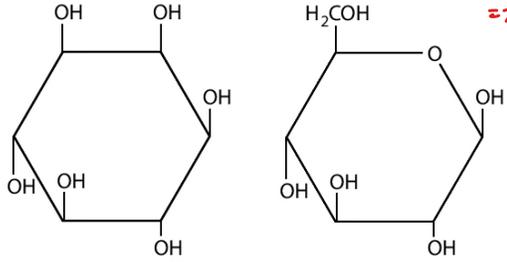
Adaptor protein: Binds to cargo receptor and clathrin at the same time and connects them to each other  
cargo receptor와 clathrin에 동시에 결합해서 연결 시켜 주는 역할

# Adaptor protein; AP2

example ↑  
(API도 존재)



# Phosphatidylinositol (PI) and phosphoinositides (PIPs)

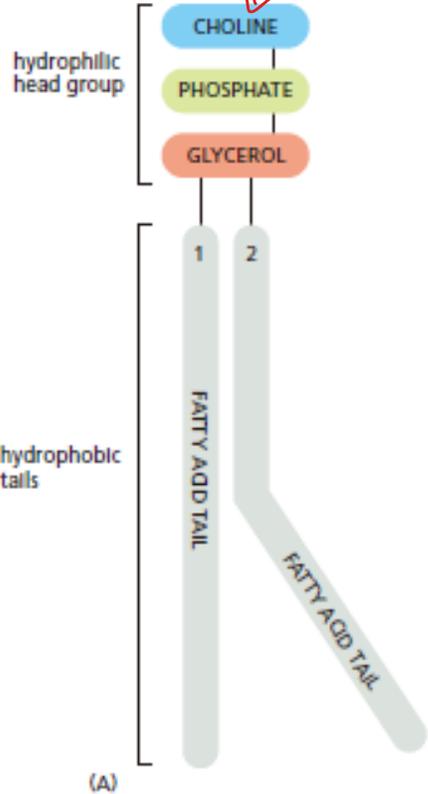


Inositol

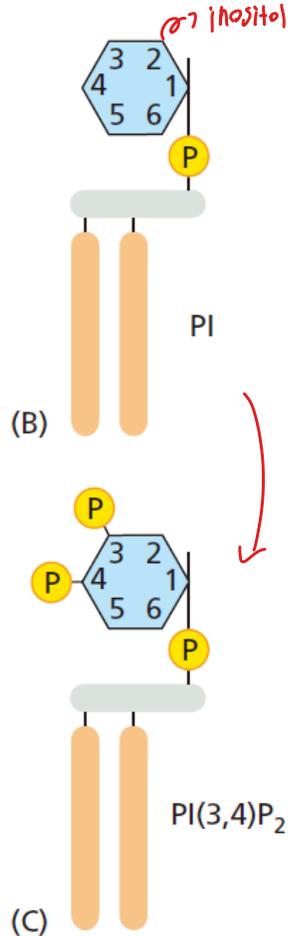
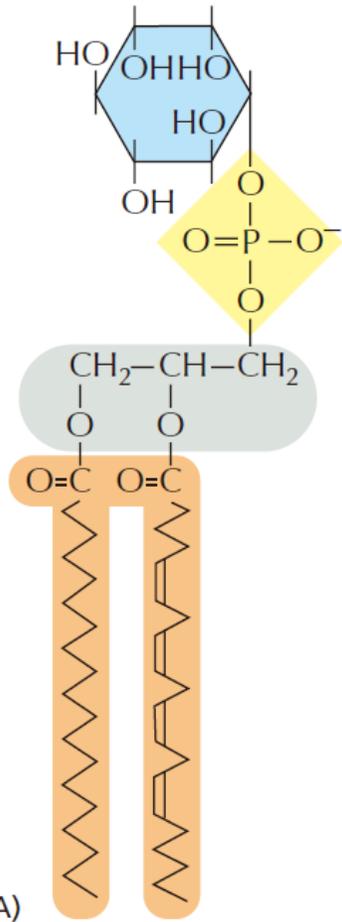
Glucose

↳ 이게 논문에 더 자주 나온  
⇒ 시그널에서 PI에

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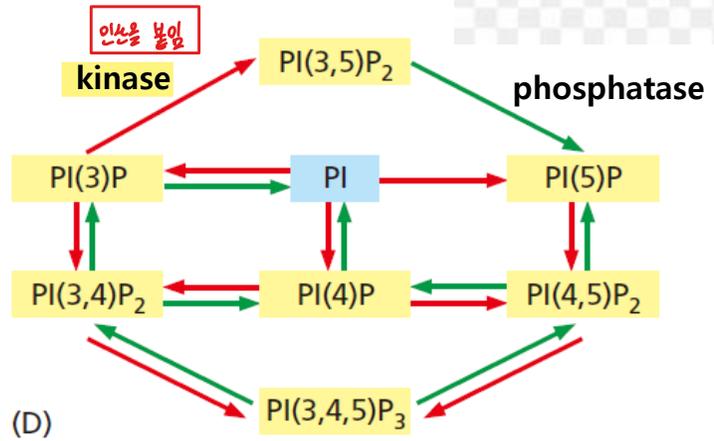
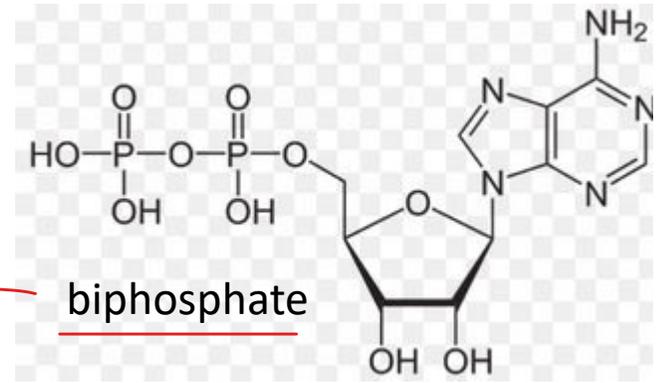


(A) Phosphatidylinositol (PI); Inositol phospholipid



(B) PI(3,4) P2:phosphatidylinositol 3,4-bisphosphate

## Adenosine Tri-Phosphate (ATP)



(D) PI(3,4,5) P3:phosphatidylinositol 3,4,5-trisphosphate



(E)



(F)

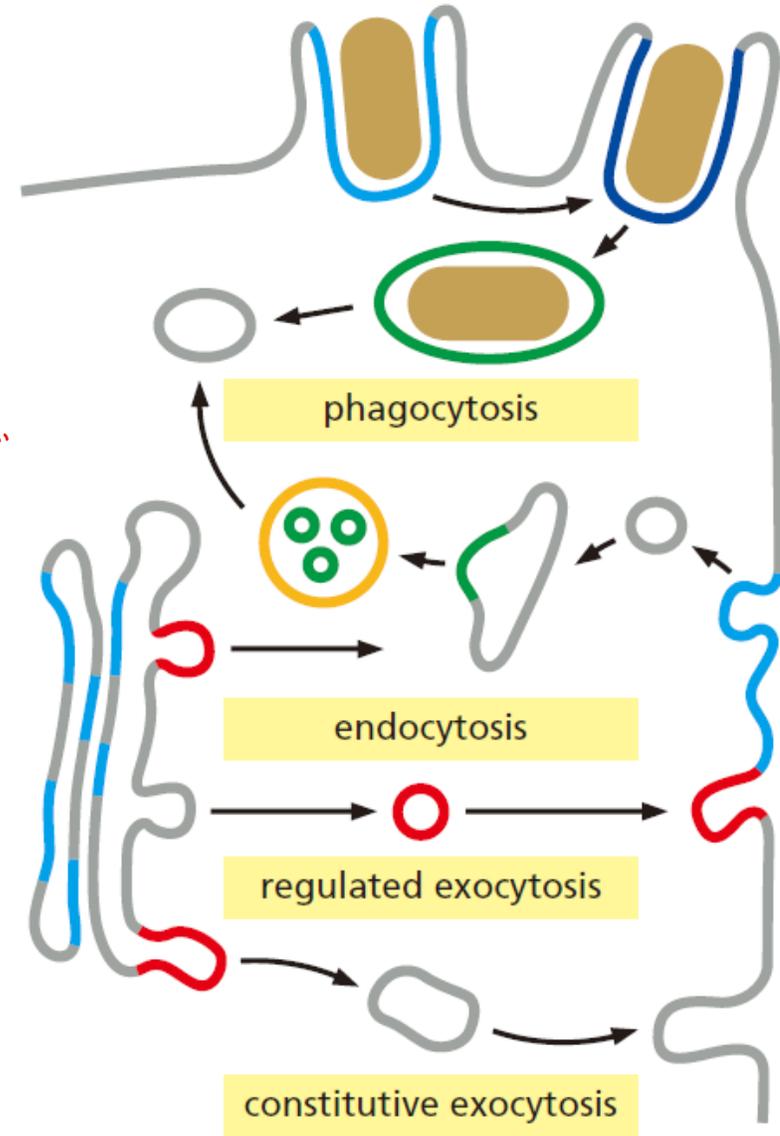
인산이 위치 따라 이름 결정

인산이 위치 따라 adaptor protein 바뀜 ⇒ receptor 바뀜

따라서 붙어 있음

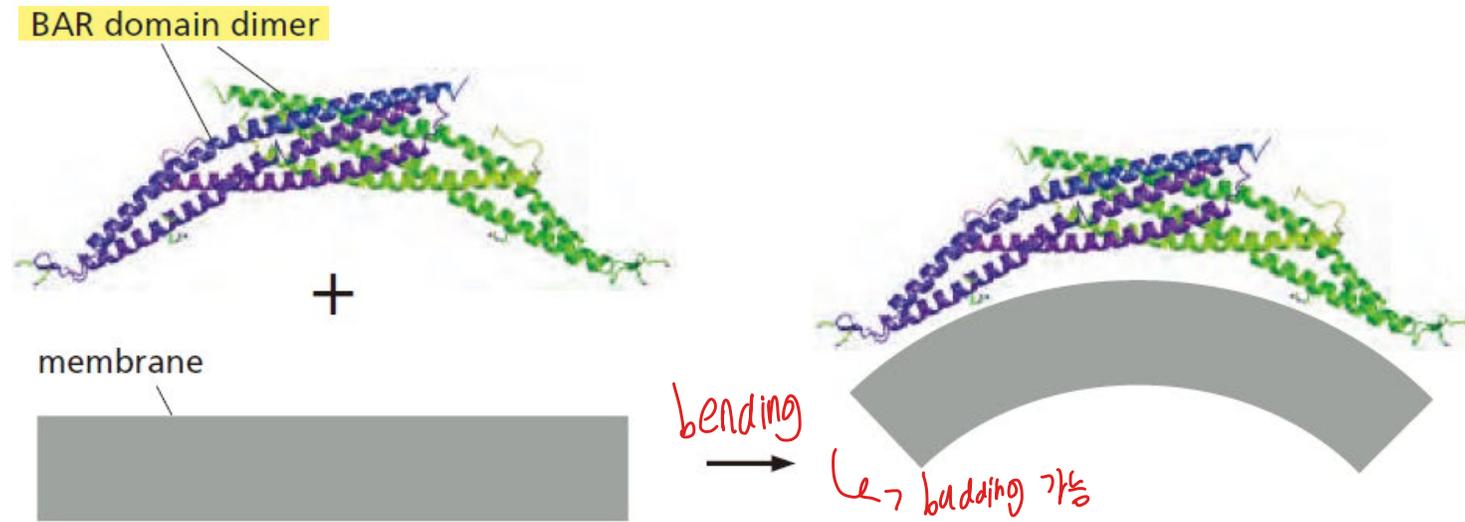
# The intracellular location of phosphoinositides

숫자 기억  
=> 단, "분포가 다르다"



KEY: PI(3)P PI(4)P PI(4,5)P<sub>2</sub> PI(3,5)P<sub>2</sub> PI(3,4,5)P<sub>3</sub>

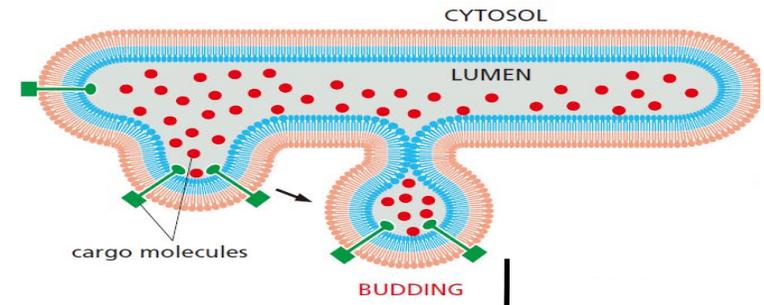
# Membrane-Bending Proteins Help Deform the Membrane During Vesicle Formation



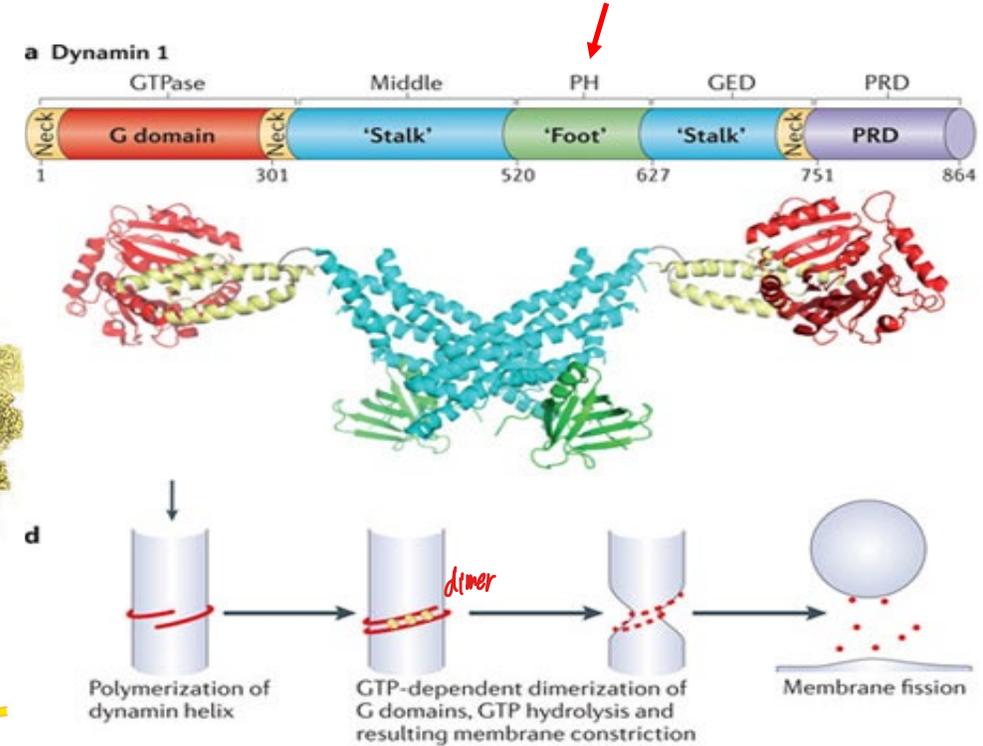
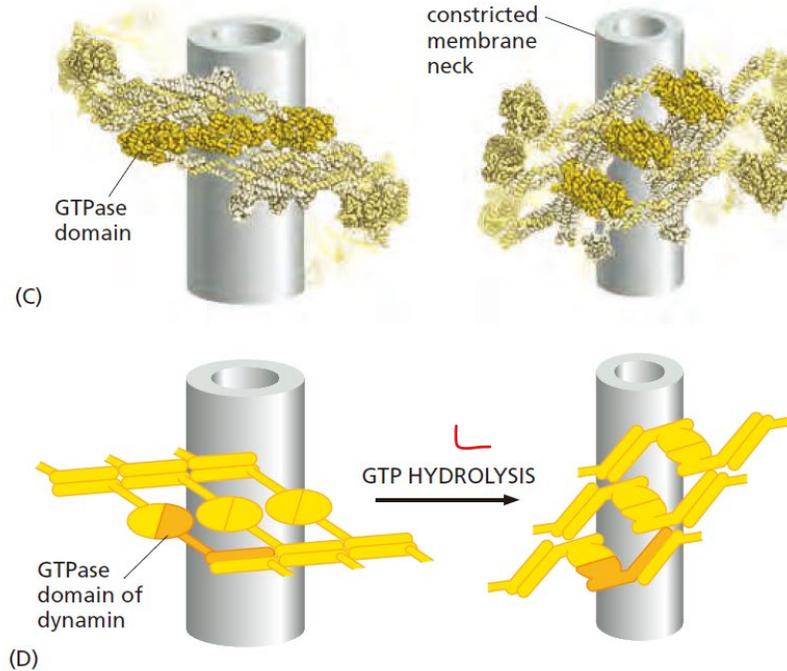
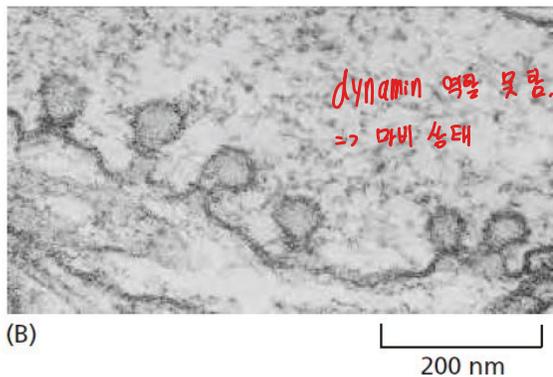
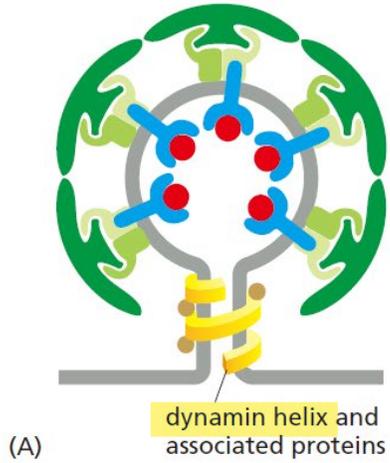
# Cytoplasmic Proteins Regulate the **Pinching-Off** and Uncoating of Coated Vesicles

**Dynamin:** GTPase domain and PI(4,5)P<sub>2</sub> binding domain

- Allows its membrane translocation
- Mediates membrane scission via PI(4,5)P<sub>2</sub> clustering

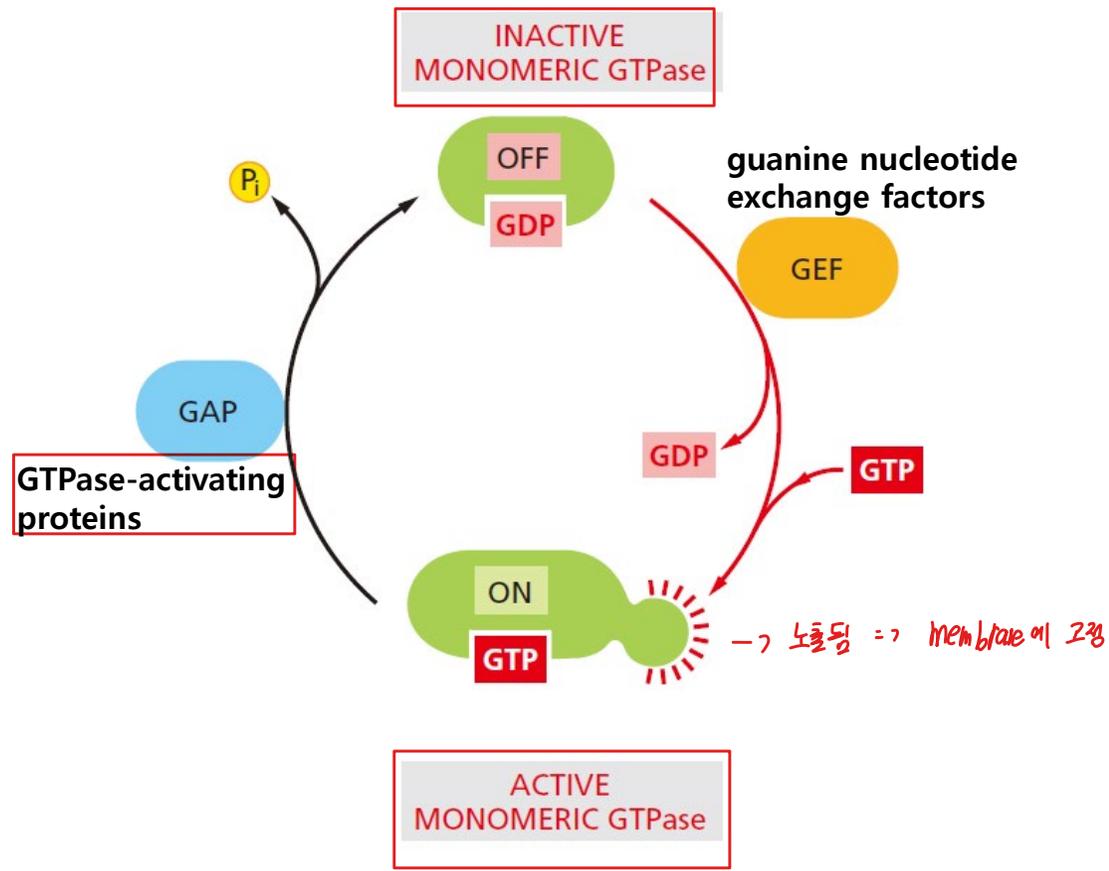


Noncytosolic leaflet이 서로 모이게 조임

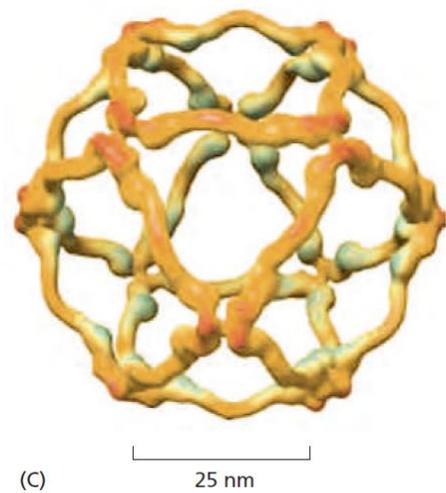
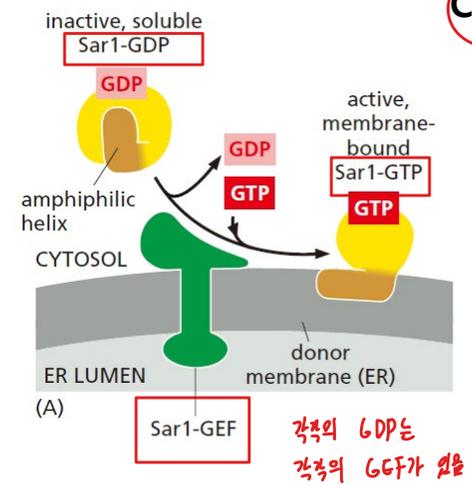


# Monomeric **GTPases** Control Coat Assembly

- Coat-recruitment GTPases:
1. ARF → COPI & clathrin ← AP2 (PIP2) ← API 이 붙으면 ARF에 의해 activation
  2. Sar1 protein → COPII

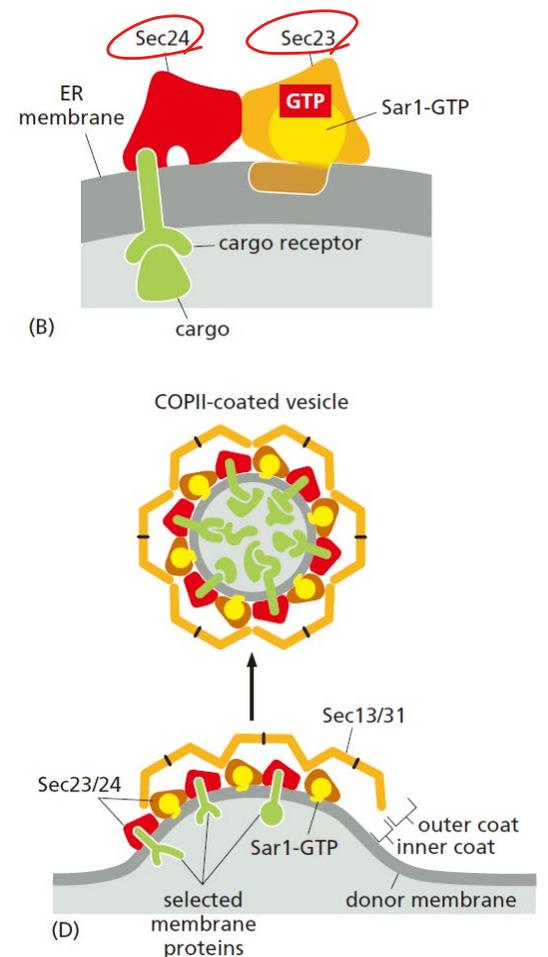


GTP-binding proteins as molecular switches



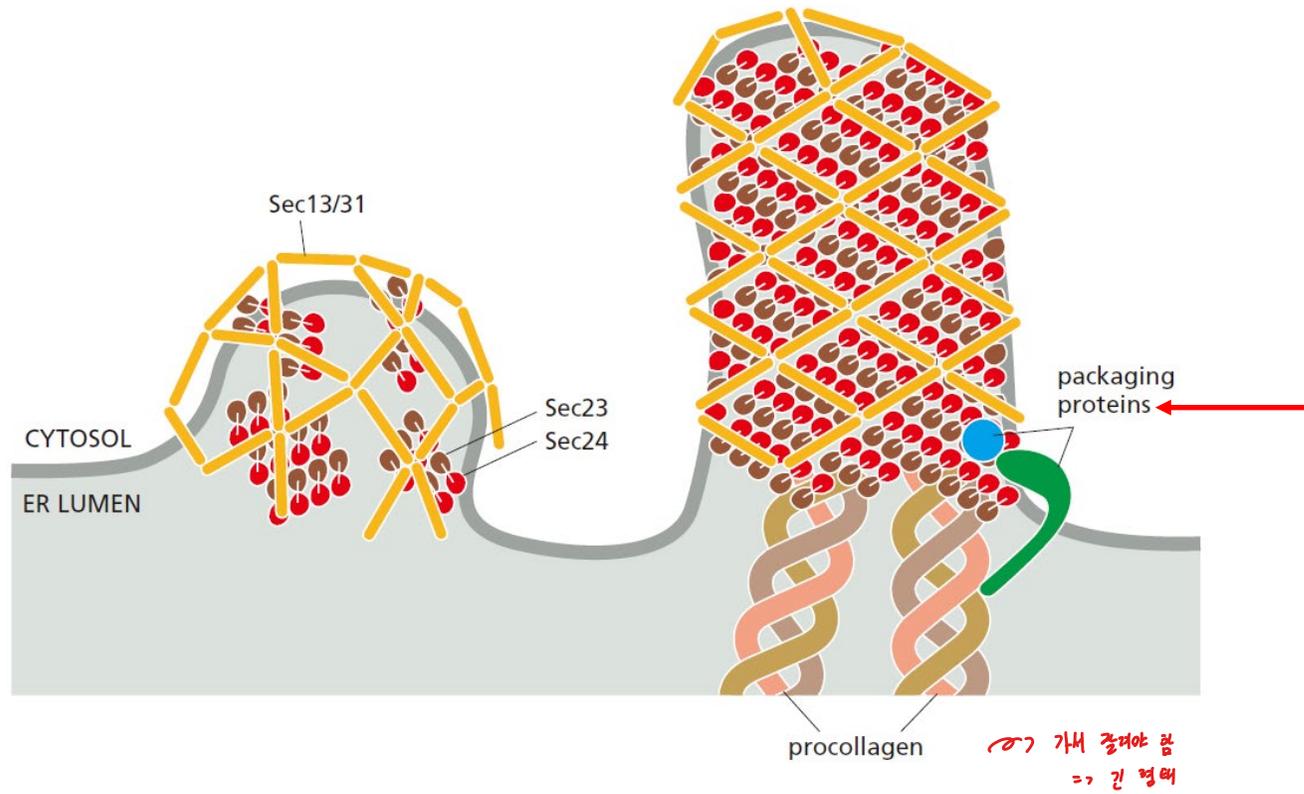
**COPII: Sar1, Sec23, Sec24, Sec13, Sec31**

= AP2 역할      = clathrin 역할



# Not All Transport Vesicles Are Spherical

제목만 기억



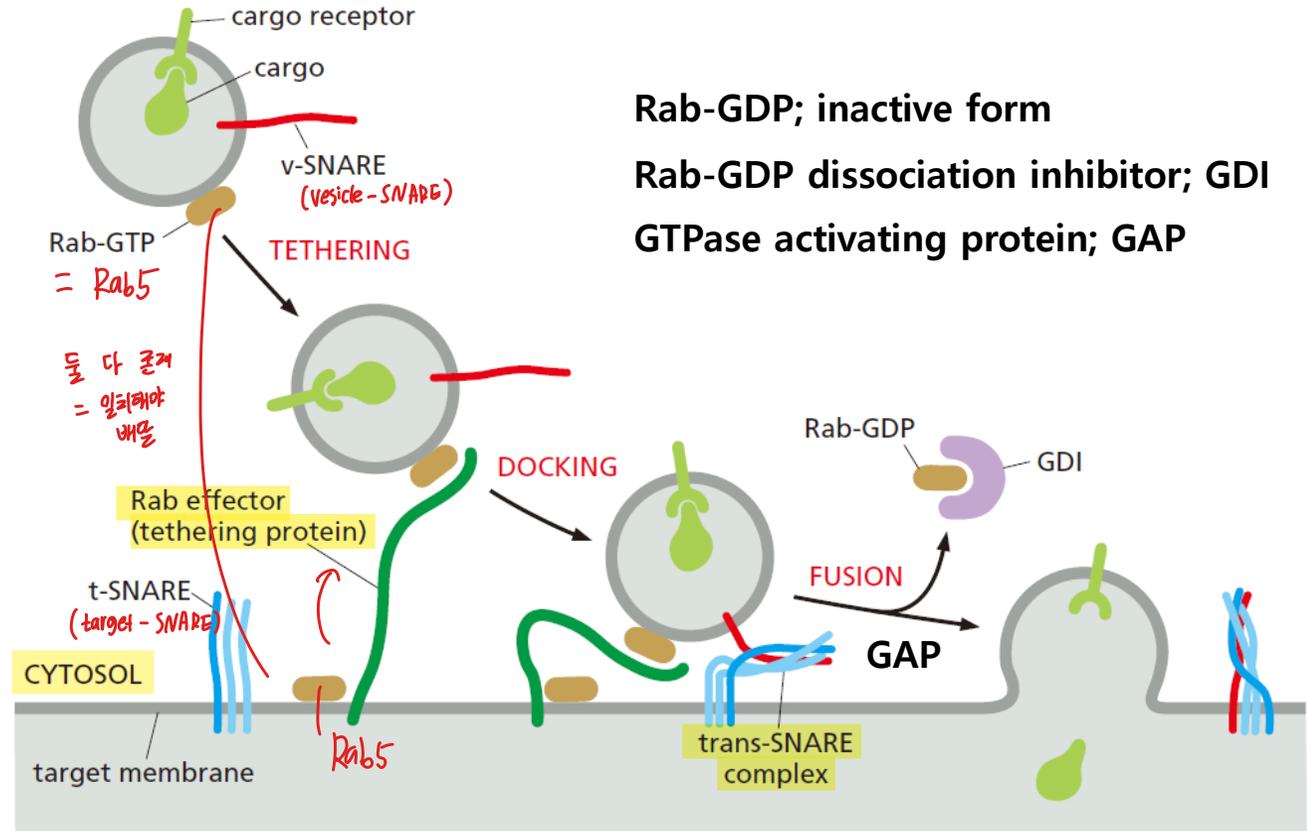
# Rab Proteins Guide Transport Vesicles to Their Target Membrane

= GTPase

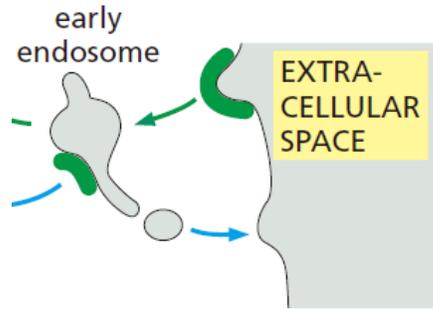
1. Rab proteins and Rab effectors direct the vesicle to specific spots on the correct target membrane
2. SNARE proteins and SNARE regulators mediate the fusion of the lipid bilayers

TABLE 13-1 Subcellular Locations of Some Rab Proteins

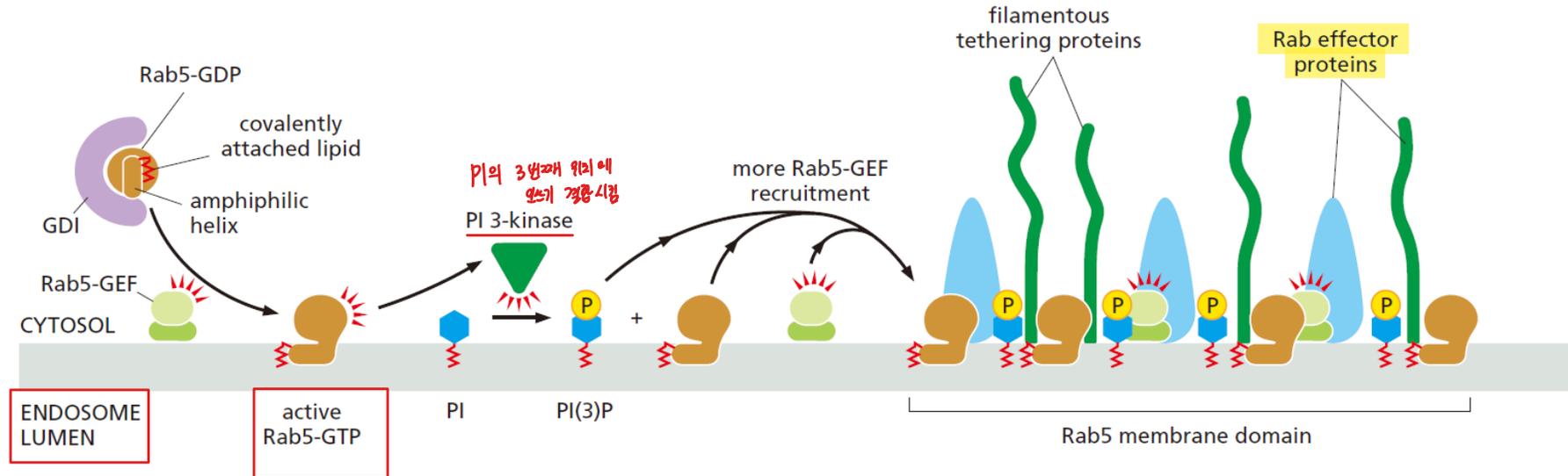
Protein	Organelle
Rab1	ER and Golgi complex
Rab2	cis Golgi network
Rab3A	Synaptic vesicles, secretory vesicles
Rab4/Rab11	Recycling endosomes
Rab5	Early endosomes, plasma membrane, clathrin-coated vesicles
Rab6	Medial and trans Golgi
Rab7	Late endosomes
Rab8	Cilia
Rab9	Late endosomes, trans Golgi



# The formation of a **Rab5** domain on the endosome membrane

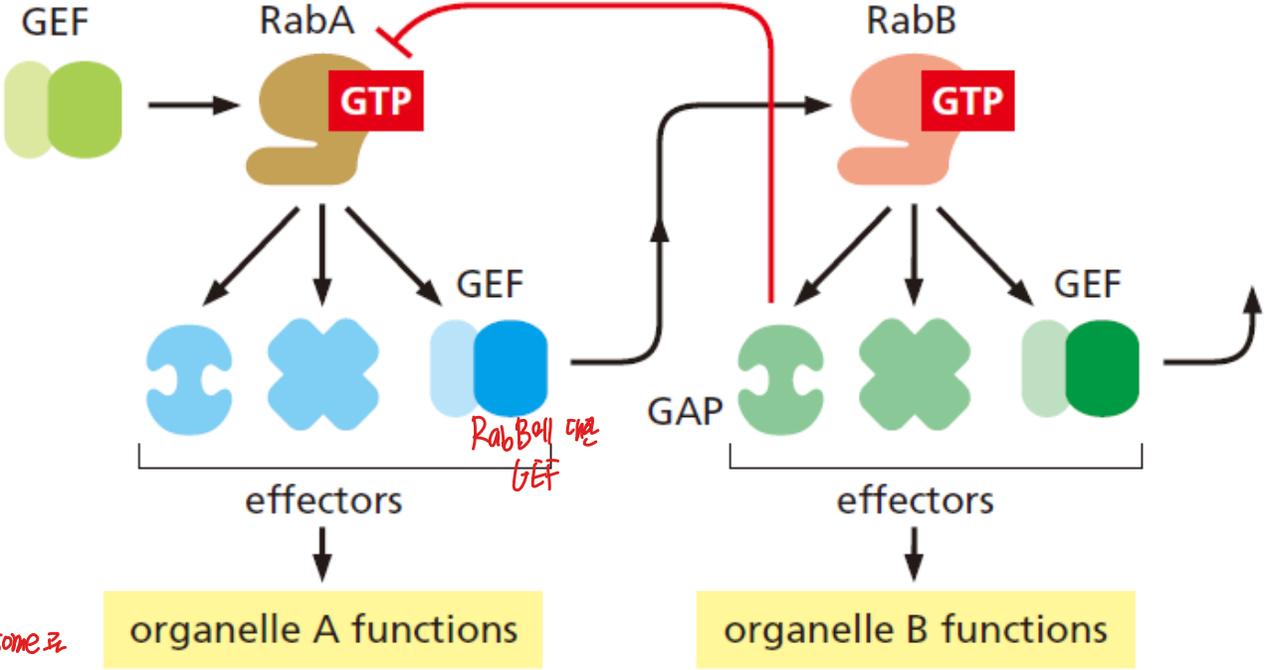


☆ Vesicle Rab = 3번의 Rab



# Rab Cascades Can Change the Identity of an Organelle

\* important 문제는 병목 조건된 것들

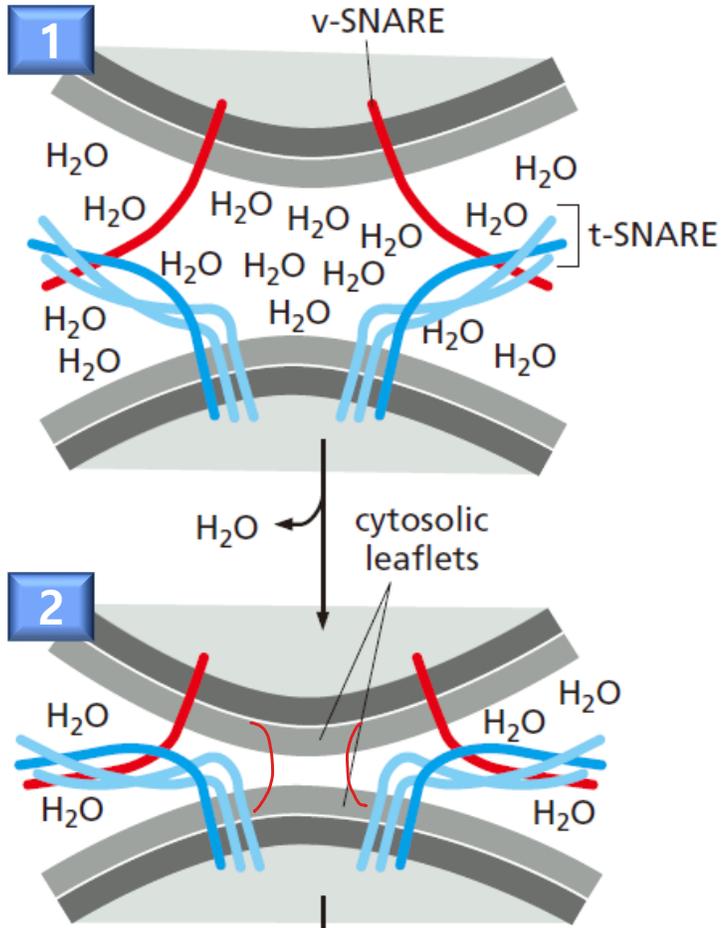


lysosome은 early endosome로 결함 X  
 → Rab7 GEF 결함

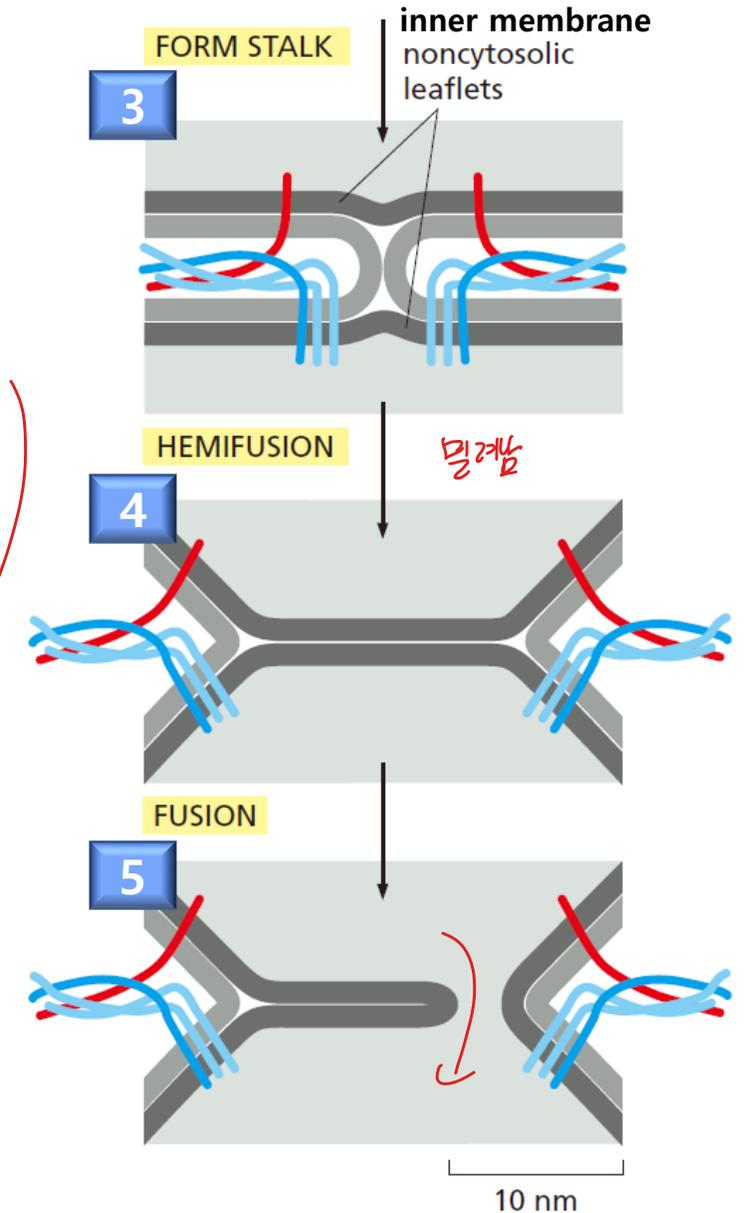
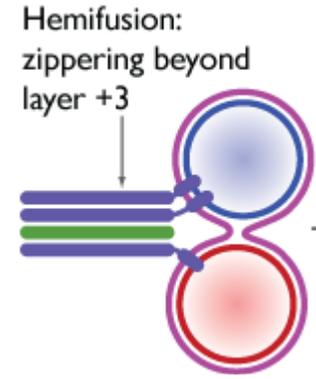
Rab5 (early endosome) → Rab7 (late endosome) 전환. Rab5 → Rab7 전환이 실패하면, cargo는 lysosome에 도달하지 불가

# SNAREs Mediate Membrane Fusion

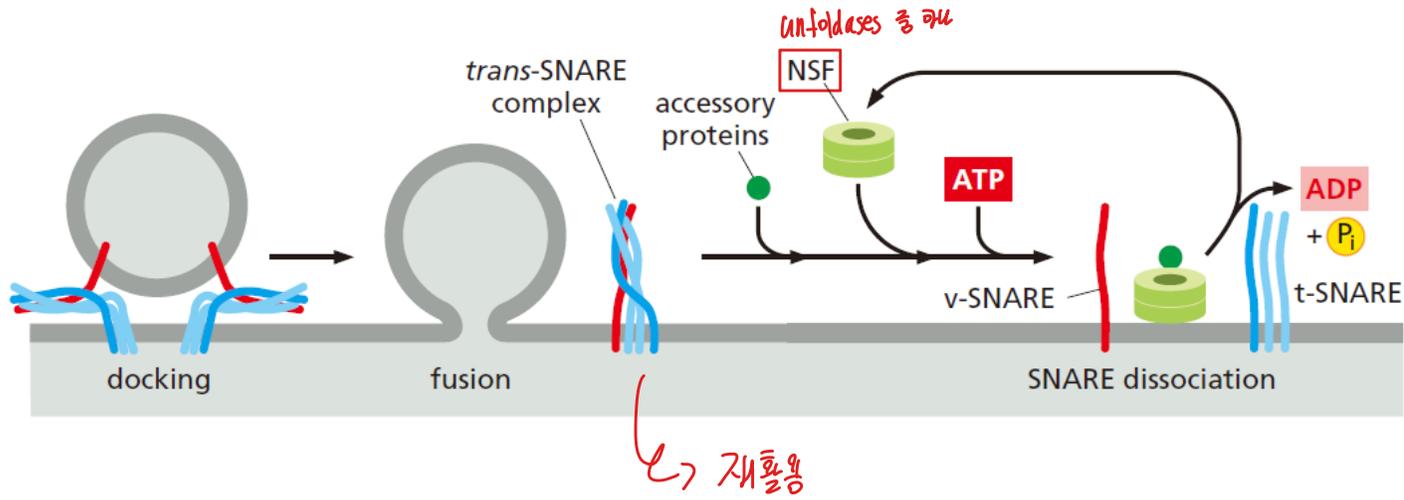
<https://sites.uw.edu/golgi/membrane-fusion/>



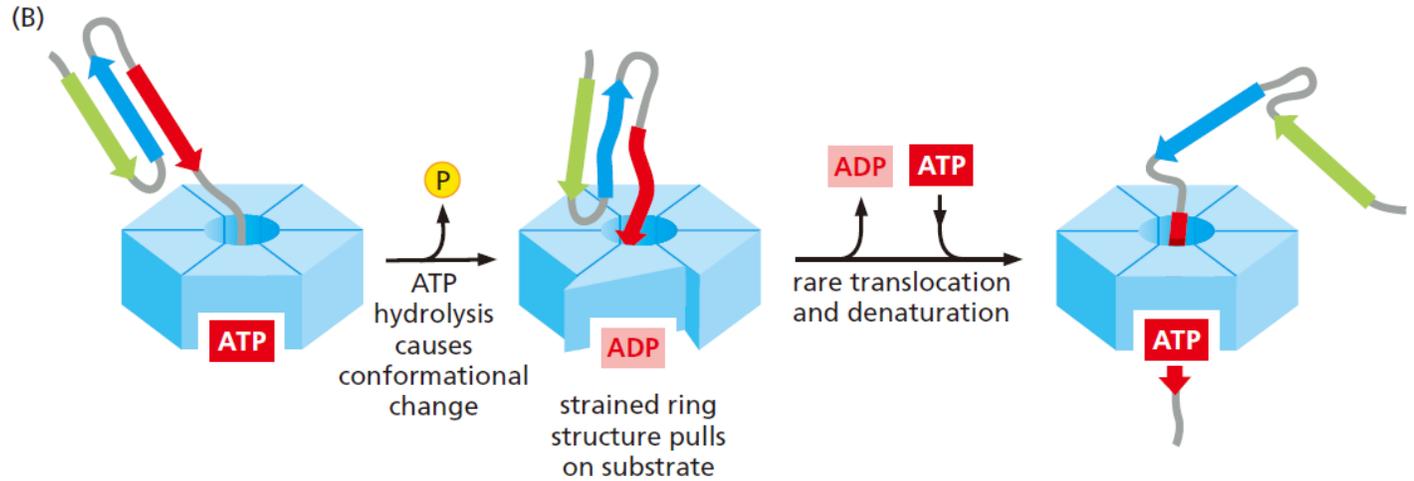
1. A tight pairing between v- and t-SNAREs  
-close apposition
2. Expels water molecules
3. Form a connecting stalk
4. Forming a new bilayer  
(hemifusion, or half-fusion)
5. Rupture of the new bilayer



# Interacting SNAREs Need to Be Pried Apart Before They Can Function Again



## 동형 Unfoldases; AAA proteins



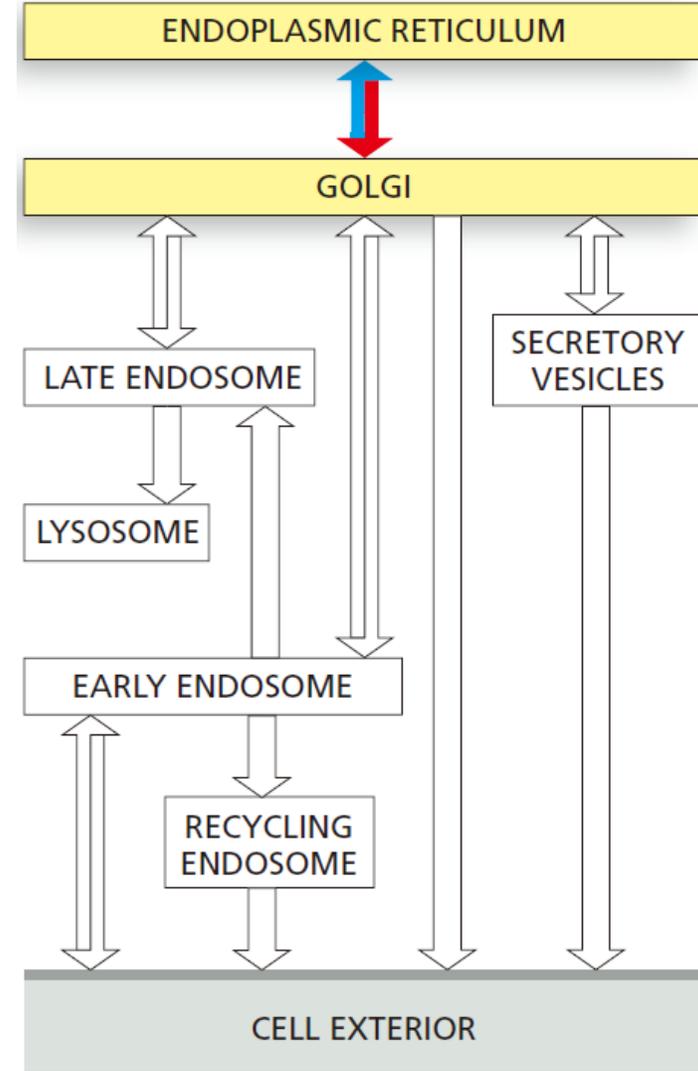
## Summary

1. Vesicle 이 형성되는 과정 –coating proteins
2. Clathrin 의 assembly
3. Adaptor protein
4. PI& PIP
5. Pinch off –dynamin
6. Coat assembly regulator– Sar1 for COPII
7. Final destination- Rab protein
8. SNARE – fusion regulator

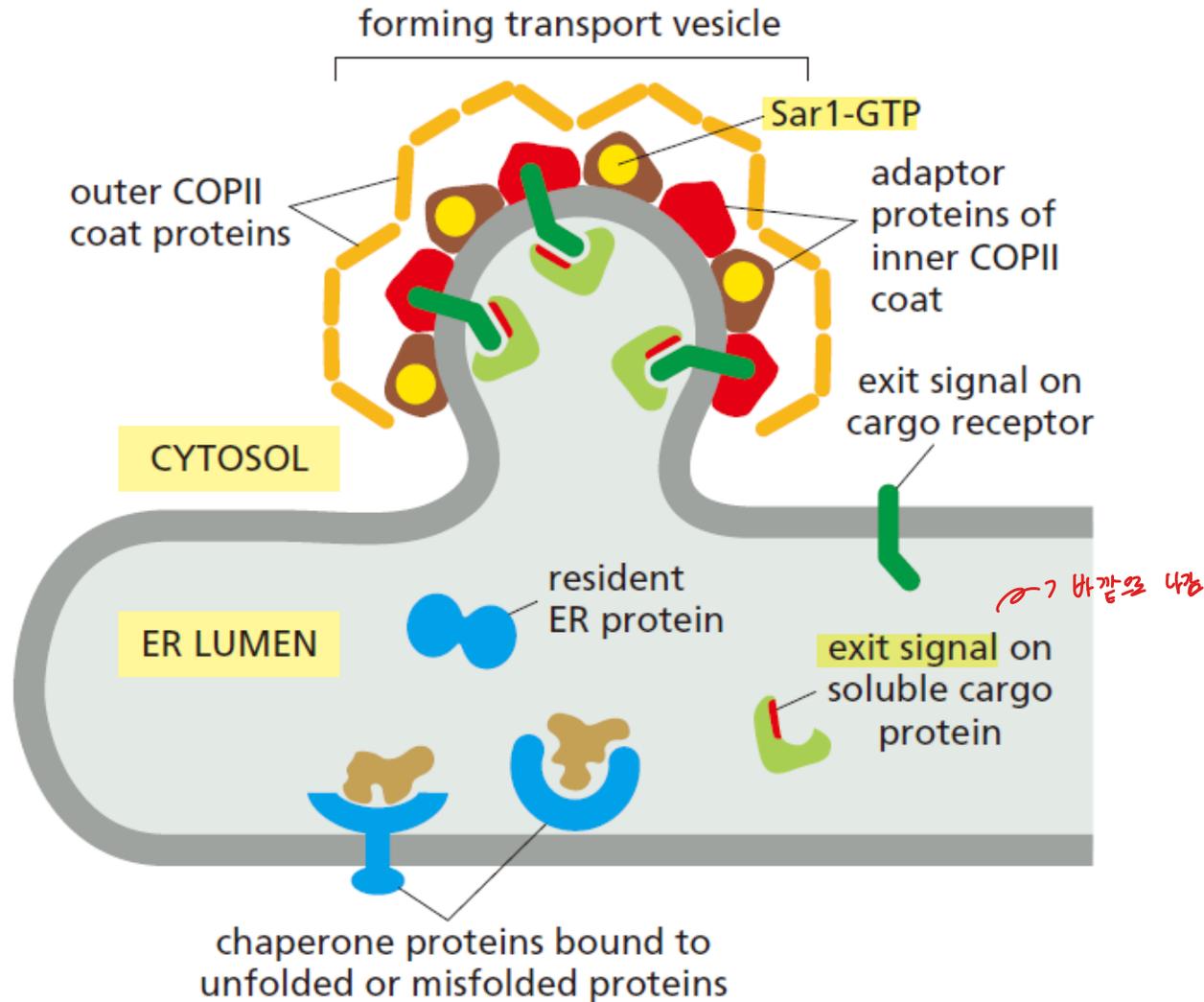
수송 소포 (transport vesicle)에 대한 설명으로 옳은 것은? (E 2점)

- ① 세포막이 튀어나온 부분에서 버딩이 시작된다.
- ② Coating 단백질만 있으면 버딩이 일어날 수 있다.
- ③ Coating 단백질이 cargo receptor를 직접 recruit 한다.
- ④ 소포의 안쪽과 세포의 안쪽 (cytosol)은 위상적으로 같다.
- ⑤ Cargo receptor들은 원래 세포 바깥쪽 (extracellular)에 존재하는 receptor들이다.

- Transport from the ER Through the Golgi Apparatus



# Proteins Leave the ER in **COPII**-Coated Transport Vesicles



## Cystic fibrosis (CF)

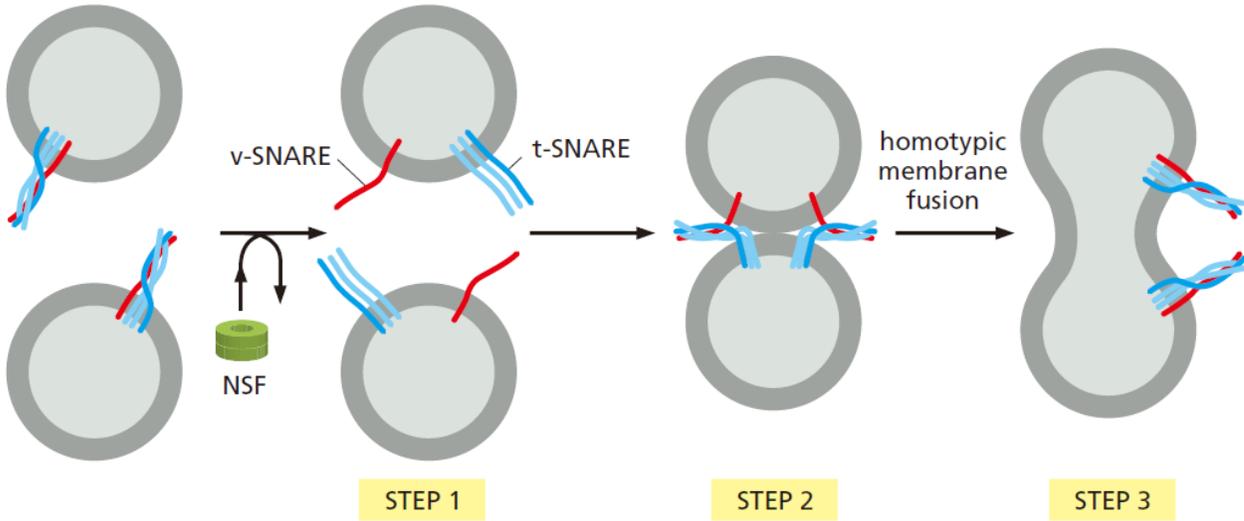
- Inherited disorder that causes severe damage to the lungs, digestive system and other organs
- **CFTR (cystic fibrosis transmembrane conductance regulator)**- the flow of salt such as  $\text{Cl}^-$
- In the most common genetic form of CF ( $\Delta\text{F508}/\Delta\text{F508}$ ), incorrectly folded CFTR is **retained in the ER and partially degraded**

amino acid  
개만 4개접는데,  
ER에서 exit 불가  
=> 나기도 못해는 있음

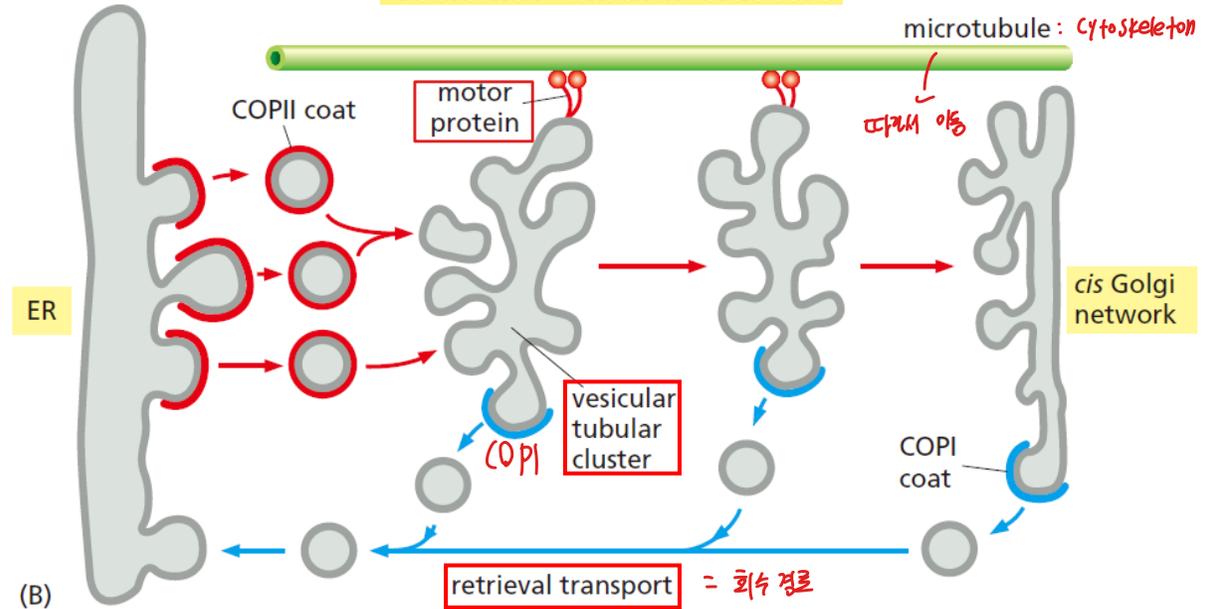
# Vesicular Tubular Clusters Mediate Transport from the ER to the Golgi Apparatus

같은 곳에서 나온 애들끼리 fusion

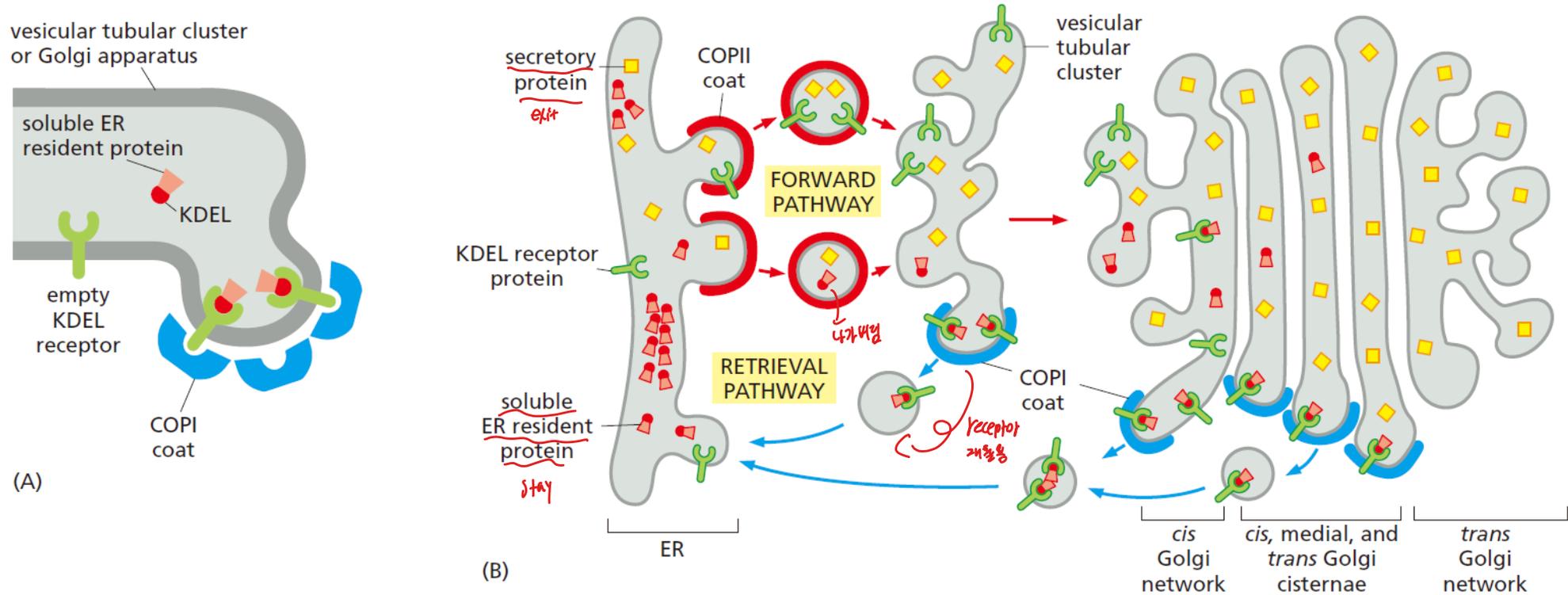
**homotypic fusion** vs heterotypic fusion



## Vesicular tubular clusters

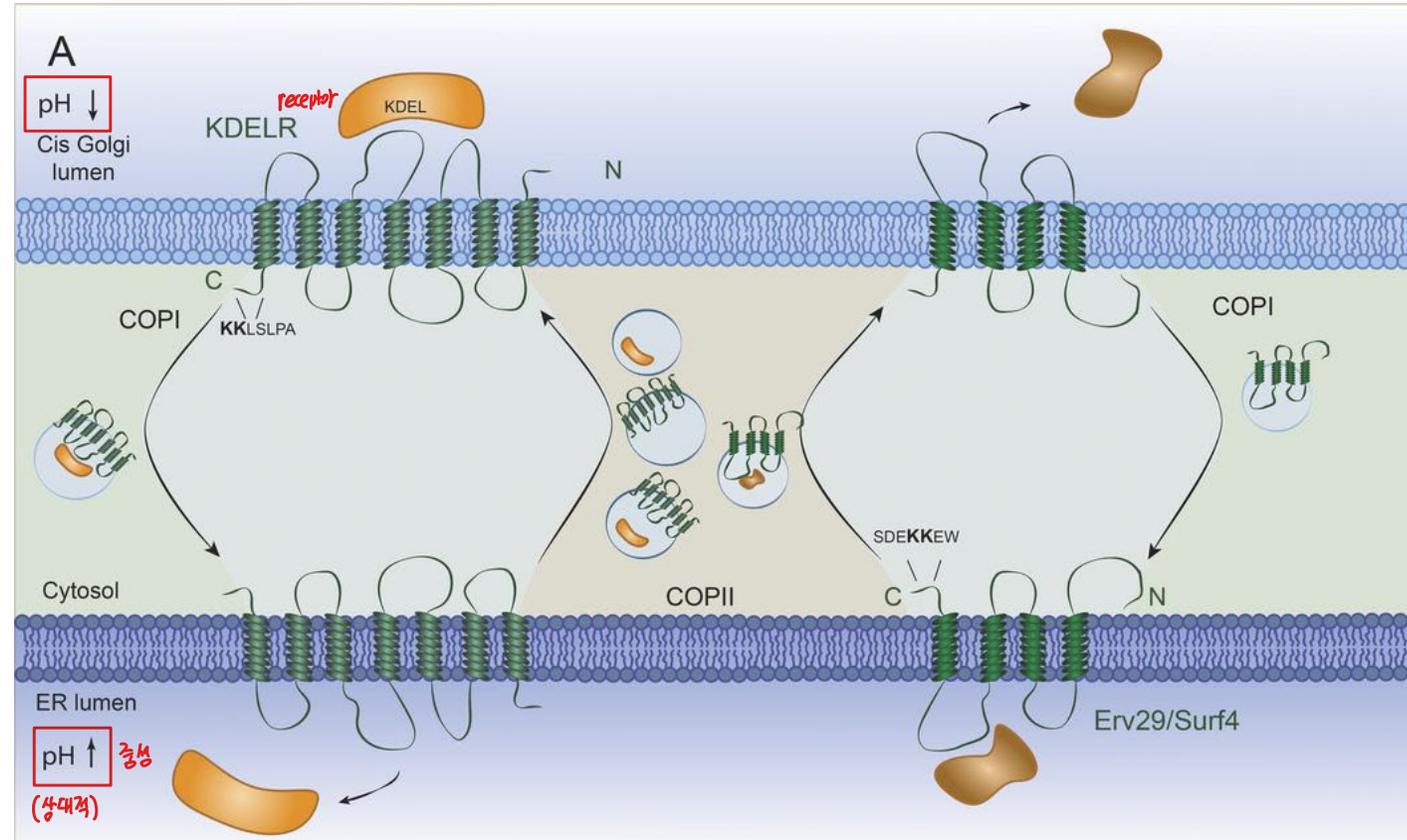


# The Retrieval Pathway to the ER Uses Sorting Signals



- **KKXX:** COPI binding signal → membrane protein
  - **KDEL:** ER retrieval signal → soluble protein
- sequence*
- 언제는 볼로, 안 볼로 => how?*

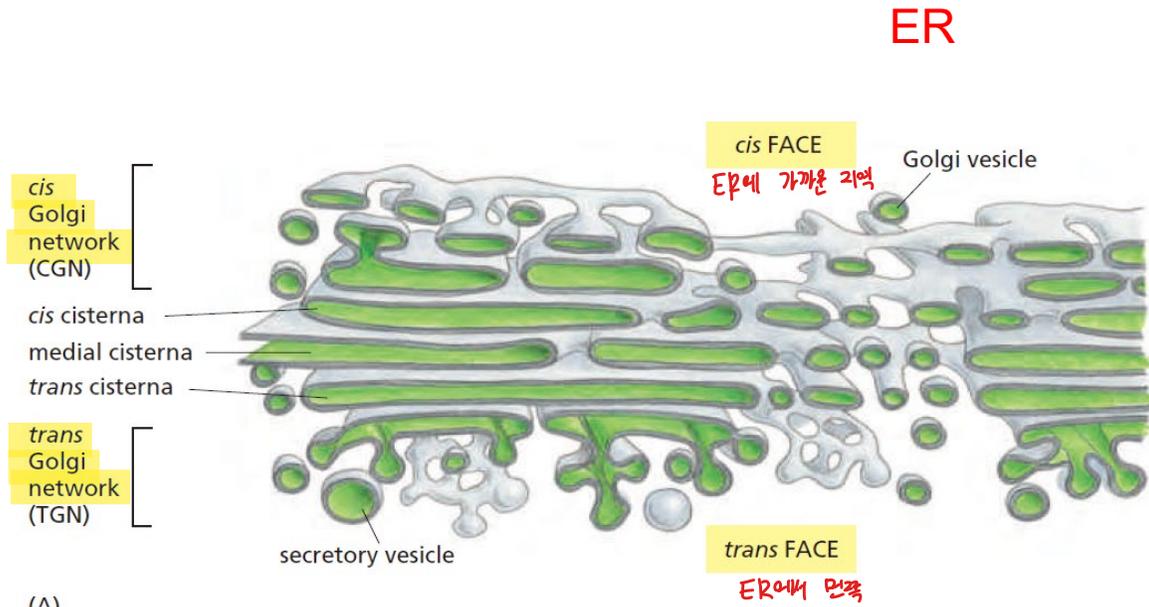
## How cargo receptors mediate traffic by cycling between the ER and Golgi?



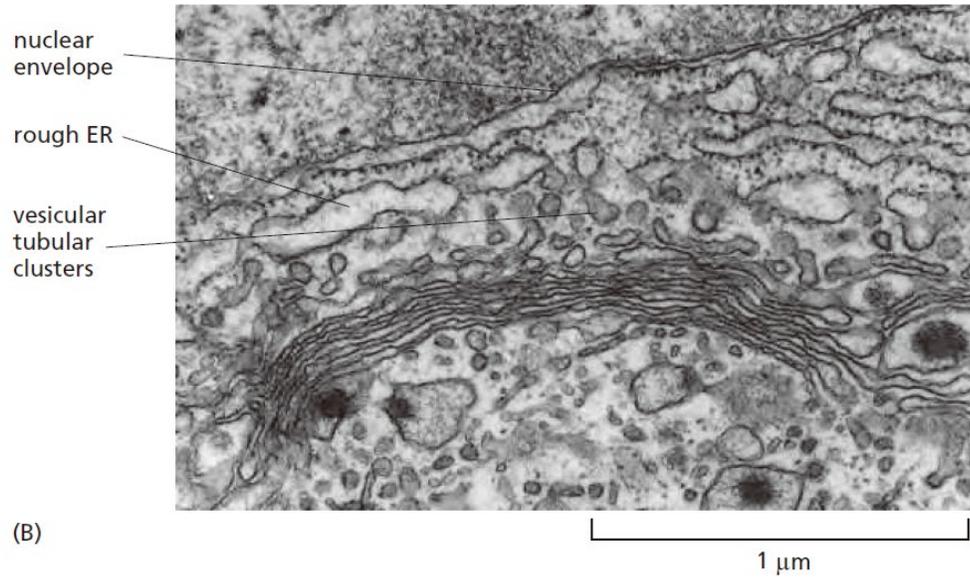
doi:10.1083/jcb.201610031

(A) The KDEL receptor interacts with soluble cargo proteins at the lower pH of the Golgi and it is directed to the ER via COPI vesicles. At the neutral pH of the ER, the receptor releases the cargo protein to the lumen.

# The Golgi apparatus



(A)



(B)



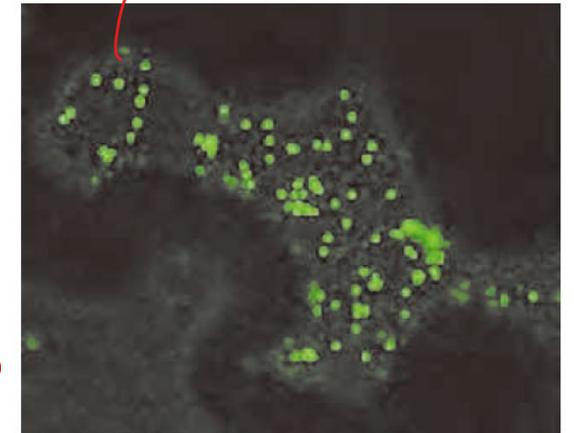
Pista bread

4~6개의 stack



(A)

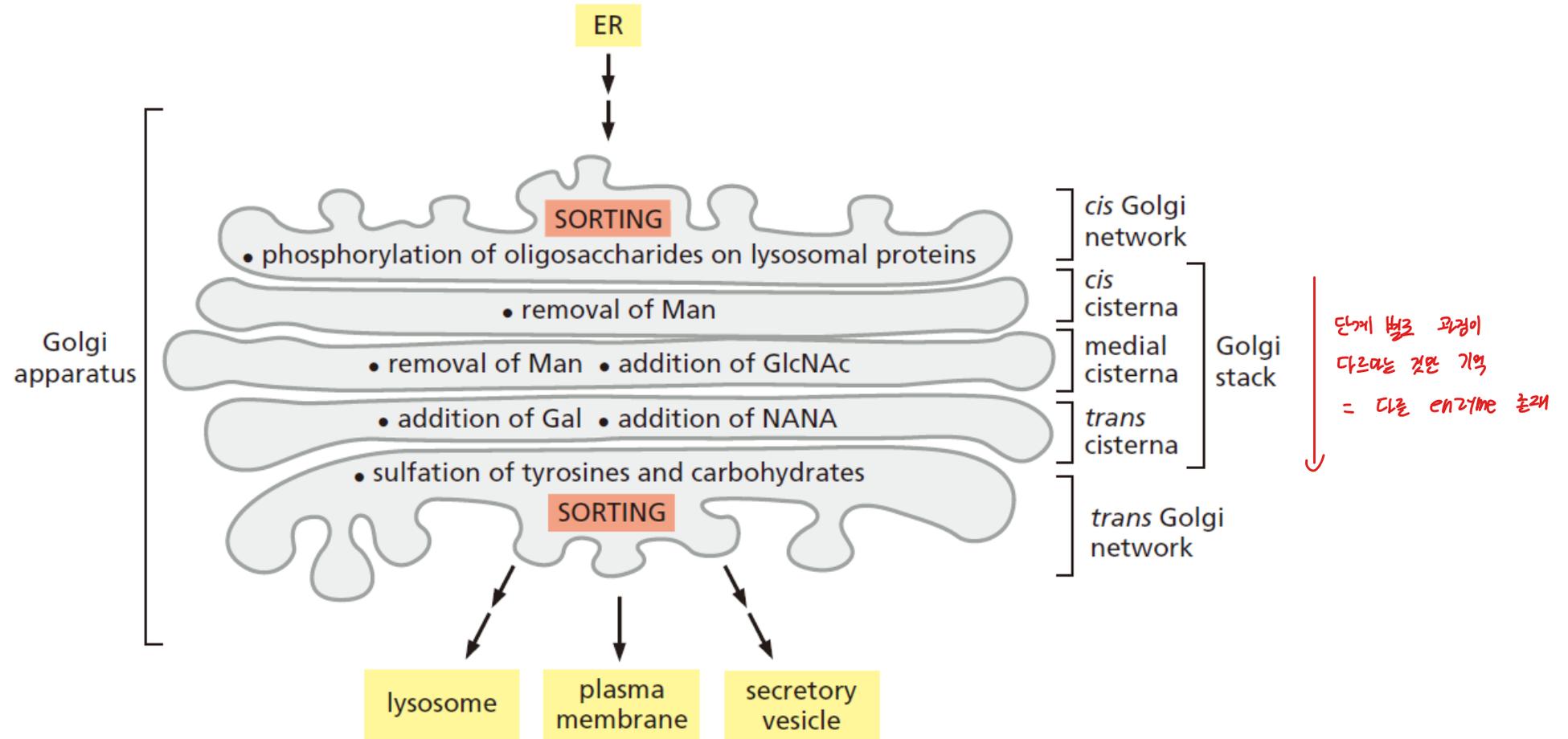
Animal



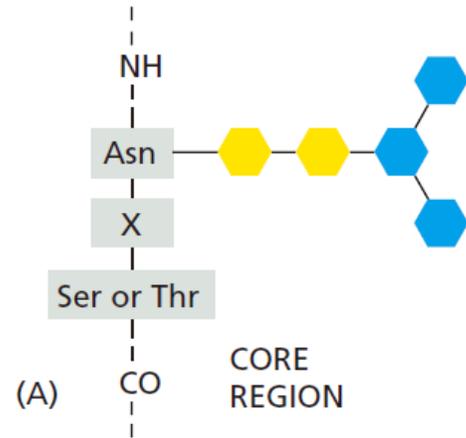
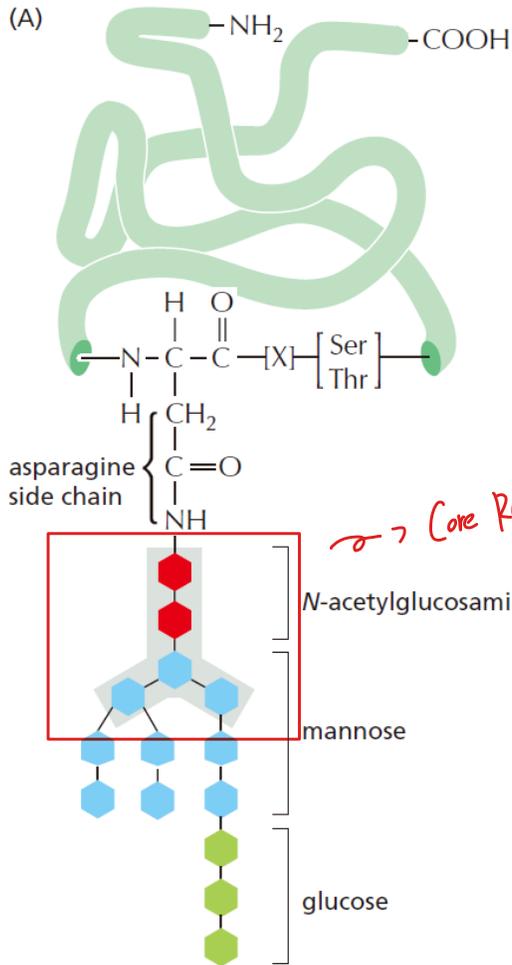
(B)

Plant

# Summarizes the functional compartmentalization of the Golgi apparatus



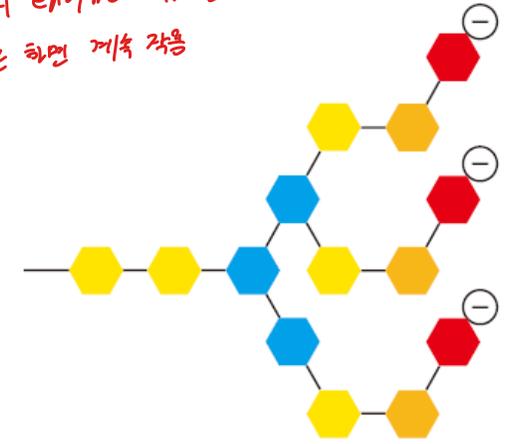
# Oligosaccharide Chains Are Processed in the Golgi Apparatus



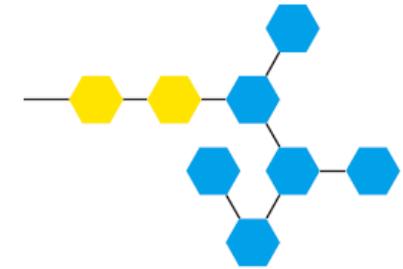
KEY

- = N-acetylglucosamine (GlcNAc)
- = mannose (Man)
- = galactose (Gal)
- = N-acetylneuraminic acid (sialic acid, or NANA)

9이기에 내의 효소 때문  
=> 접근하면 계속 각음



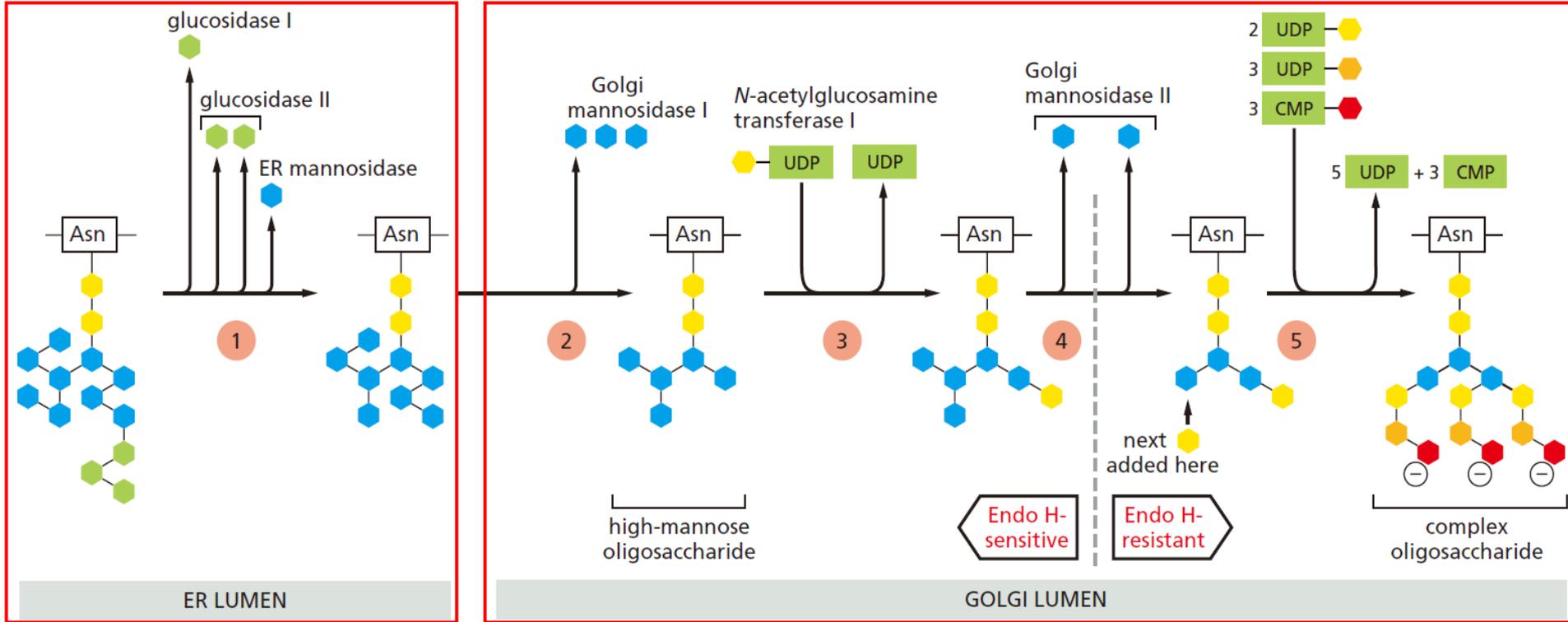
(B) COMPLEX OLIGOSACCHARIDE



(C) HIGH-MANNOSE OLIGOSACCHARIDE

- ❖ 효소 접근 가능 → **complex/hybrid glycan**으로 전환, 효소 접근 차단 → trimming이 제한되어 **high-mannose** 형태
- ❖ 단단히 접힌 구조나 특정 folding domain 내부에 묻힌 당 - 효소 접근 불가
- ❖ 표면에 노출된 당은 Golgi의 trimming·extension 효소 접근 가능

# Oligosaccharide processing in the ER and the Golgi apparatus



KEY:

● = N-acetylglucosamine (GlcNAc)  
 ● = mannose (Man)  
 ● = glucose (Glc)  
 ● = galactose (Gal)  
 ● ⊖ = N-acetylneuraminic acid (sialic acid, or NANA)

1단계: Glucose와 특정 mannose를 제거하고 이동 - (ER)

2단계: Golgi mannosidase I은 3개의 만노스를 더 제거

3단계: N-아세틸글루코사민 전이효소 I이 N-아세틸글루코사민을 첨가

4단계: Mannosidase II는 두 개의 추가 만노스를 제거

5단계: N-아세틸글루코사민, 갈락토스 및 시알산이 추가

*정확하면  
CAMP의 형성  
=> enzyme 이 기대해서*

*step  
기억 X*

Step 1: Remove and transfer glucose and specific mannose – ER

Step 2: Golgi mannosidase I removes 3 more mannose

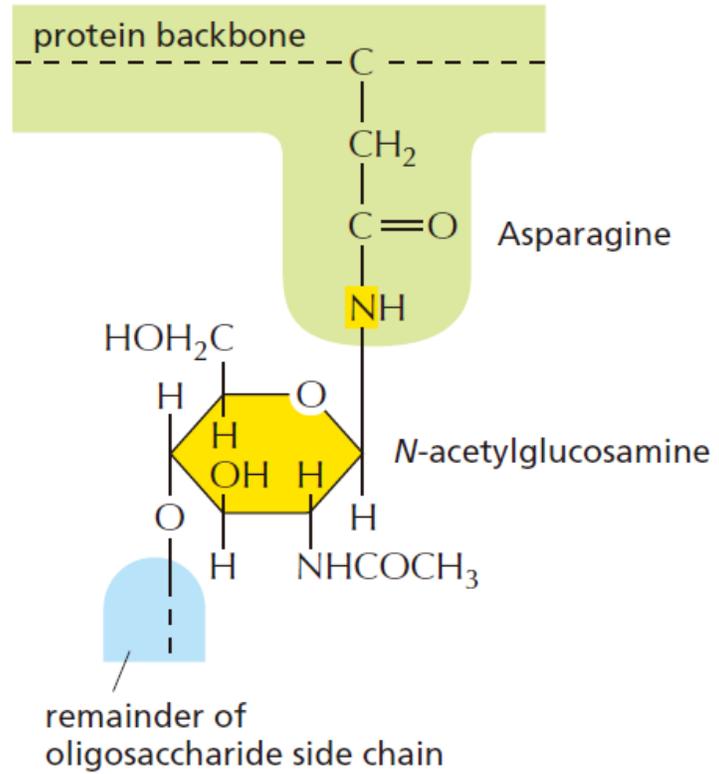
Step 3: N-acetylglucosamine transferase I adds N-acetylglucosamine

Step 4: Mannosidase II removes two additional mannose

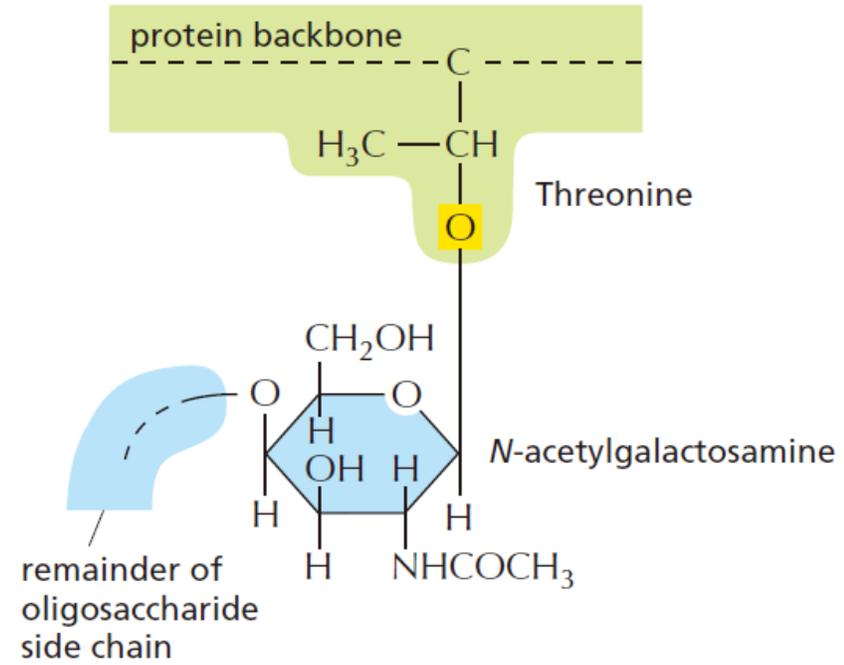
Step 5: Add N-acetylglucosamine, galactose and sialic acid

# Proteoglycans Are Assembled in the Golgi Apparatus

## N-LINKED GLYCOSYLATION

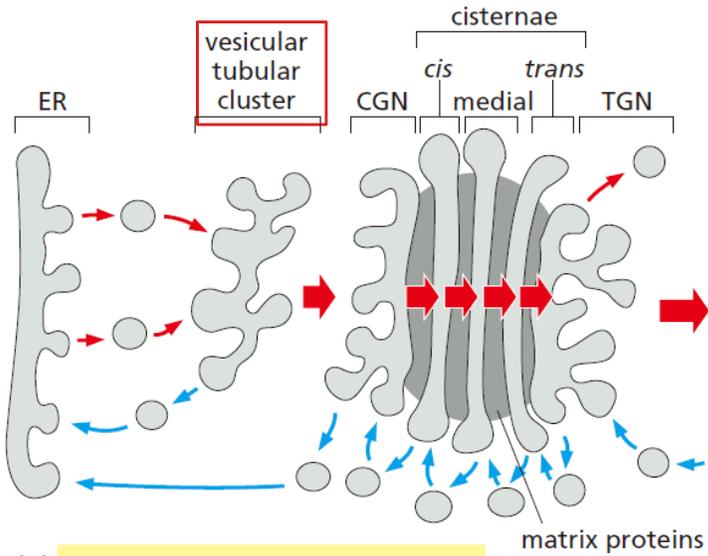


## O-LINKED GLYCOSYLATION : 이것도 끝내관찰 것만 기억



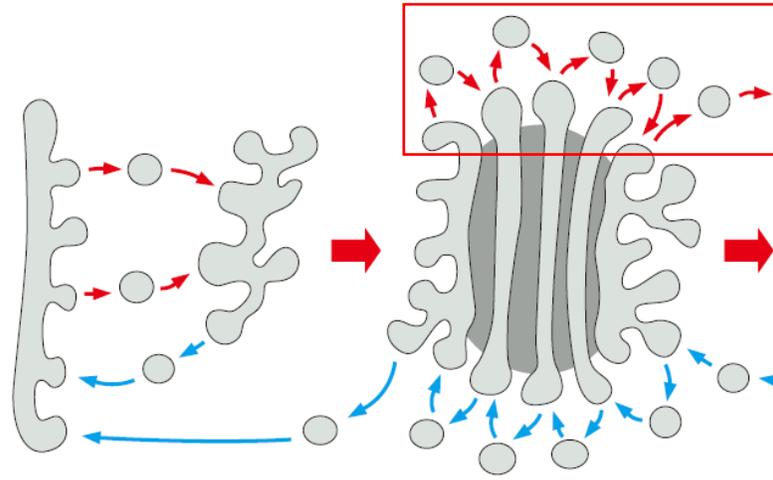


# Transport Through the Golgi Apparatus May Occur by Cisternal Maturation



(A) CISTERNAL MATURATION MODEL

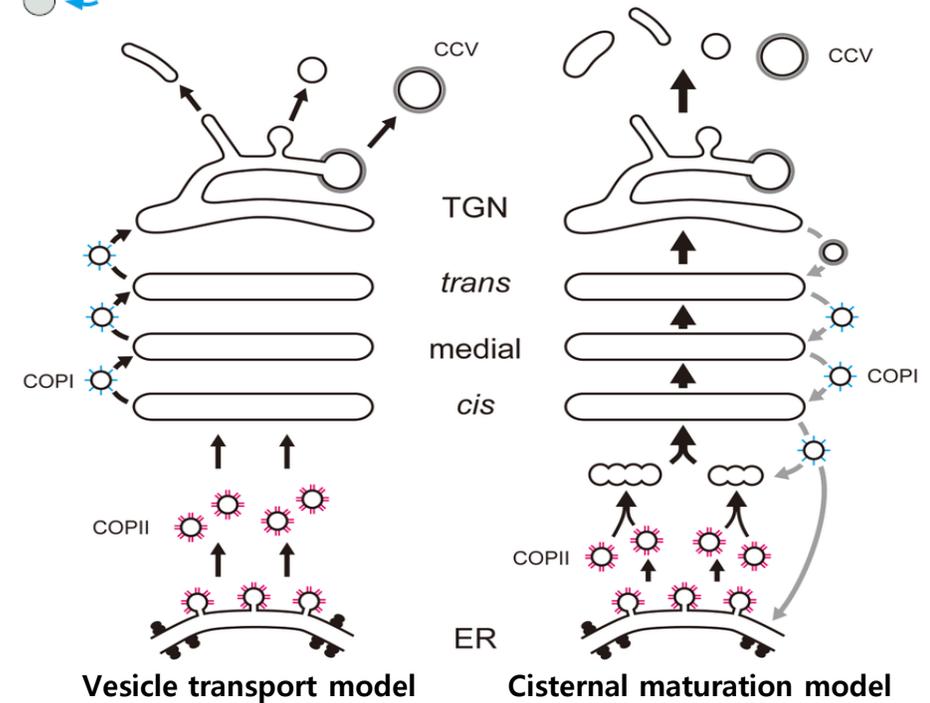
점점 오른쪽으로 maturation



(B) VESICLE TRANSPORT MODEL

6이위가 고정되어 있음

\* 많은 큰 단백질로 구성된 : Vesicle로 이동  $\Rightarrow$  (B)가 맞다면 이동 물품. 두 모델 다  
 : 근데 TGN에 이동이 있음  $\Rightarrow$  (A)가 어느정도 맞음. 확실히 있음.



Vesicle transport model

Cisternal maturation model

(a)

(b)

[10.1146/annurev.cellbio.24.110707.175421](https://www.differencebetween.com/difference-between-cisternal-maturation-and-vesicular-transport/)

**Thank you for attention**

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