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# Biology

## 4. Membrane organelles

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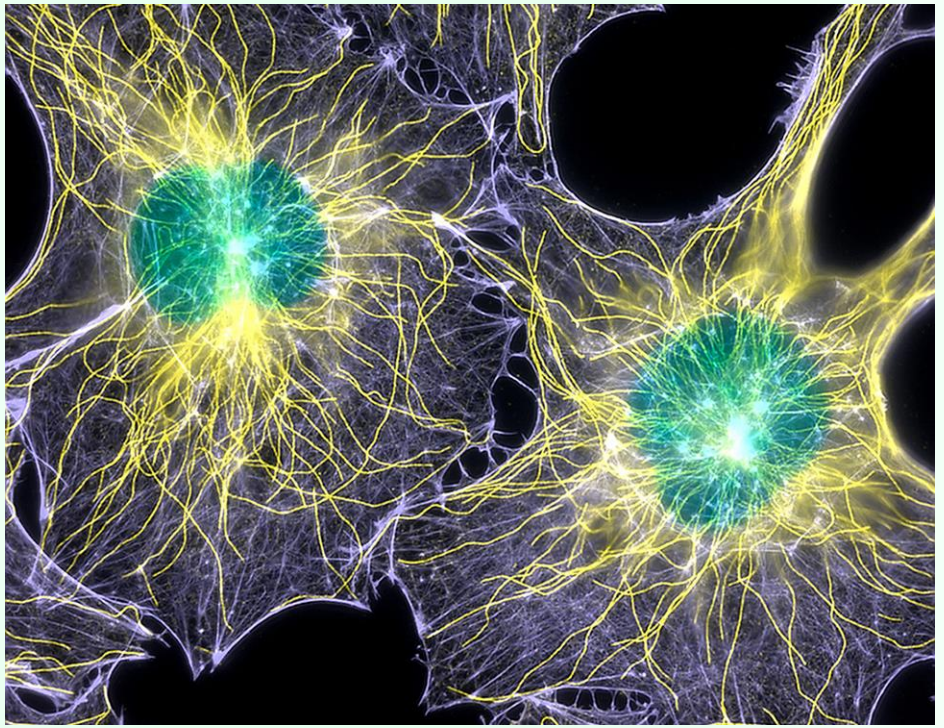
# Organisation of eukaryotic cell

- Each cell is complex hirearchicaly organised system
- Main building blocks are proteins, nucleic acids, polysaccharides, and lipids
- Cellular organelles are formed by spatial organisation of main building blocks
- Organelles themselves have multilevel organisation



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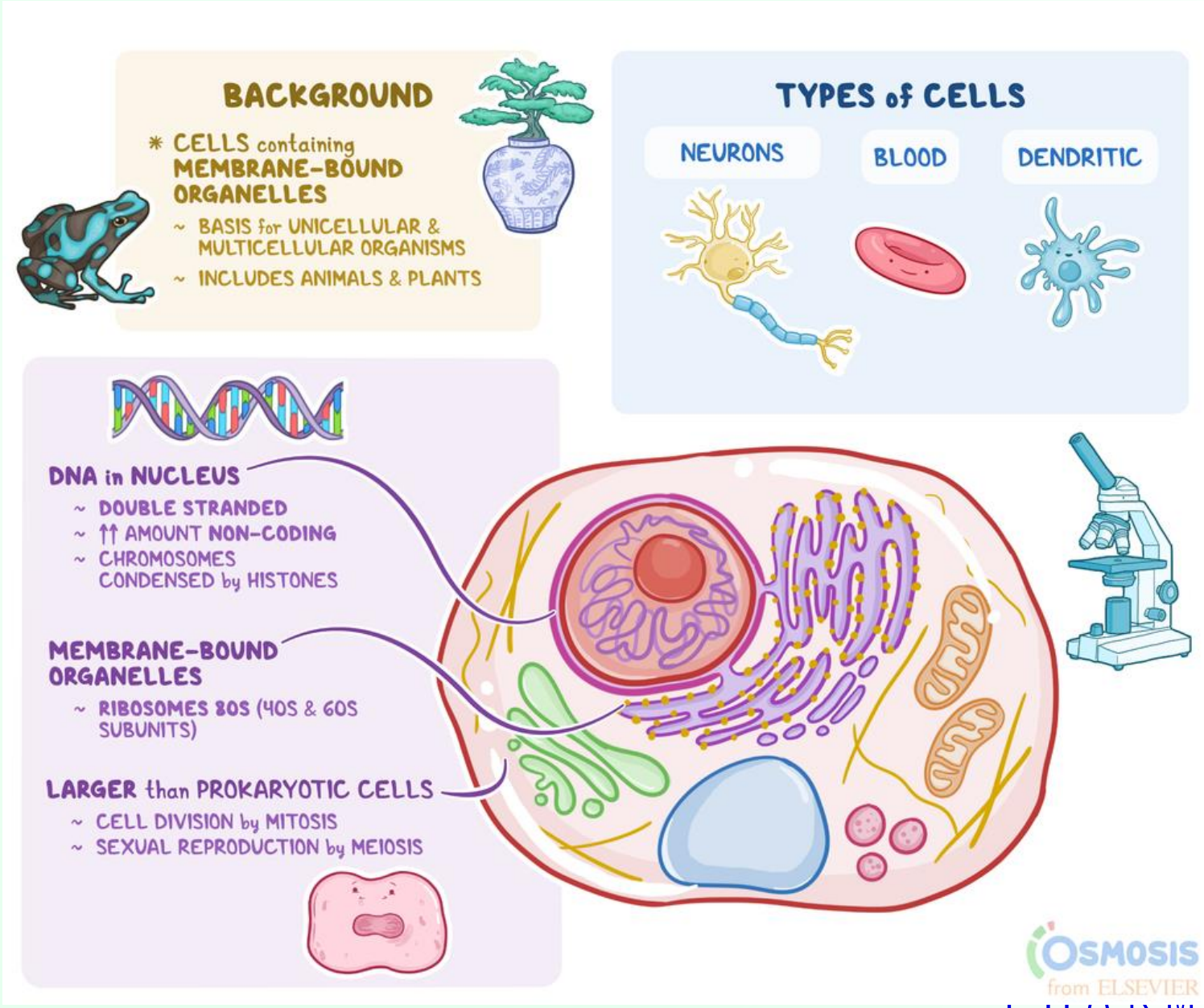
# Cellular structures

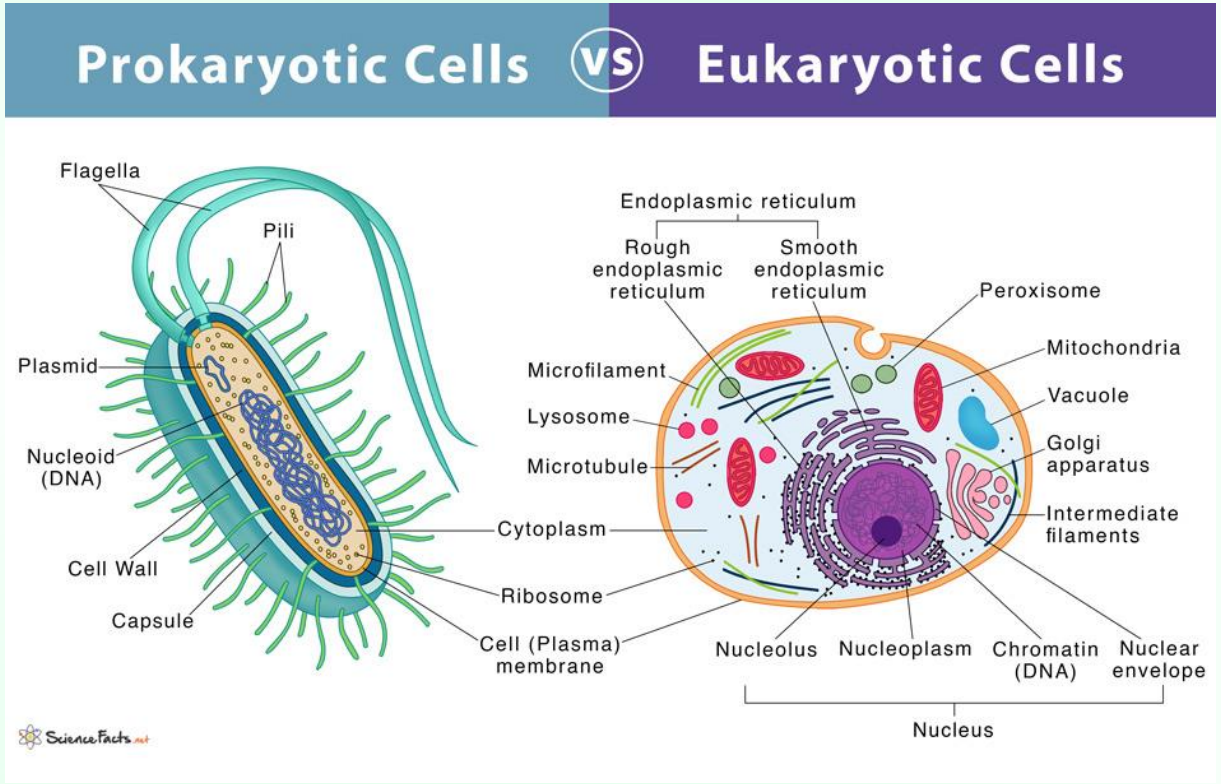
- Membrane structures
- Fibrilar structures
- Genophores
- Cytoplasm
- Ribosomes
- Cellular inclusions




https://www.osmosis.org/answers/eukaryotic-cell

# Differences between eukaryotics and prokaryotics – quick reminding

| | PROKYRYOTICS | EUKARYOTICS |
|---|---|---|
| **Cell organisation** | simple | complex |
| **Nucleus** | any nucleus (only nukleoid) | full-bodied nucleus |
| **Chromosome** | one circular | one or more linear |
| **Genes** | w/o introns | introns and exones |
| **Organelles** | Only non-membranes | membranes and non-membranes |




https://www.sciencefacts.net/prokaryotes-vs-eukaryotes.html

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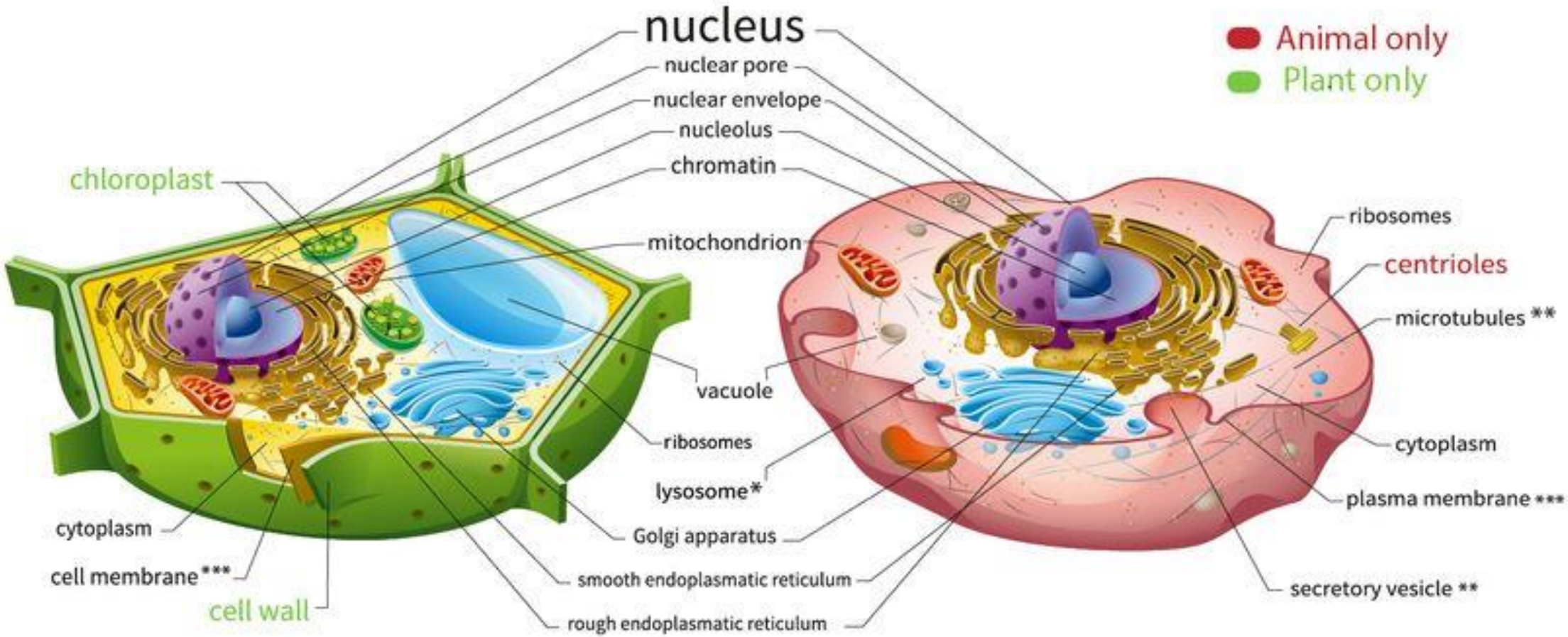
# Plant cell

# Animal cell




* Plants may have lytic vacuoles, which act like lysosomes in animal cells.

** Although they're not labelled here, plant cells have microtubules and secretory vesicles, too.

*** Cell membrane and plasma membrane are just different names for the same structure.

https://science.howstuffworks.com/life/cellular-microscopic/plant-cells-animal-cells.htm



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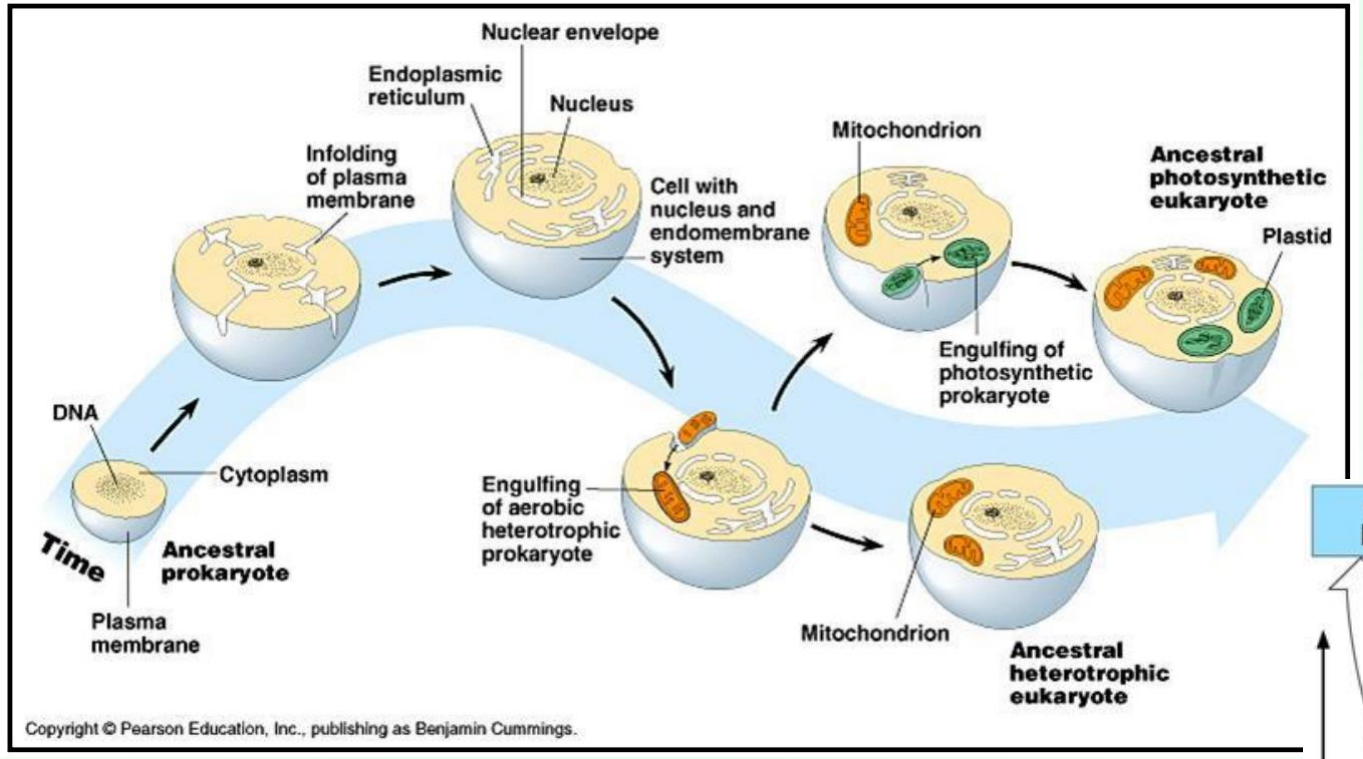
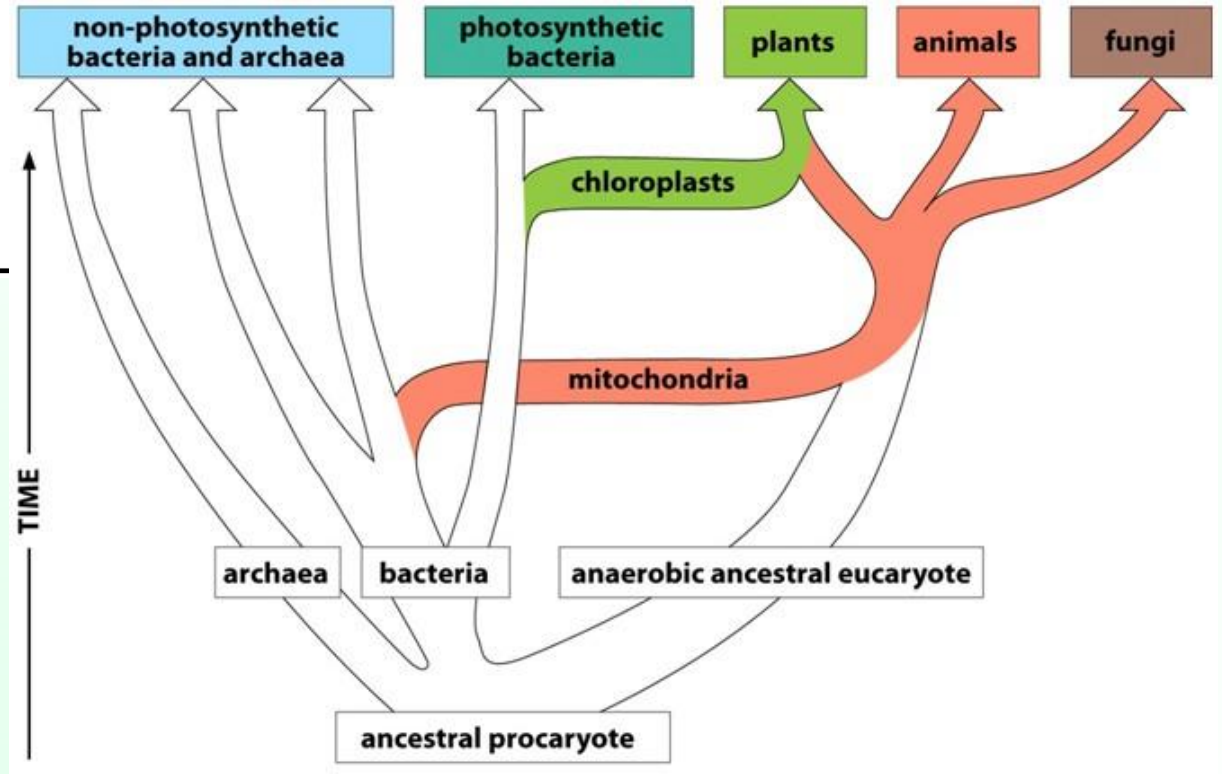
# Compartmentation – theory of endosymbiosis

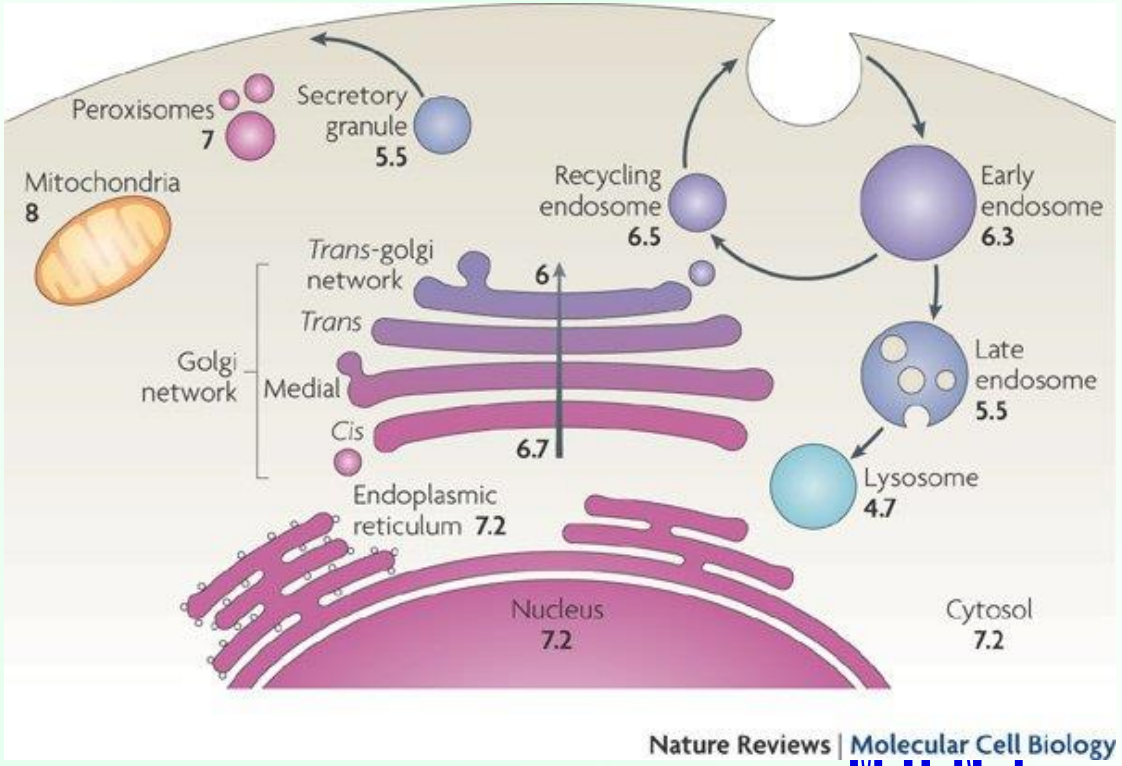



https://slideplayer.com/slide/10110785/

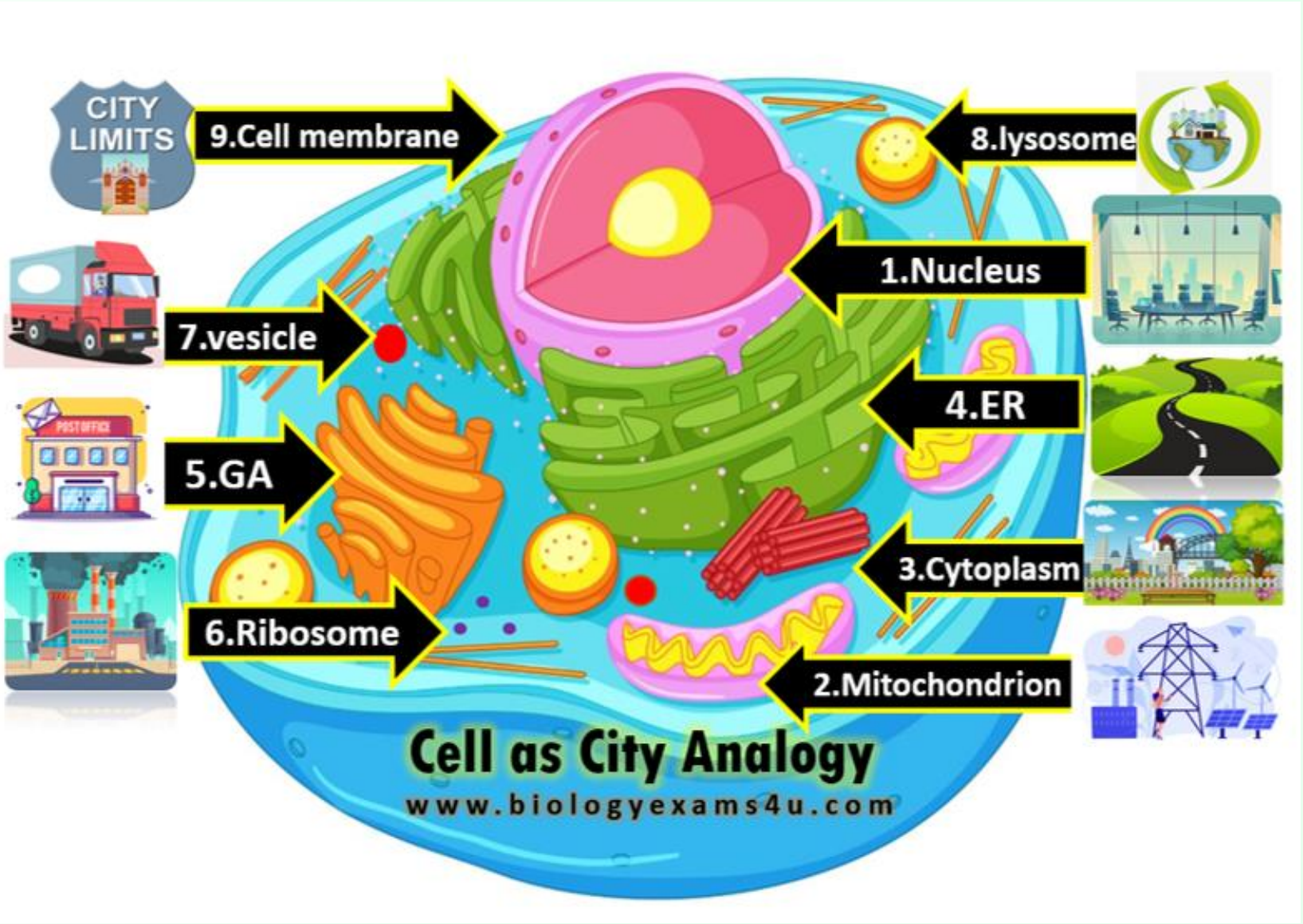
# Why do cells need organelles?

- Organelles maintain different concentrations of substances in different parts of the cell. Most important is the maintenance of ion concentration gradients on opposite sides of the membrane. At the right moment, the cell can then initiate influx or transport.
- It is advantageous to maintain each biochemical process in a specific environment and at certain concentrations. It would be possible without them, energy and metabolic transformations would not be as efficient or would be slow or some could not take place biochemically at all. The waste products would also unnecessarily interact with DNA and other useful molecules inside the cell.




pH in cell

# Cell as a city or a fabric




https://www.biologyexams4u.com/2022/12/cell-city-analogy-learn-cell-parts.html

https://prezi.com/hqun2aj4kqa5/cell-analogy-a-factory/



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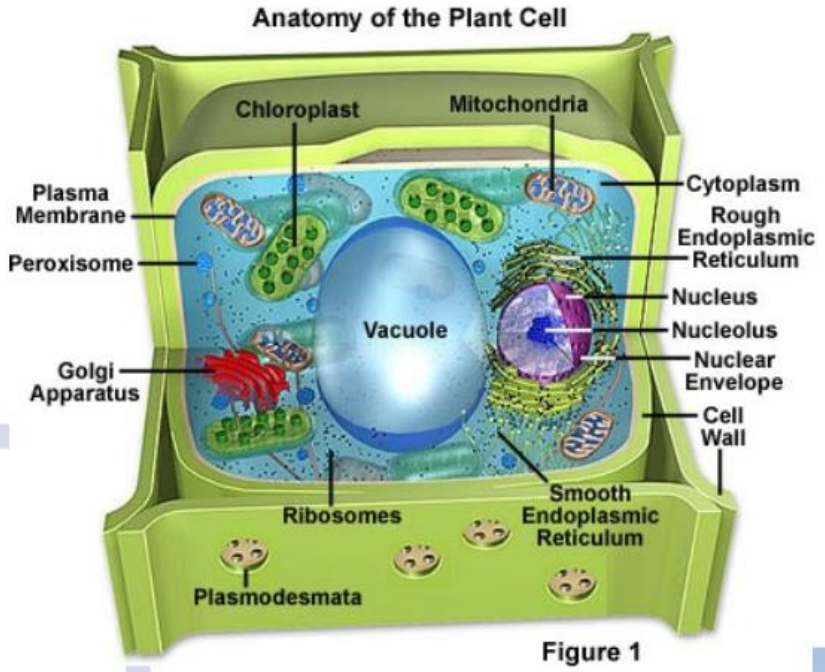


Figure 1



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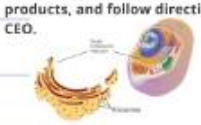
# Plant Cell Analogy: A Factory

By: Rachel Canzoneri, Megan McGee, and Angie Florimbio


### Ribosomes
**Factory Workers**

Ribosomes are one of the smallest organelles in the cell. They make proteins, and are located on the endoplasmic reticulum (ER). These ribosomes are similar to the factory workers, since they both create products, and follow directions from the nucleus/ CEO.

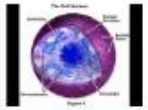


### Mitochondria
**Local Power Plant**

In a cell, "mighty mitochondria" produces energy-rich molecules. Like the local power plant that provides power to most parts of the factory, mitochondria powers and produces energy in a cell.

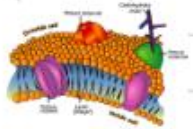
### Nucleus
**The CEO**

The nucleus is the part of the cell that controls and directs all of the activity. Like the CEO of the factory, who makes all the major decisions and is responsible for most activity, the nucleus and CEO are clearly similar.



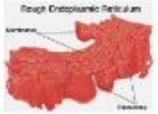
### Cell Membrane
**Doors of the Factory**

The cell membrane is similar to the doors of the factory. In a cell, the cell membrane is part of the outer lining, and it controls what comes in and out, like the doors of the factory allow people to enter and leave.



### Rough Endoplasmic Reticulum (Rough ER)
**Assembly Line**

The rough ER is where the ribosomes are located. So, it's where proteins, and other molecules, are made. Therefore, the rough ER is like the factory's assembly line, because it's where the ribosomes make the proteins, or where the workers make the products.



### Golgi Bodies
**Shipping Department**

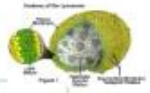
The golgi body is located near the cell membrane. It's responsible for grouping vesicles, finalizing them, and shipping them elsewhere. A shipping department is like the golgi body because it takes the final product and ships to where they need to go. Therefore, the golgi body is like our shipping department.

### Cytoplasm:
**Floors of the Factory**

Cytoplasm is the jelly-like fluid that takes up most of the space in the cell, besides the organelles. Like the floors of the factory, it's where everything happens and it takes up quite a lot of space.

### Lysosomes
**Maintanence Crew**

In a cell, lysosome are responsible for breaking waste down, and handle the movement of trash and waste. Therefore, lysosomes are like the maintenance crew or janitors, because both handle waste and general trash.



### Vacuole
**Storage Area**

The large, central vacuole is one of the cell's biggest organelles. It stores water and nutrients. This is very similar to the way the factory's storage closet stores tools, machines, and other supplies.

### Cell Wall
**Structure/Walls of the Factory**

The cell wall is the outermost lining of the cell. Found only in plant cells, it protects the cell and maintains it's shape. Like the cell wall, the walls of the factory protect the factory workers, protection, and maintain the building structure.

### Chloroplast
**Solar-powered Rooftop**

Since plants don't eat food, they use chloroplast to transform energy they absorb from the sun for the cell to use in a process called photosynthesis. Since solar power panels absorb light from the sun and transform the energy to power the factory, chloroplast and the solar-powered rooftop of the factory are very analogus to each other.



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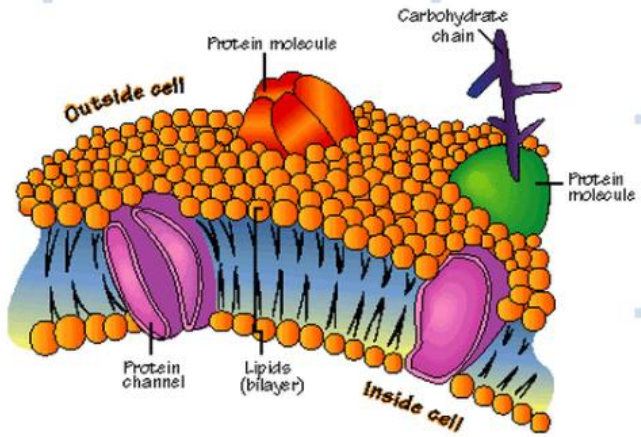


# *Cytoplasm:*
# *Floors of the Factory*

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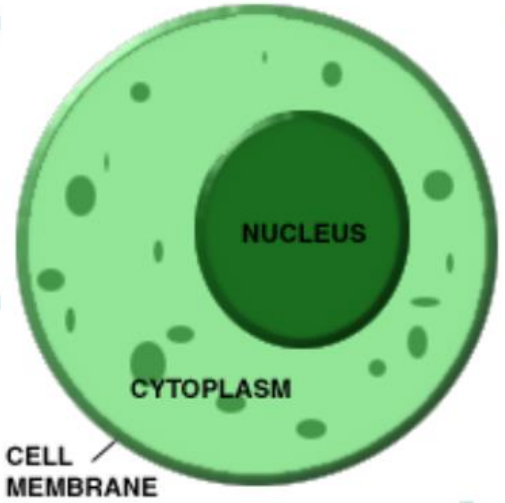


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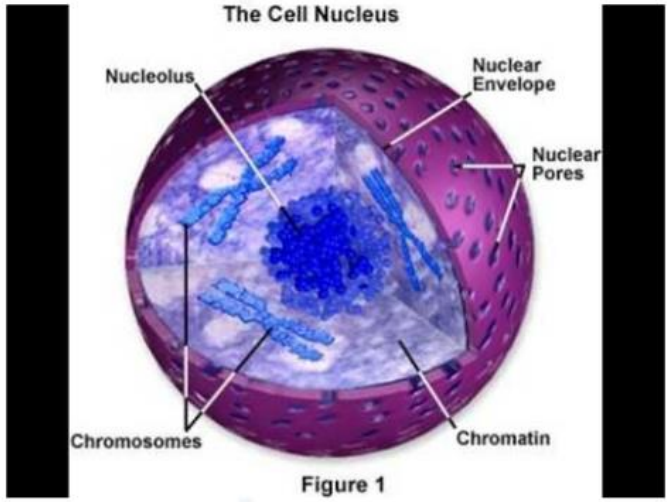

Figure 1

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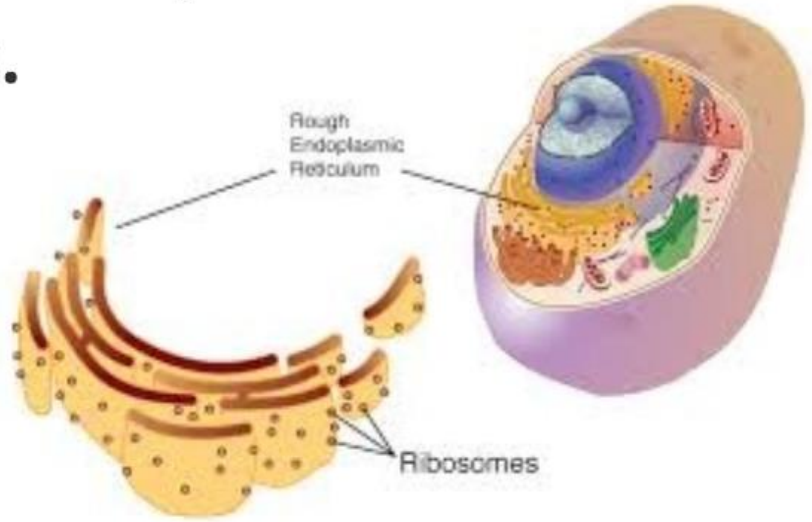


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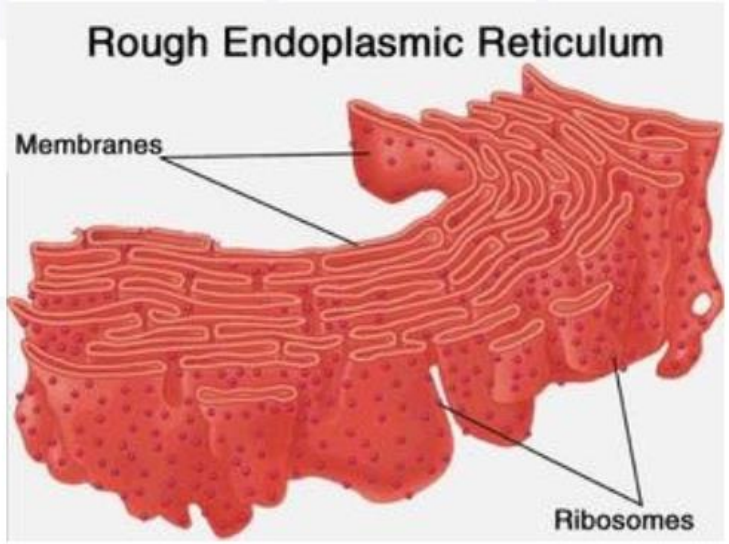


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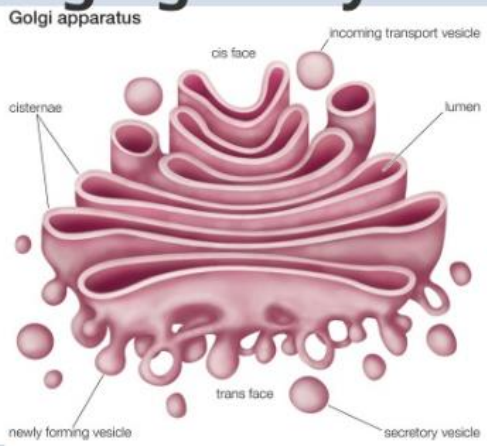




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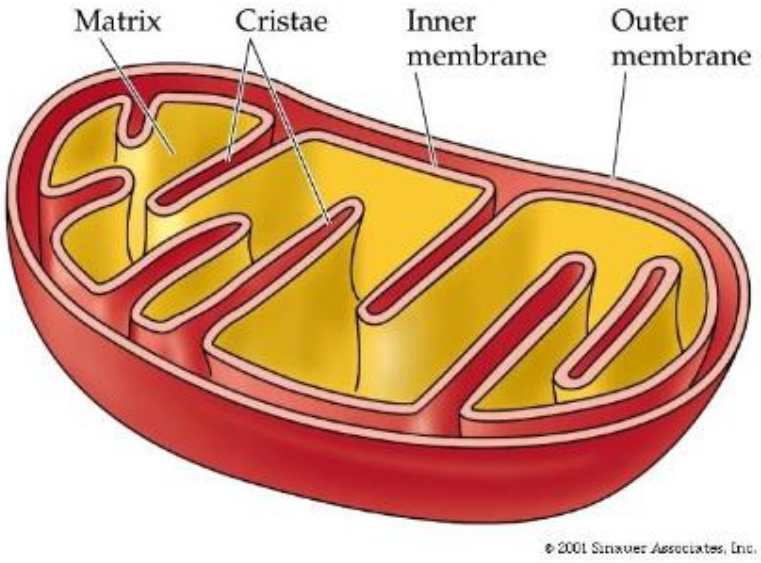




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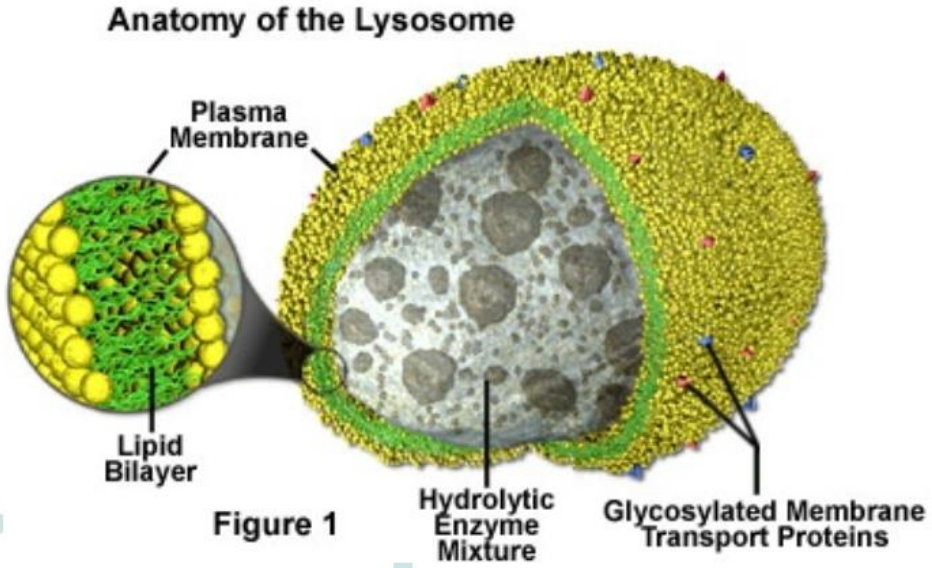


Figure 1



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# Vacuole

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Plant Cell Central Vacuole

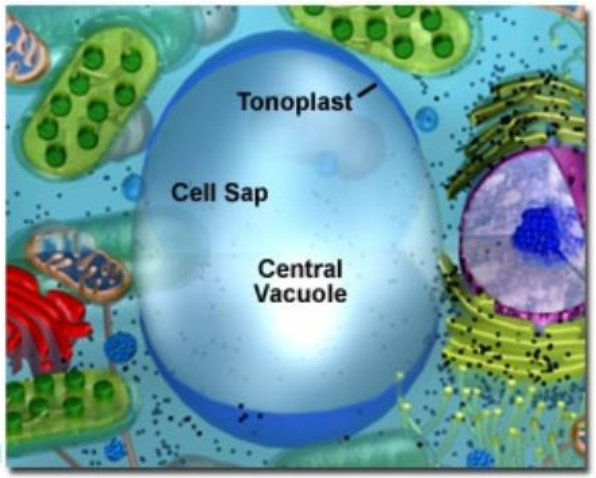


Figure 1



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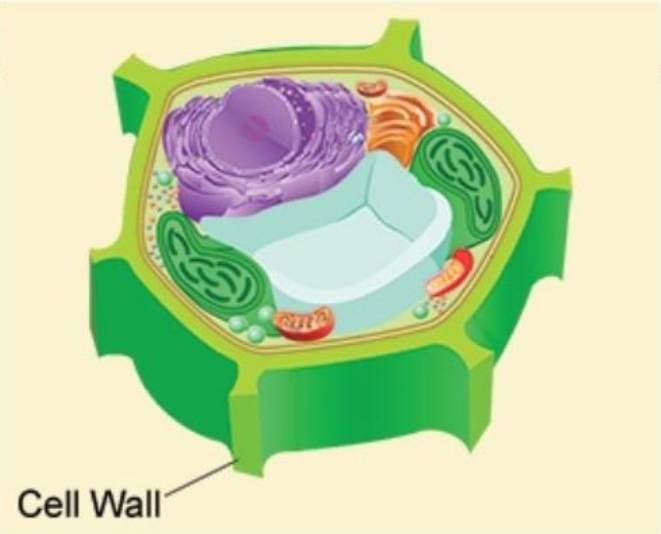





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# Chloroplast

# Solar-powered Rooftop

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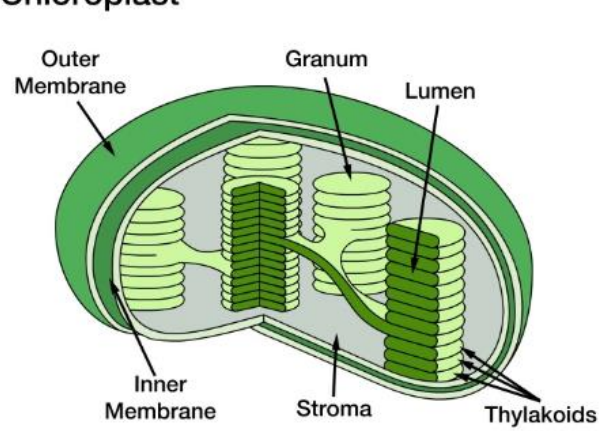




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# Homeostasis Scenario

## Cell

Problem: The vacuole is too full of water and nutrients.

Solution: The vacuole stops taking in water and the other organelles take the water when -needed. Once the vacuole isn't at maximum capacity, the cell can start absorbing water again.

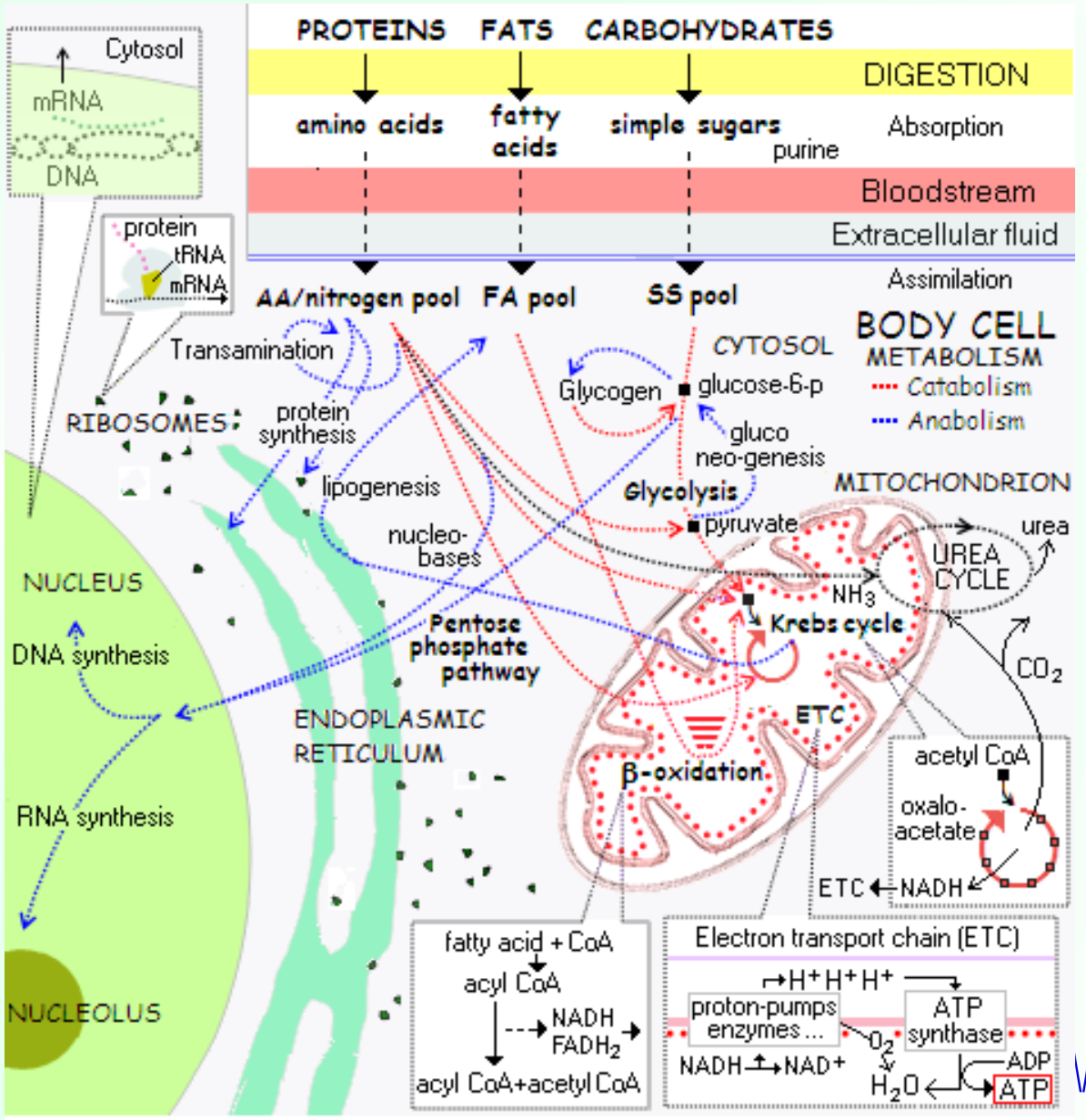
## Factory

Problem: The storage area is overflowing with tools and other supplies.

Solution: Production is put on hold until most of the supplies are shipped out or used. Production can then be resumed because there is space in the storage area.

# Metabolic net of organelles

- Each organelle has its role
- An intensive exchange of substances and energy takes place between the organelles

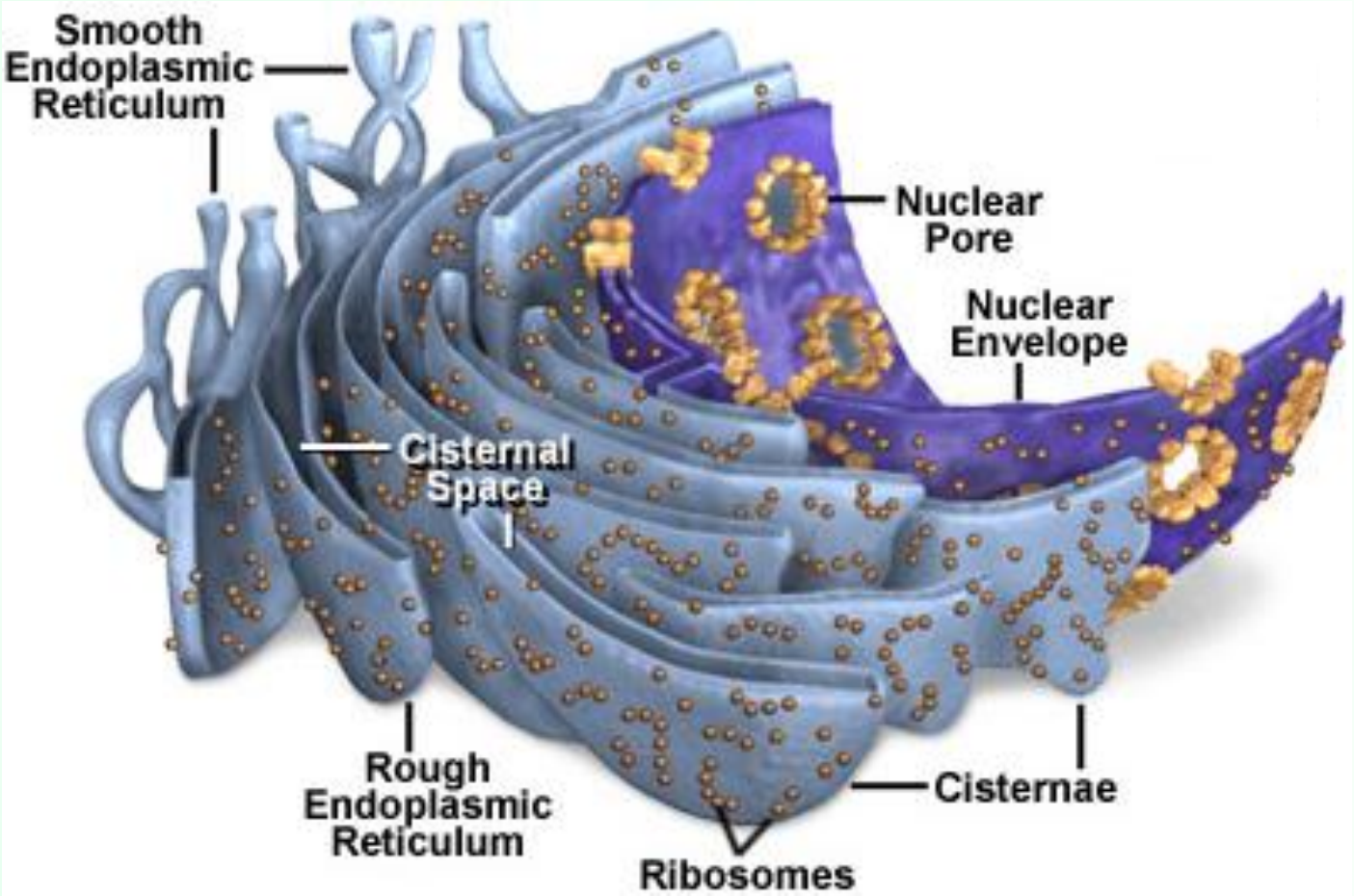



https://www.healthknot.com/cellular_metabolism.html

# Endoplasmic reticulum (ER)

- Assambly line of cells
- Multiple curved membrane sheet, which forms closed sac - **endoplasmic lumen (cisternal space)**
- Connected with nucleoplasm
- Membrane of ER represent more than 50 % of total cell membranes
- ER lumen occupates up to 10% of cell volume

https://micro.magnet.fsu.edu/cells/endoplasmicreticulum/endoplasmicreticulum.html



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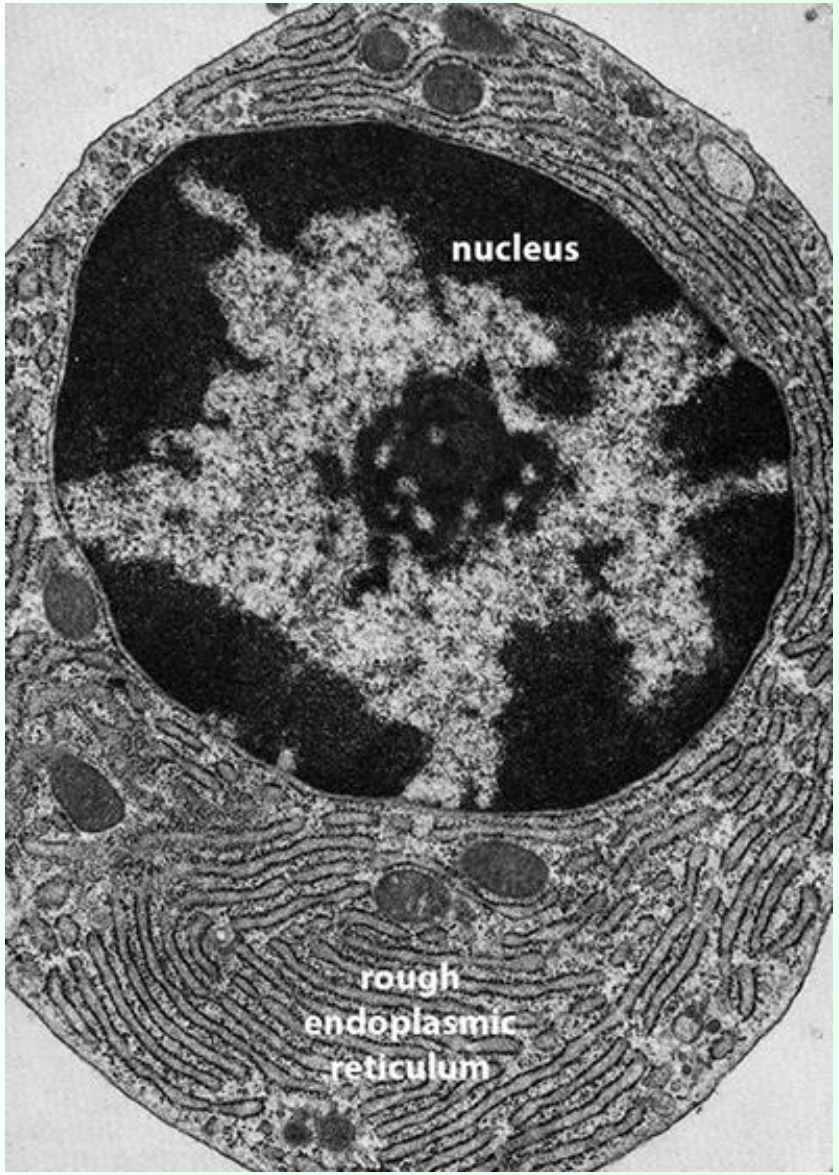
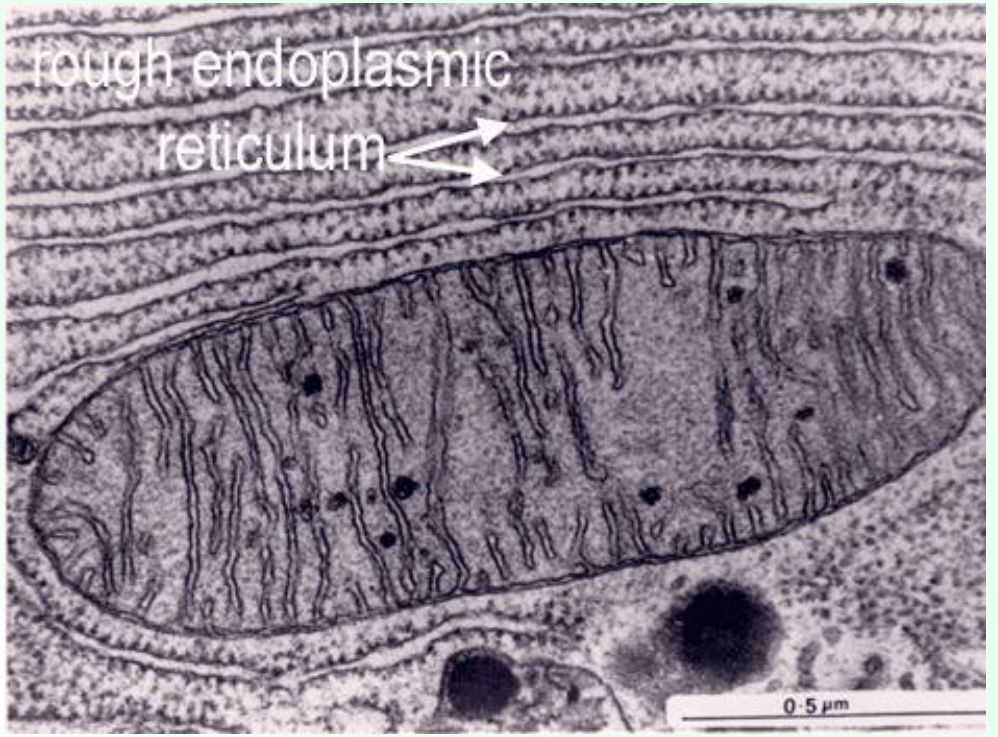
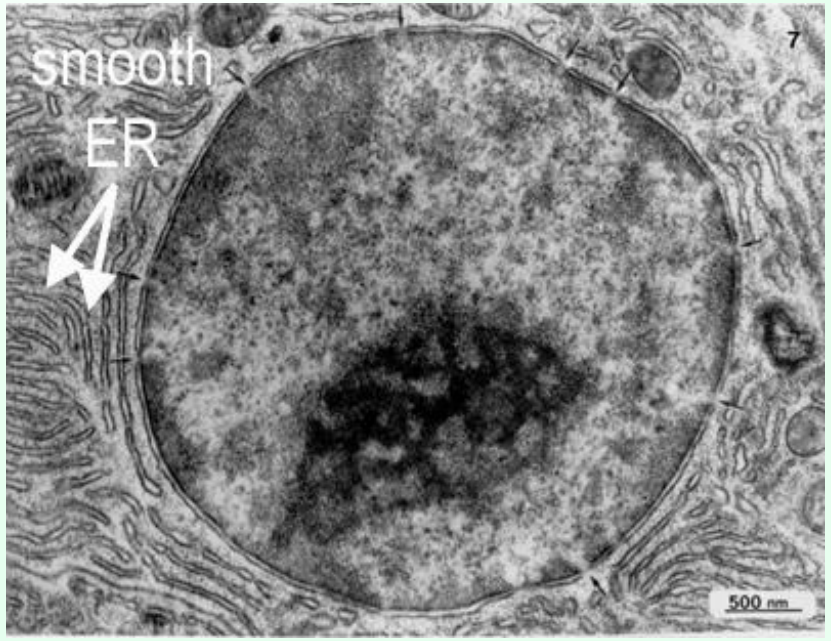



https://www.ncbi.nlm.nih.gov/books/NBK563126/figure/article-28660.image.f1/




https://www.histology.leeds.ac.uk/cell/cell_organelles.php



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# ER functions

- **central role in the synthesis of lipids, proteins, steroids**
- **biosynthesis and metabolism of own substances and xenobiotics**
- it facilitates the formation of the correct tertiary or quaternary structure of proteins
- transport system – distribution of proteins to the cytoplasm or organelles
- maintaining of osmotic pressure
- **storage and deposition of $Ca^{2+}$ ions**
- **chemical modification of proteins**
  - disulfide bridges are formed by oxidation of cysteine pairs of side chains
- formation of glycoproteins by covalent attachment of a short oligosaccharide side chain – **is finished in GA**
- the oligosaccharide precursor is linked by an O- or N-bonds to a protein molecule
- protein output is controlled = misfolded protein is retained by **chaperone** or degraded

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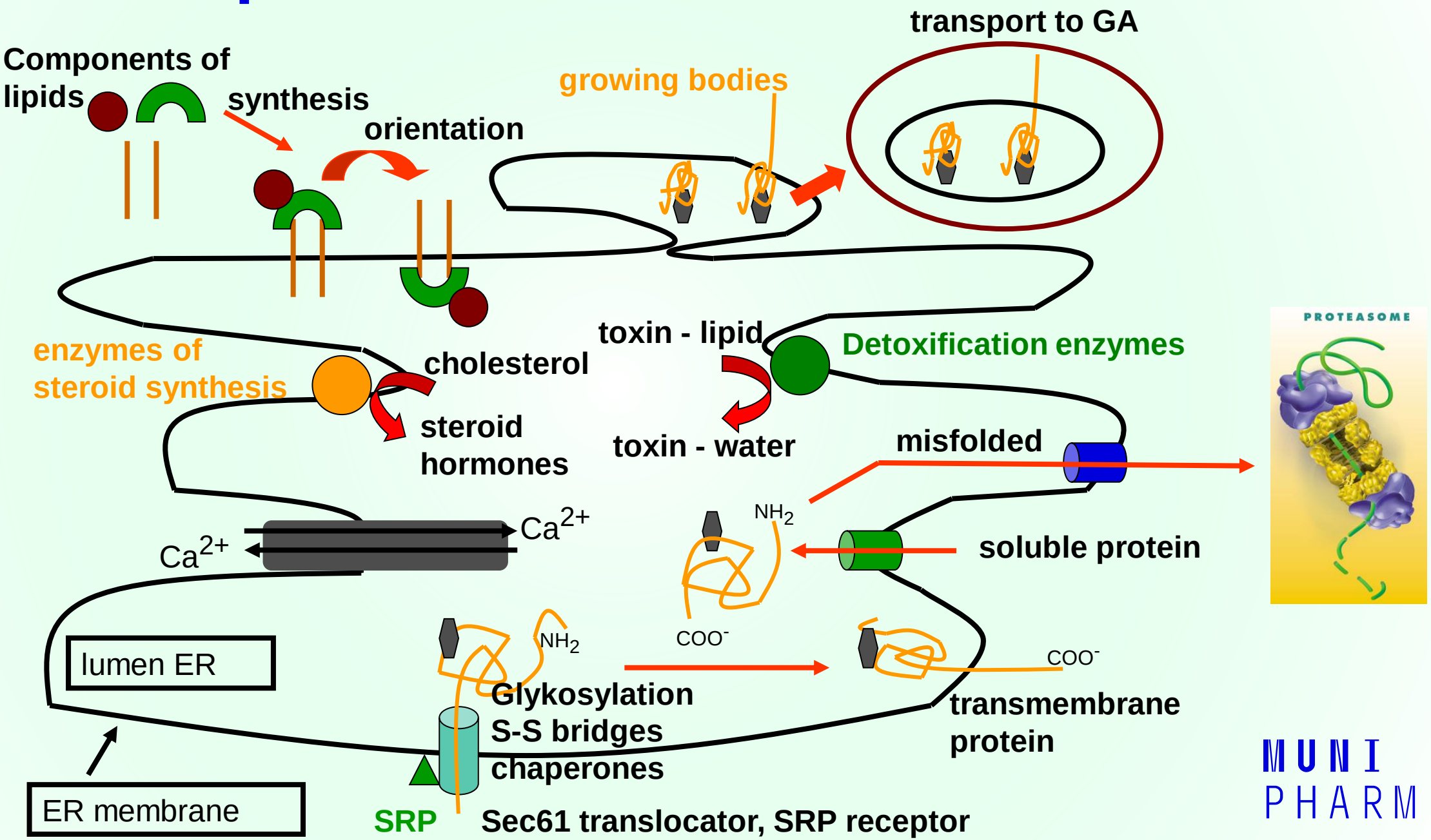
# Schematic representation of ER functions



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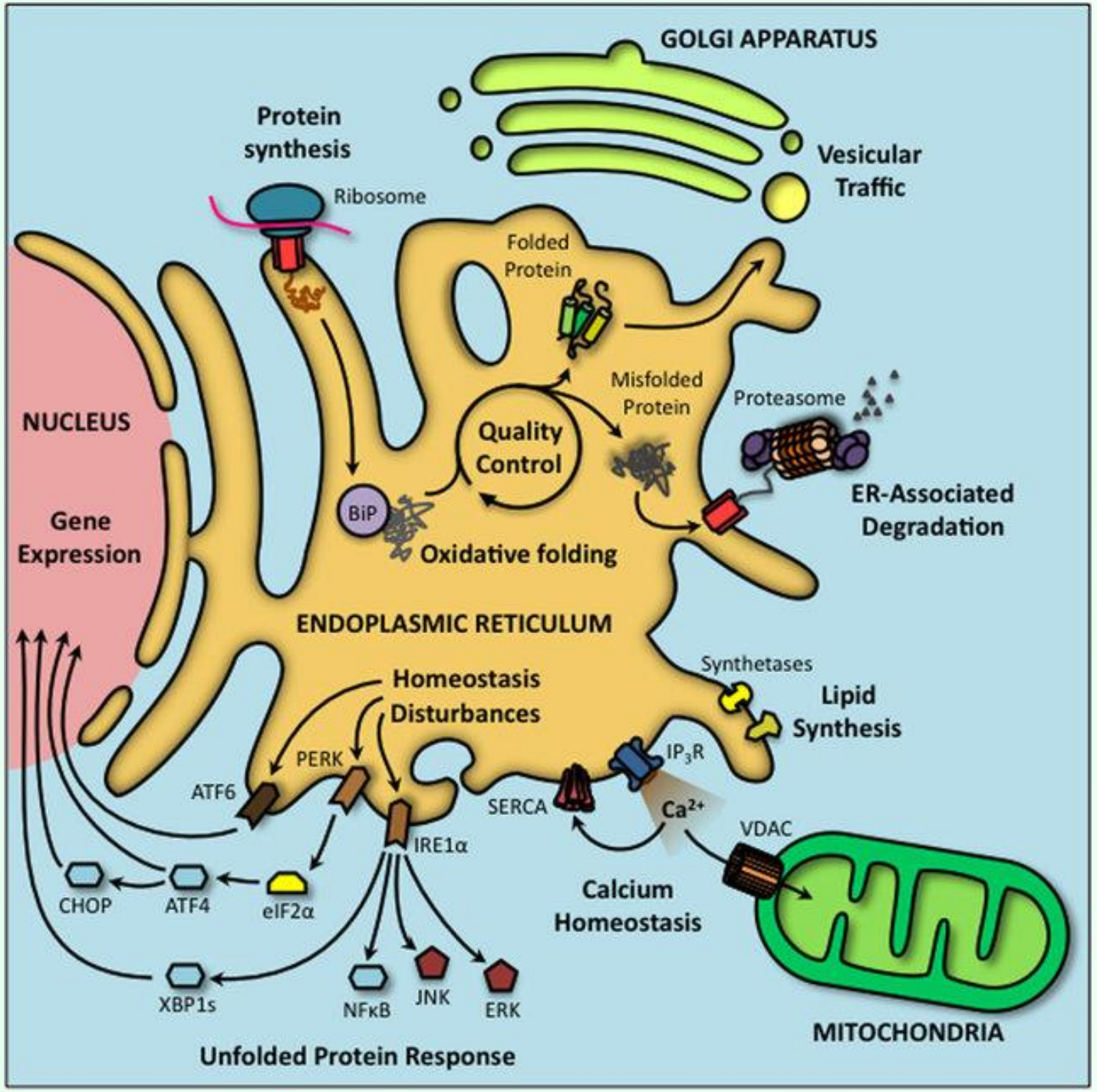




DOI: 10.1016/j.biocel.2011.10.012

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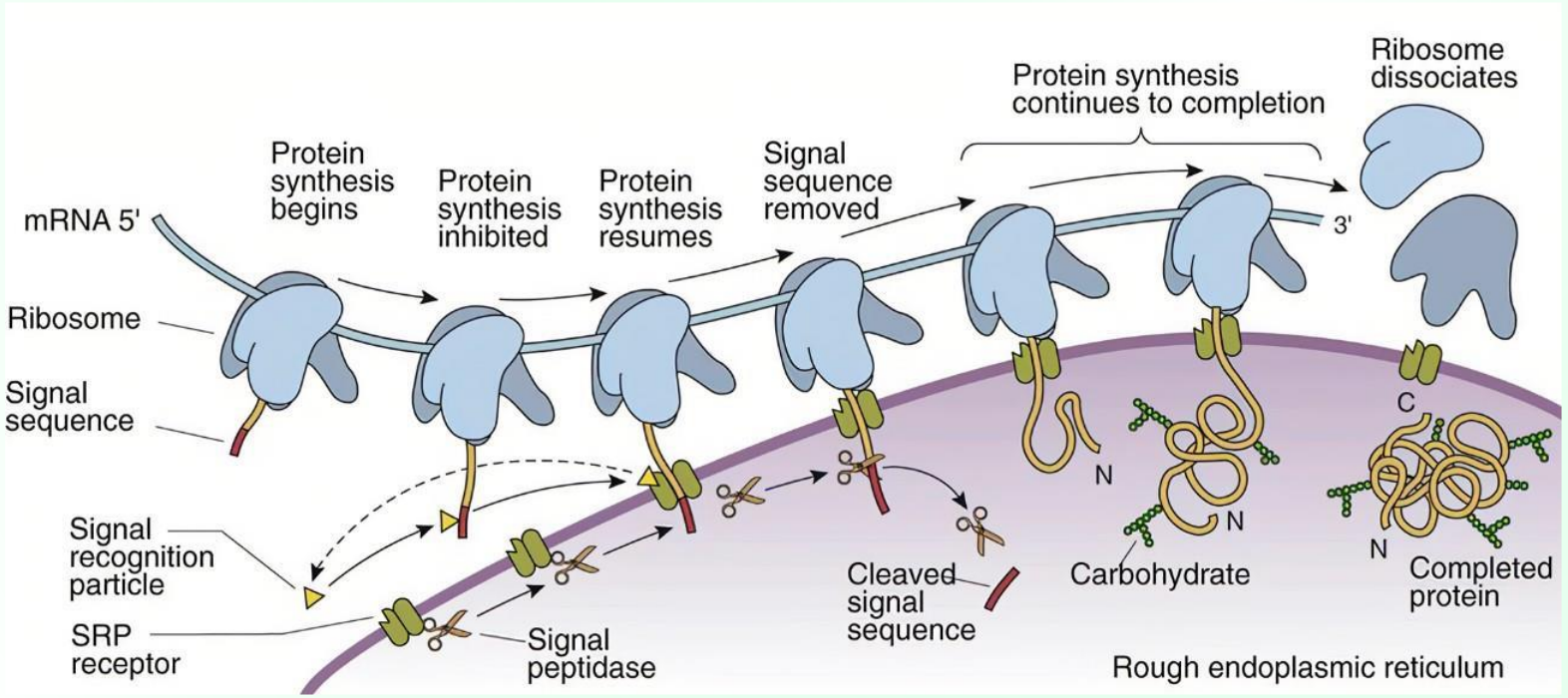
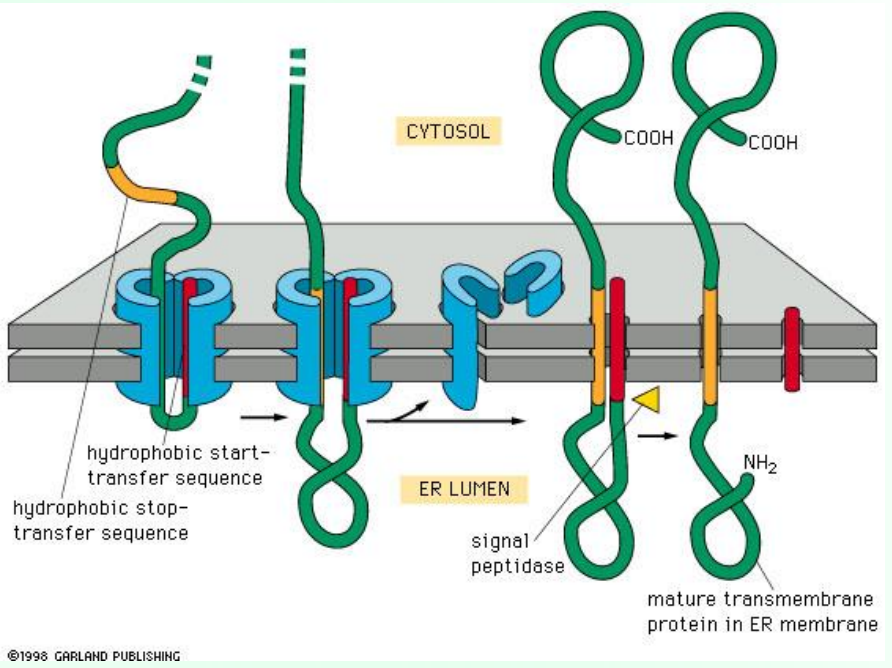
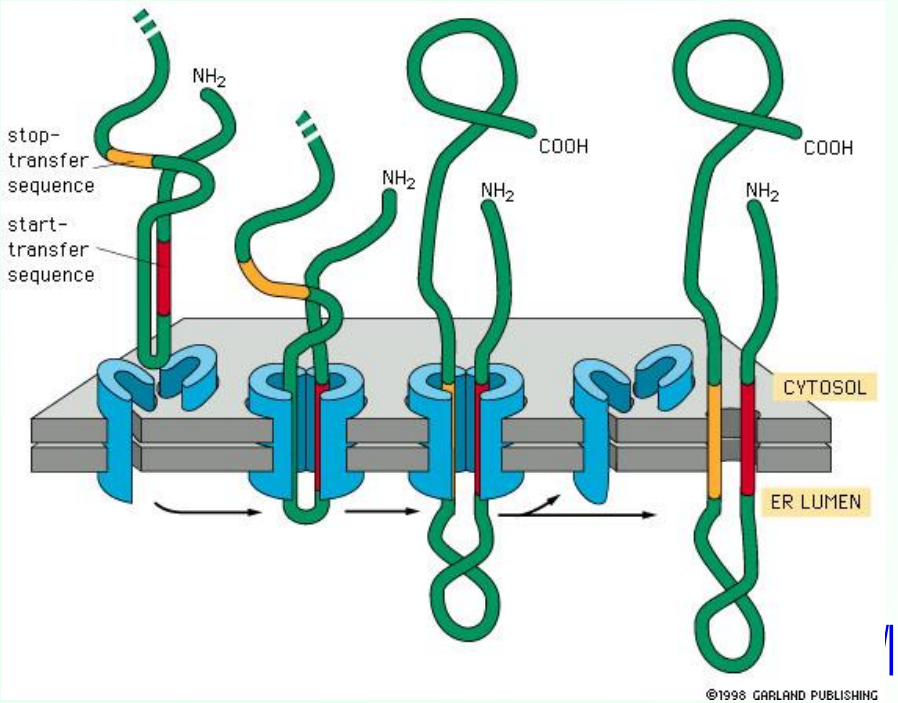
https://www.zoology.ubc.ca/~berger/B200sample/unit_8_protein_processing/er_targeting/lect27.htm

# ER – protein synthesis

- Extracellular proteins and membrane-bound proteins are formed in ER
- Proteosynthesis starts in cytoplasm
- Proteins are formed by ribosomes on **rough ER**
- Post-translation modifications in ER – **formation of disulfidic bridges** and **starting of glycosylationní** (continuing in GA)

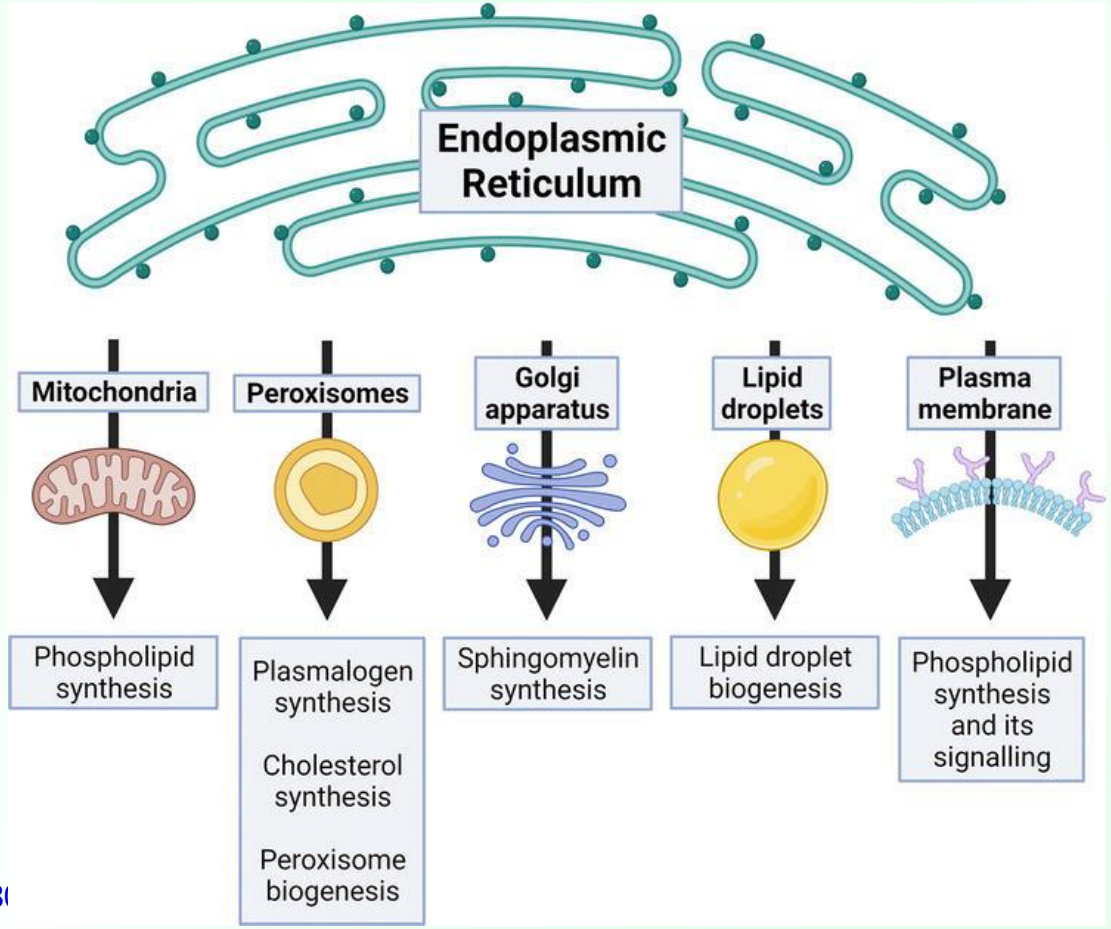


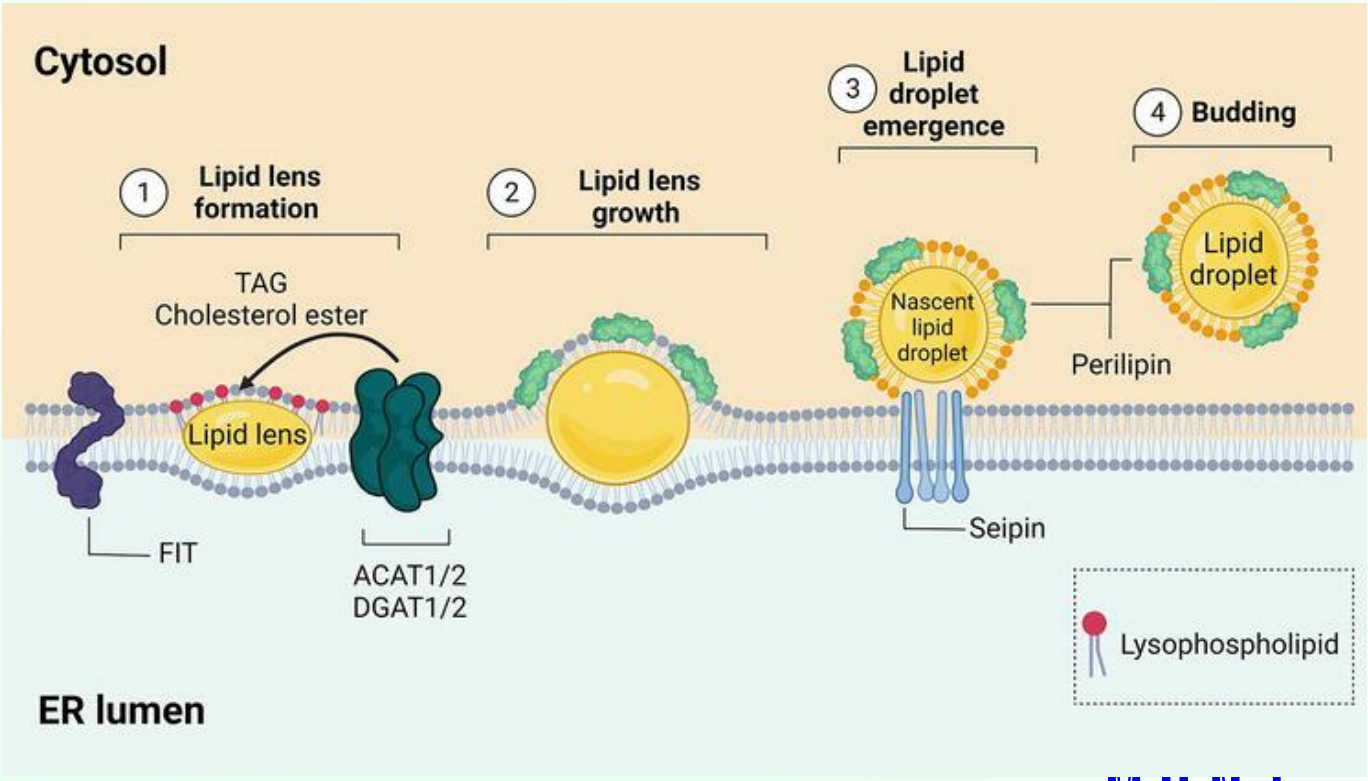



# ER – lipid synthesis

- Lipids are formed in smooth ER in cooperation with other organelles
- In the ER, storage lipid droplets are also created by a special process by dislodging and throttling a segment of the ER membrane into the cytoplasm




https://www.intechopen.com/online-first/82195



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# ER – detoxification of metabolites and xenobiotics

- Mainly in smooth ER of hepatocytes
- (Probably) the most important is **group of P450 cytochromes**
  - P450 oxidoreductases are very important enzymes for pharmacology
  - we know several subtypes - subtypes 3A4 and 2C9 metabolize most of drugs and a number of toxins and xenobiotics (e.g. into more polar molecules for easier elimination from the body)
- P450 is also involved in the metabolism and synthesis of a number of important substances, e.g. **vitamins, cholesterol, bile acids, steroid hormones,...**

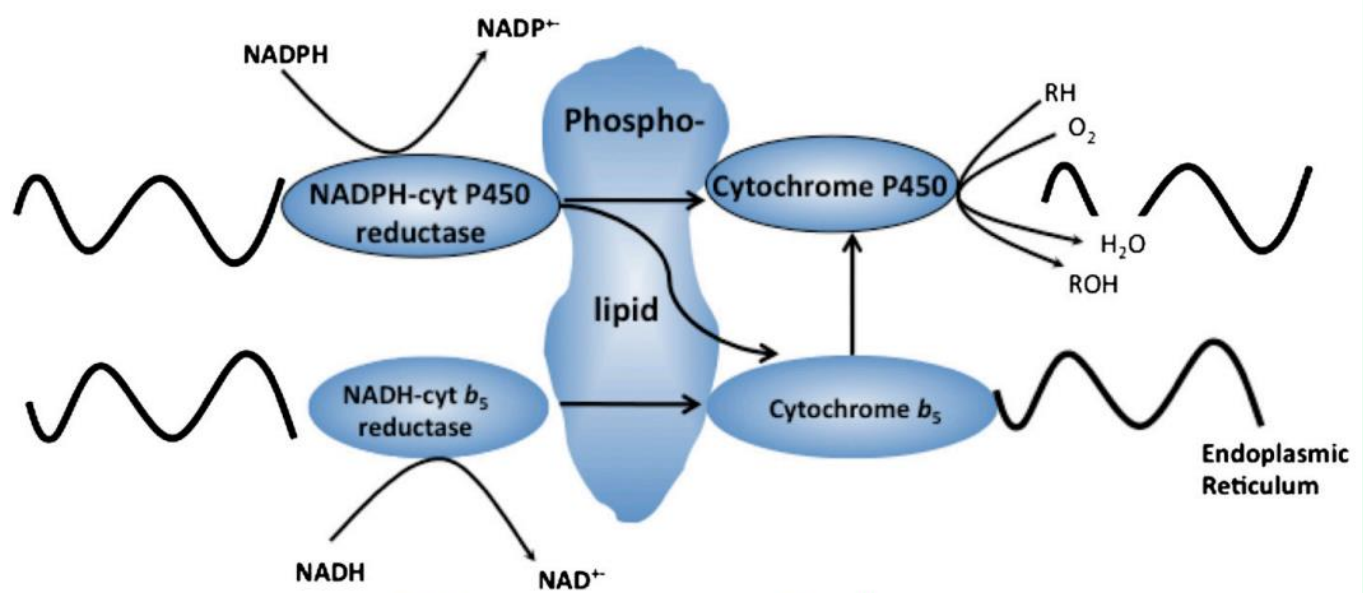
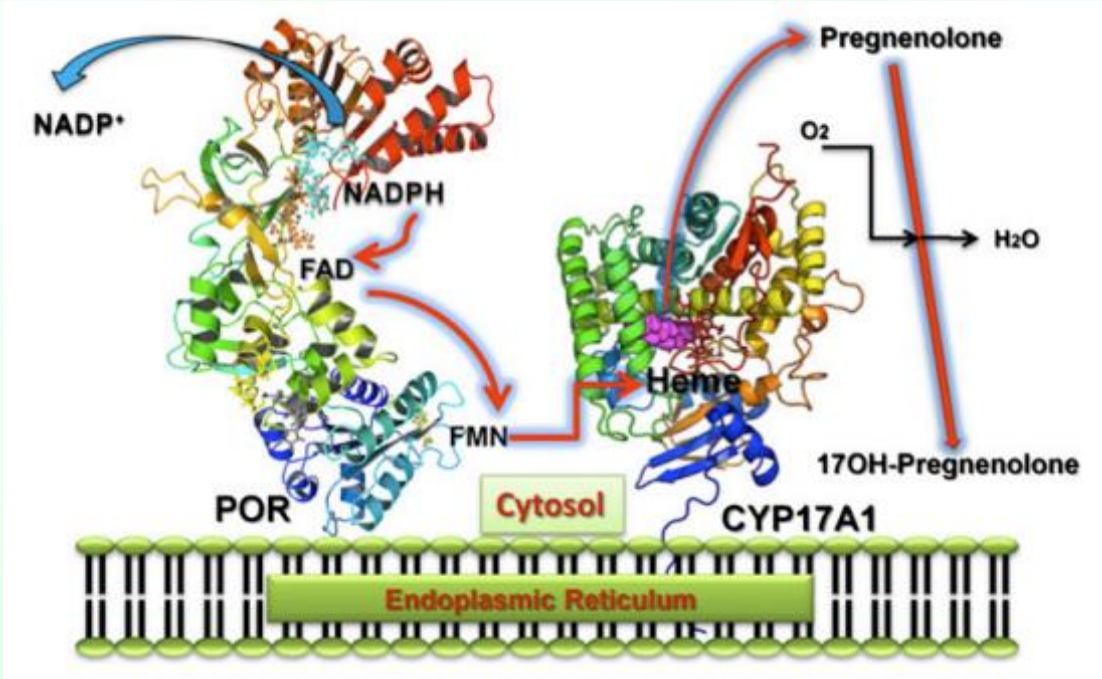



Fig. 3. Electron-transport pathways in the cytochrome P450 system.

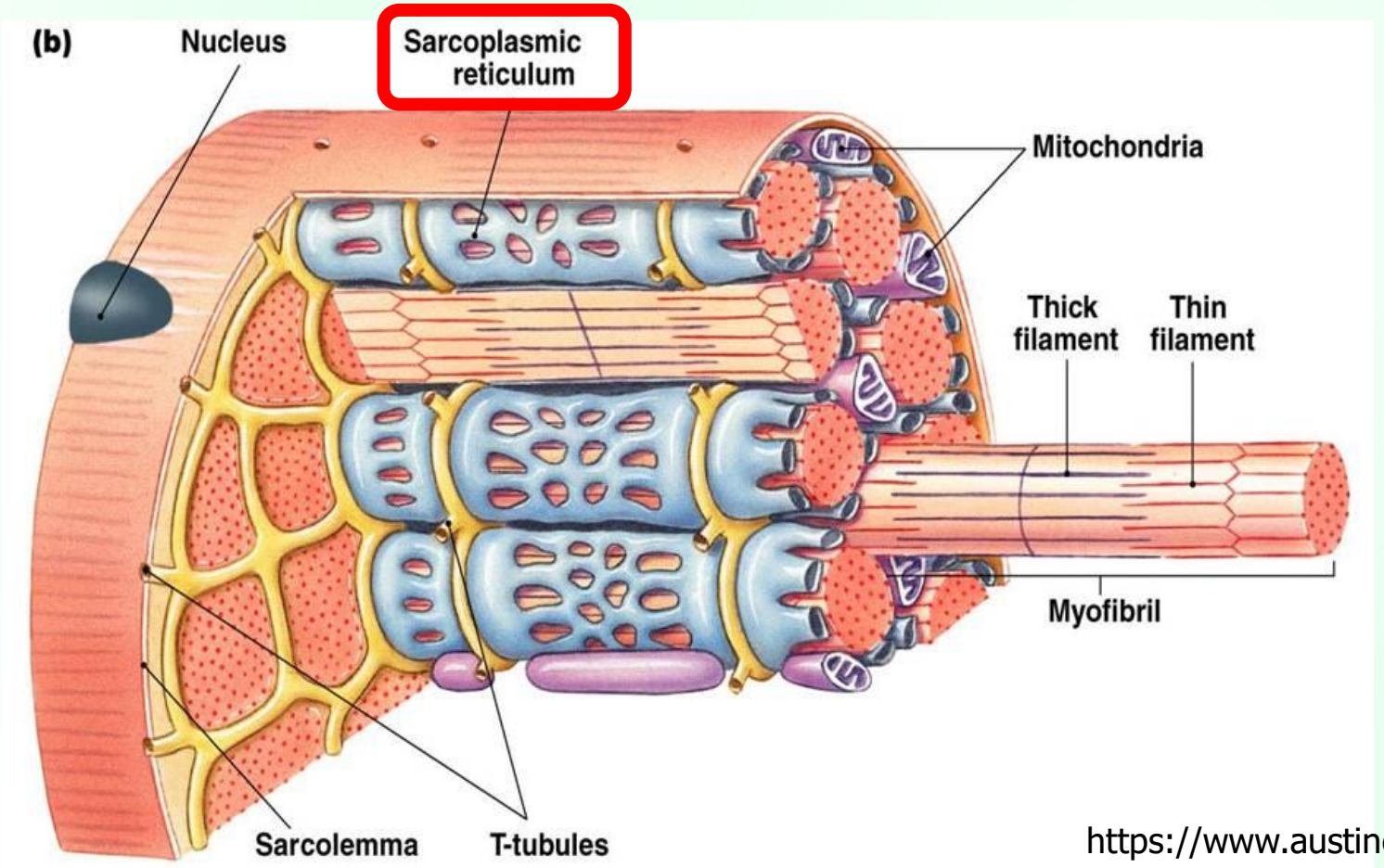


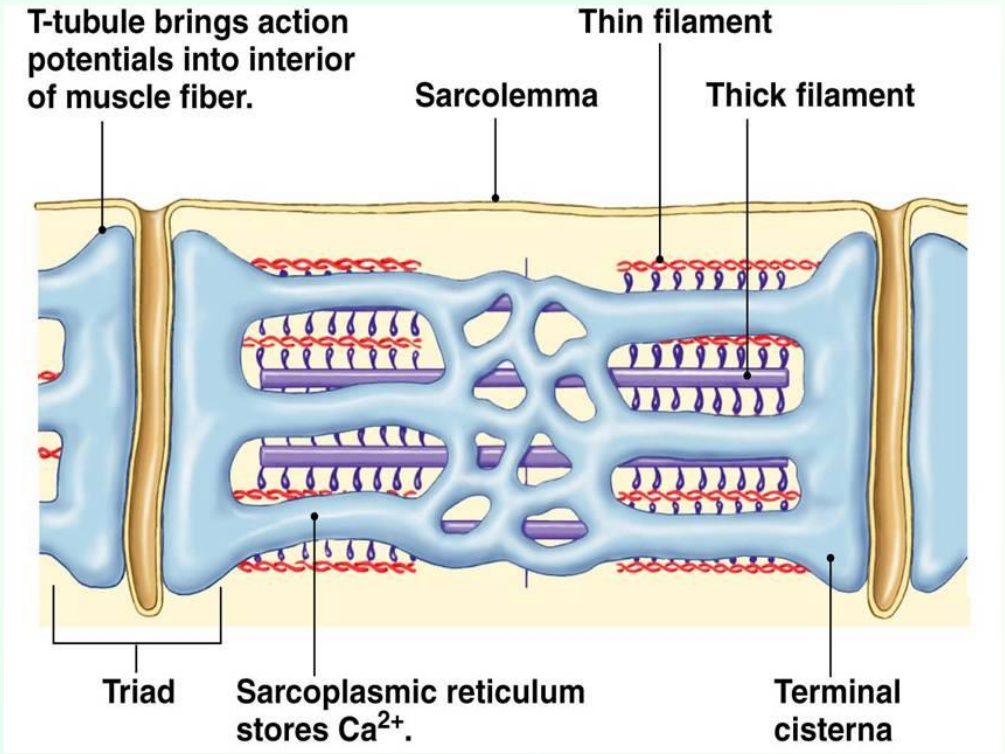



https://doi.org/10.1124/dmd.112.048991

# ER → Sarcoplasmic reticulum (SR)

- Sarcoplasmic reticulum = ER in muscle cells
- SR releases $Ca^{2+}$ ionts and start muscle contraction




https://www.austincc.edu/apreview/PhysText/Muscle.html

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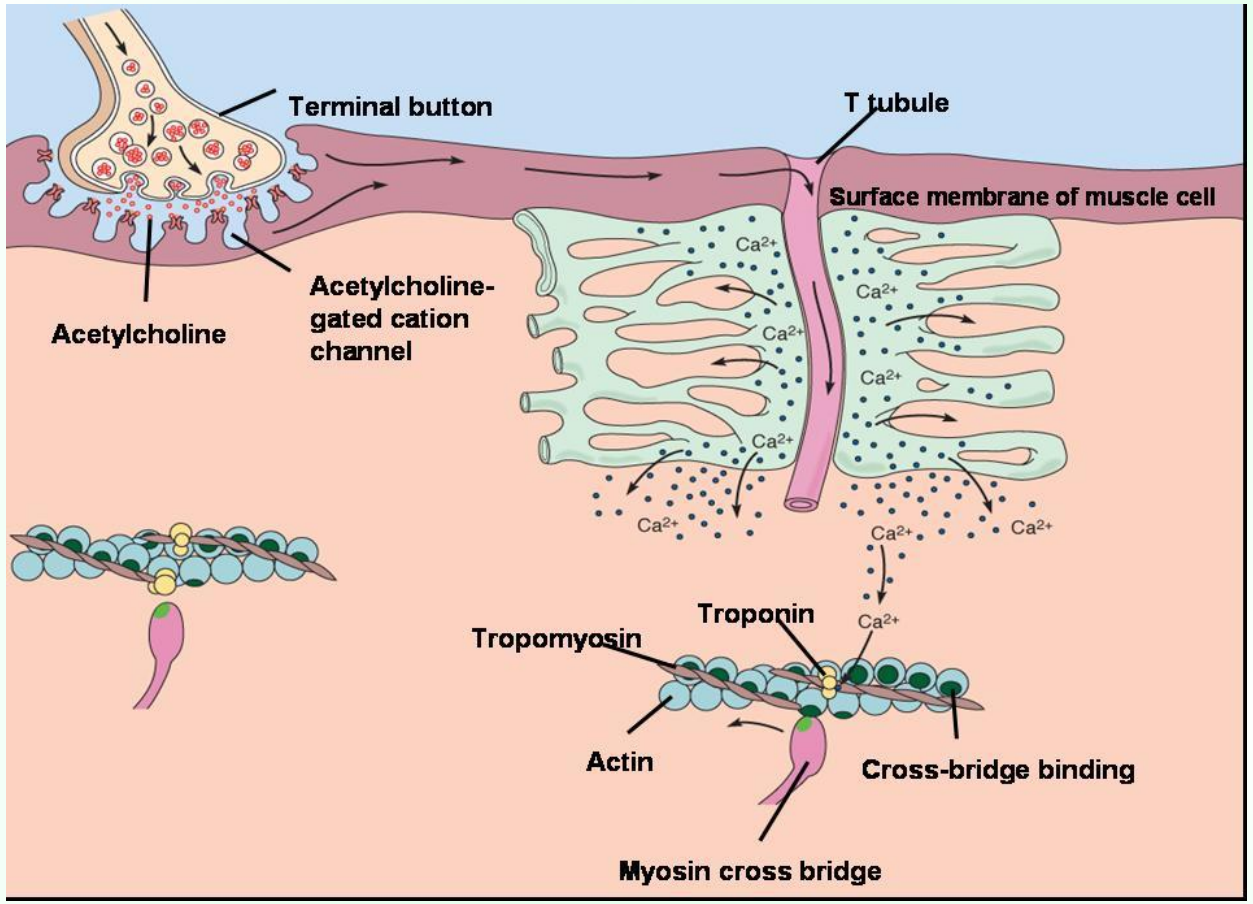


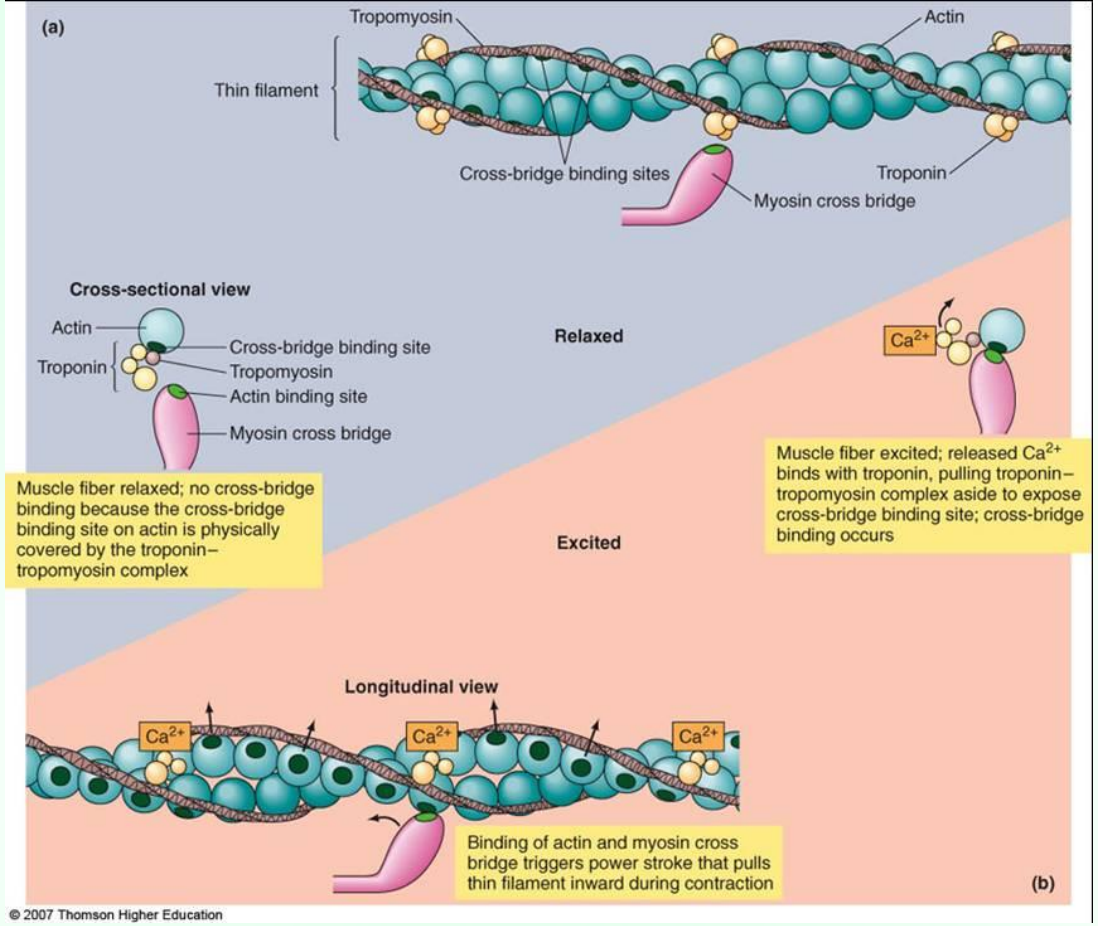


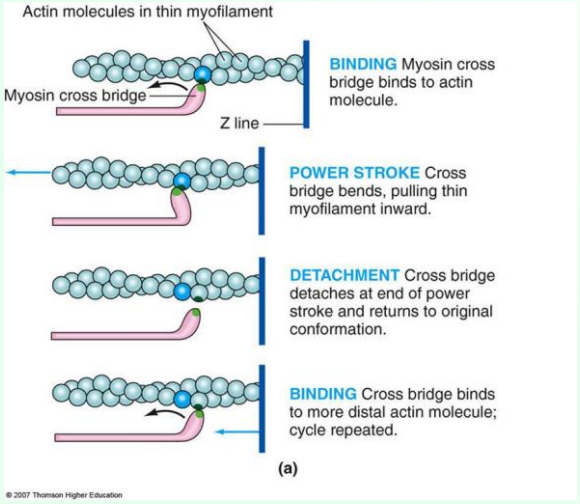


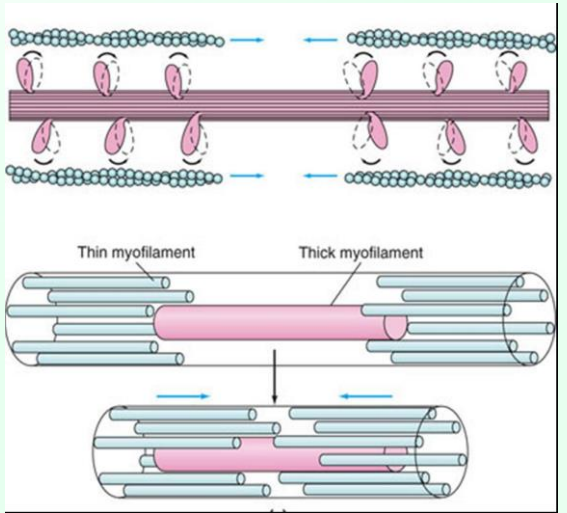


https://www.austincc.edu/apreview/PhysText/Muscle.html

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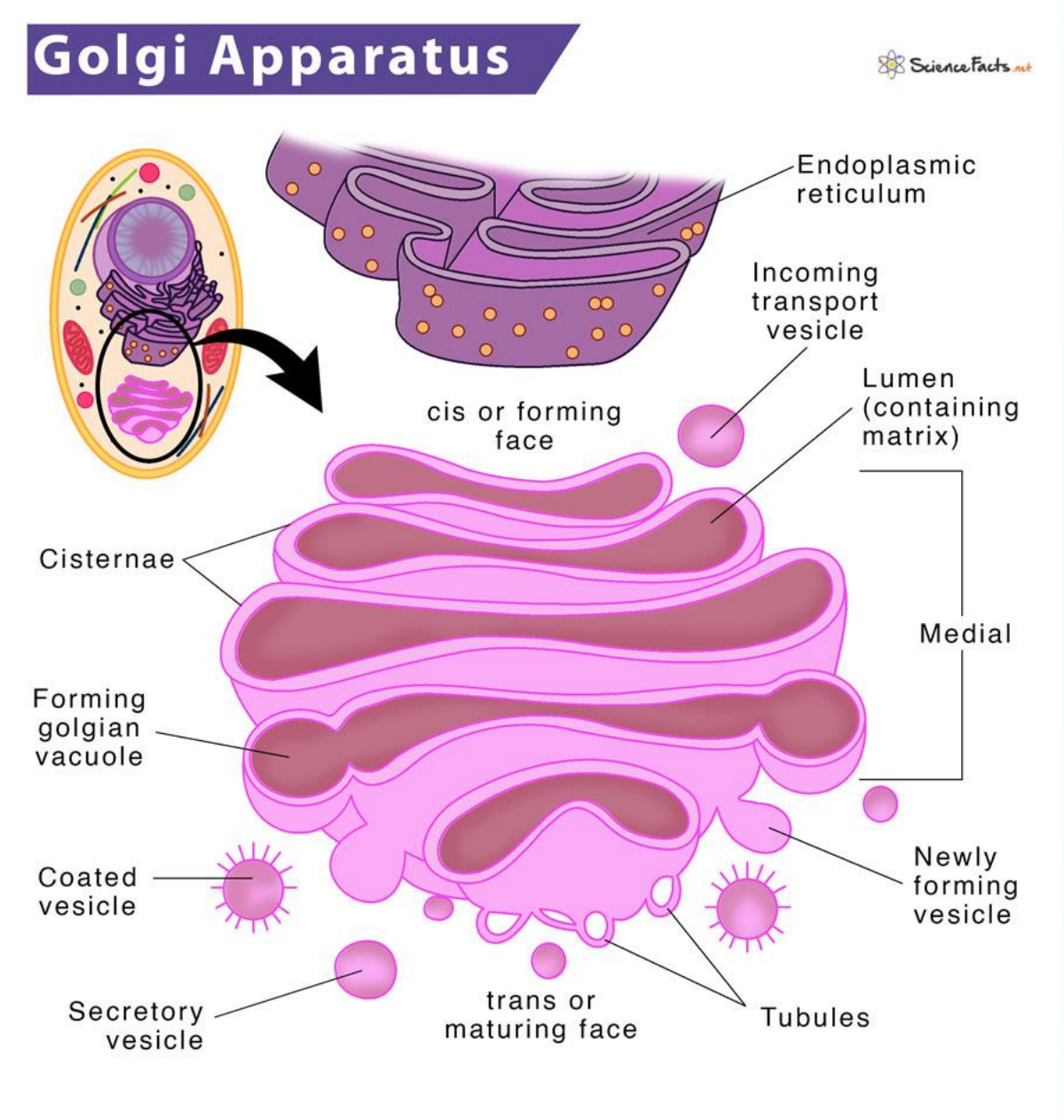
# Golgi apparatus (GA) – I.

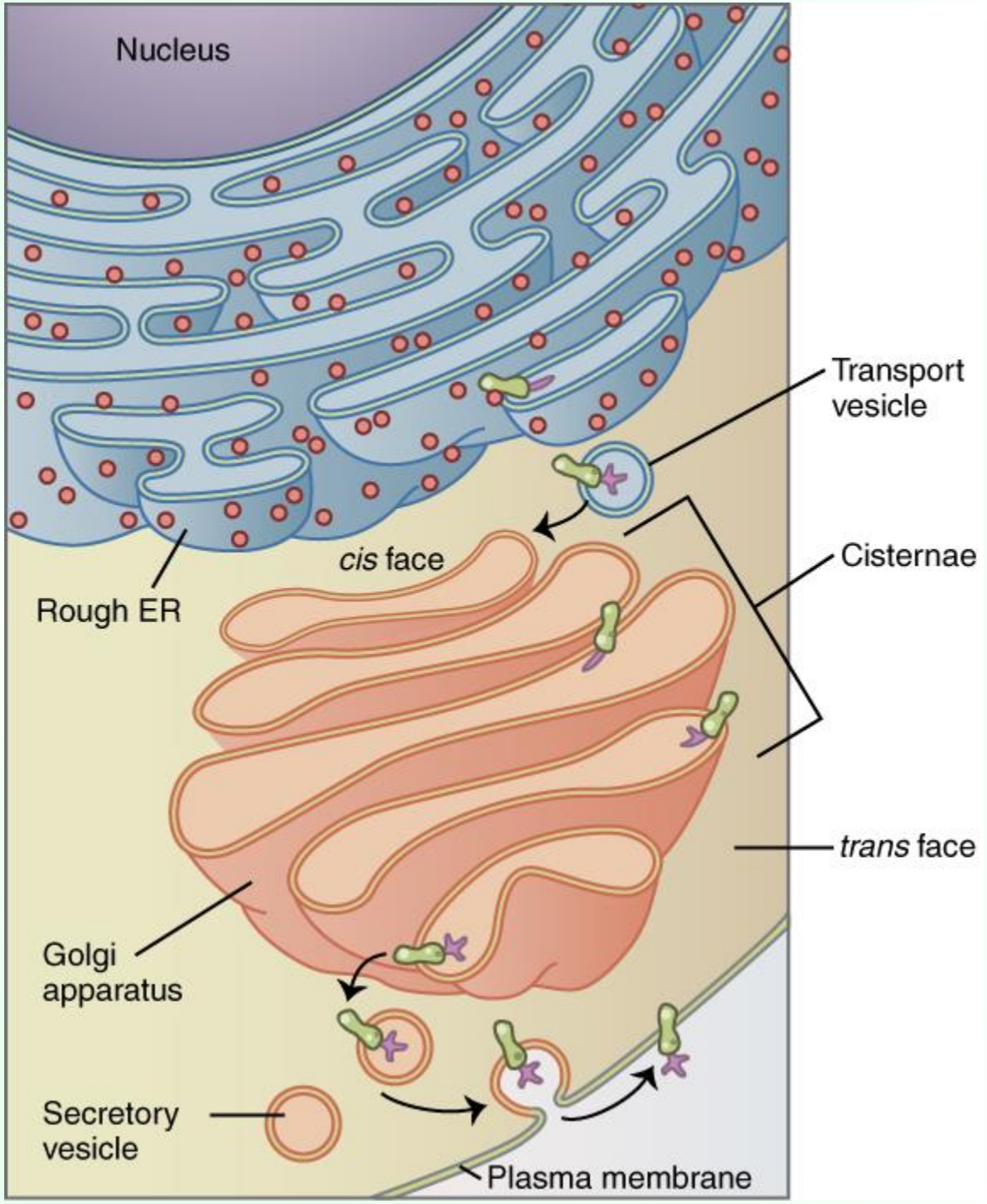
- Complex of **cisternae** and **vesicles**
- Located close to nukleus and ER
- **Vesicles** – sacs containing proteins produced in the rough ER deliver their contents to the **cis face** of the GA with which they fuse
- **Secretory vesicles** – vesicles containing processed proteins and suffocating from the **trans face** of the GA from where they move to the plasma membrane where they excrete their contents into the extracellular environment




https://www.sciencefacts.net/golgi-apparatus.html

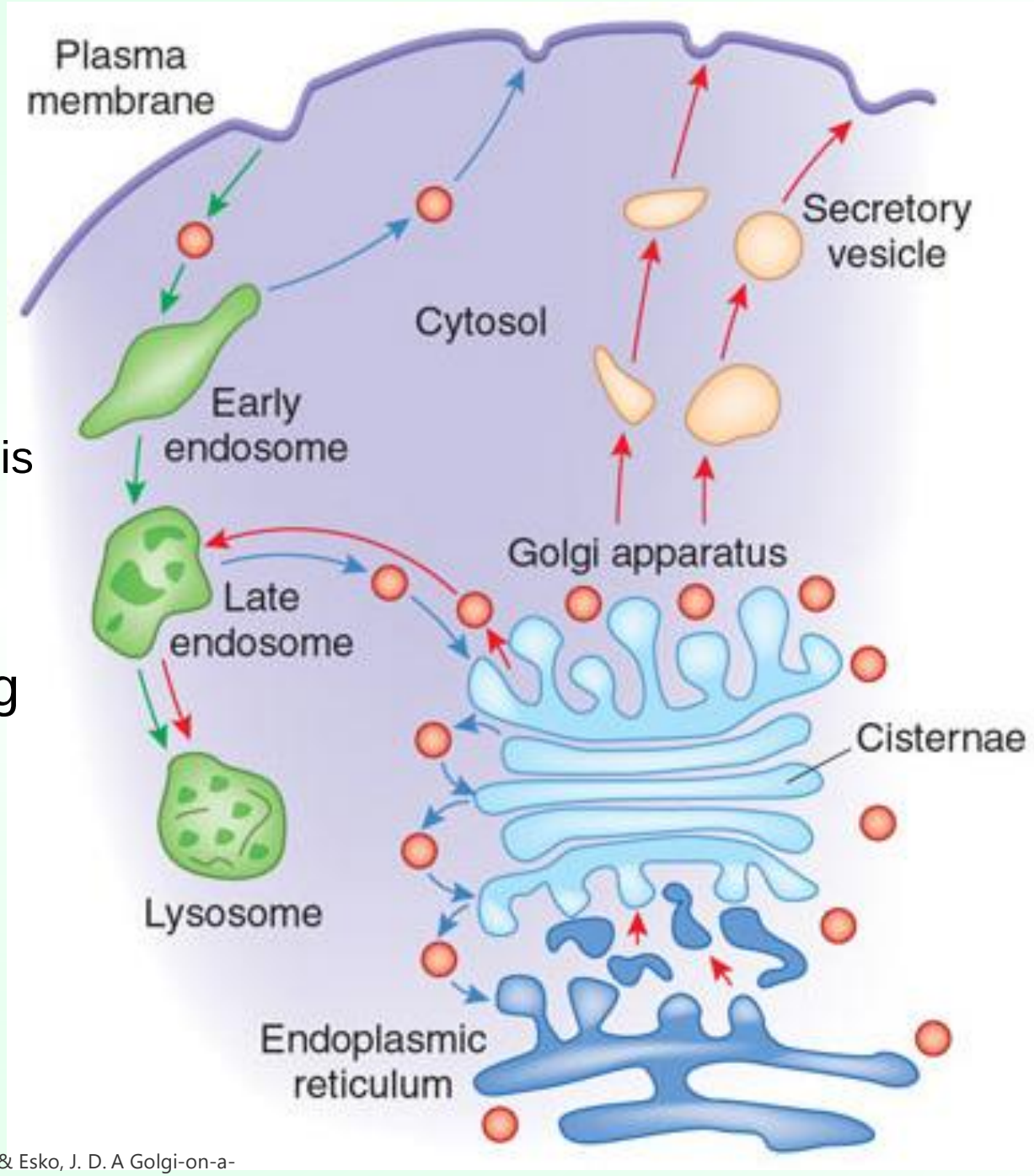
# Golgi apparatus (GA) – II.

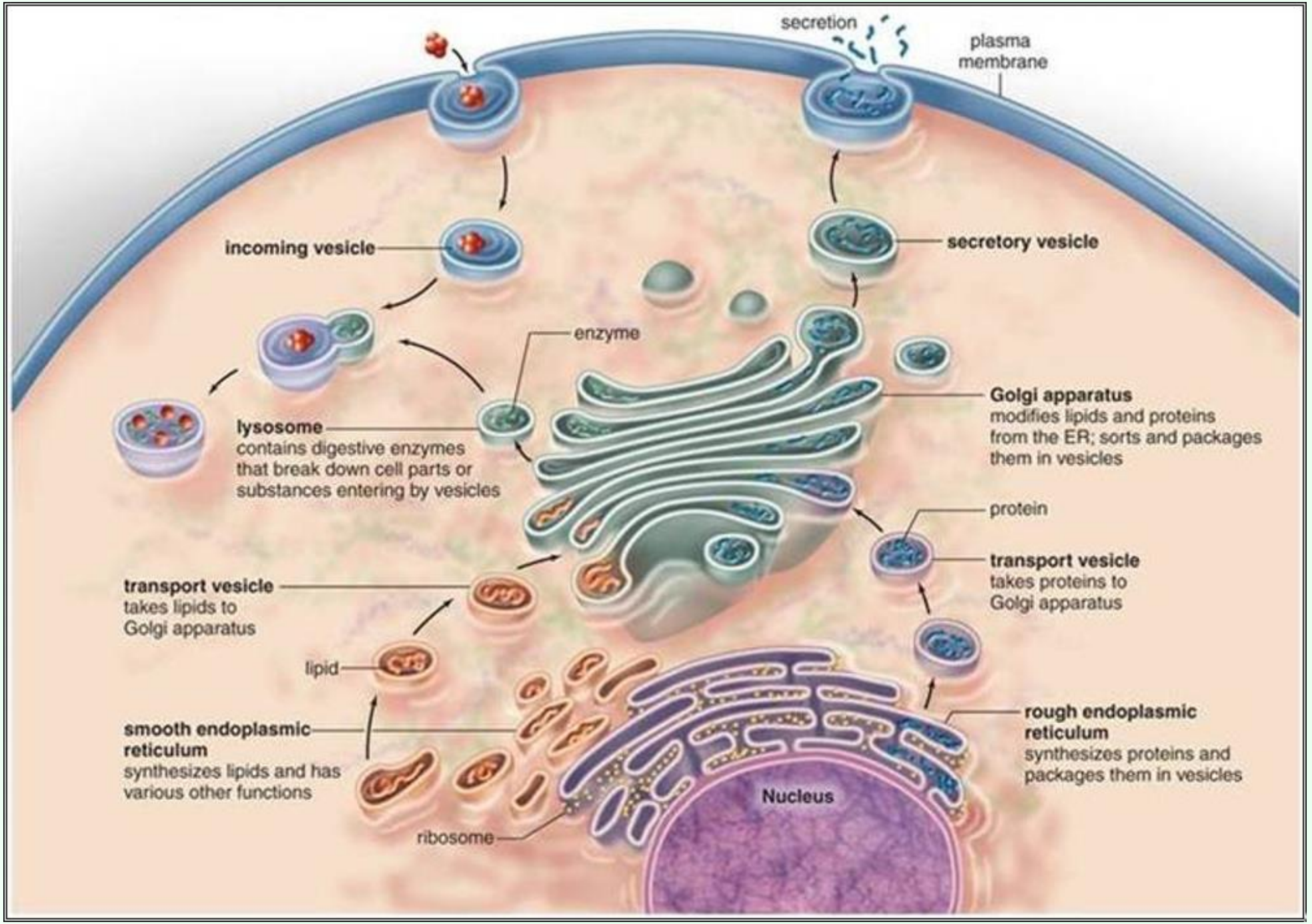
- Cisternae are connected to each other and on the side facing the nucleus (cis face), they constantly receive vesicles split off from the ER and intensively split vesicles filled with various cell secretions (trans face)



# GA functions

- Transport and storage of differnt compounds
- Posttranslation modification of proteins
  - The most common are glycosylation, phosphorylation, sulphatation, specific proteolysis
- Synthesis of polysaccharides and immunoglobulins
- Creation of secretory vesicles used during exocytosis
- Production of materiál for cell wall
- Creation and diferentiation of lysosomes
- Reparation of cell surface
- Creation of vacuols








https://doi.org/10.1016/B978-0-444-63772-7.00017-8

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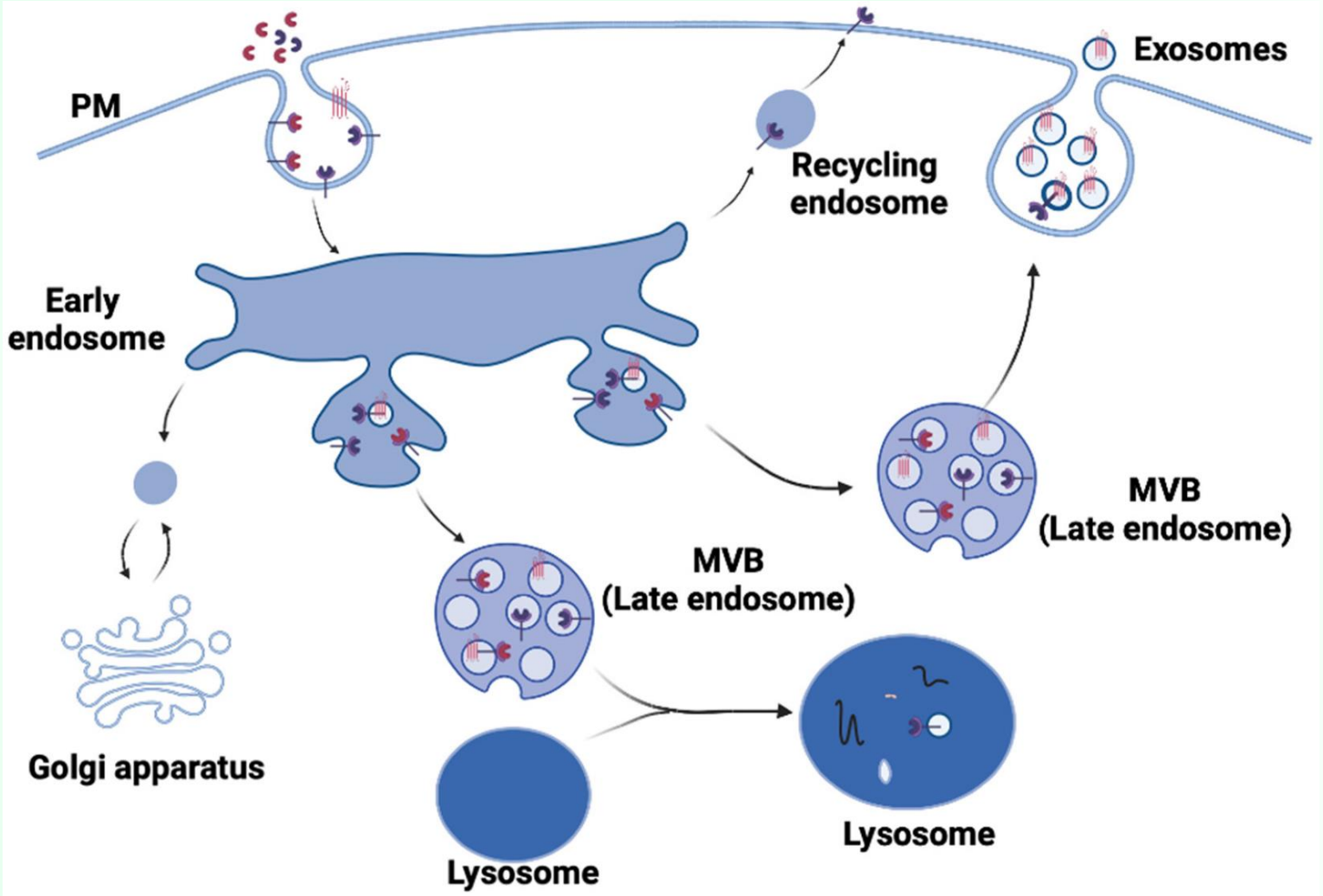
# Exosomes, endosomes and lysosomes

- Organelles/vesicles with recycling function
- **Exosomes** – transport material outside the cell
- **Endosomes** - transport material into cell
- **Lysosomes** – organelles digesting phagocytated material




https://doi.org/10.3390/ijms24021337

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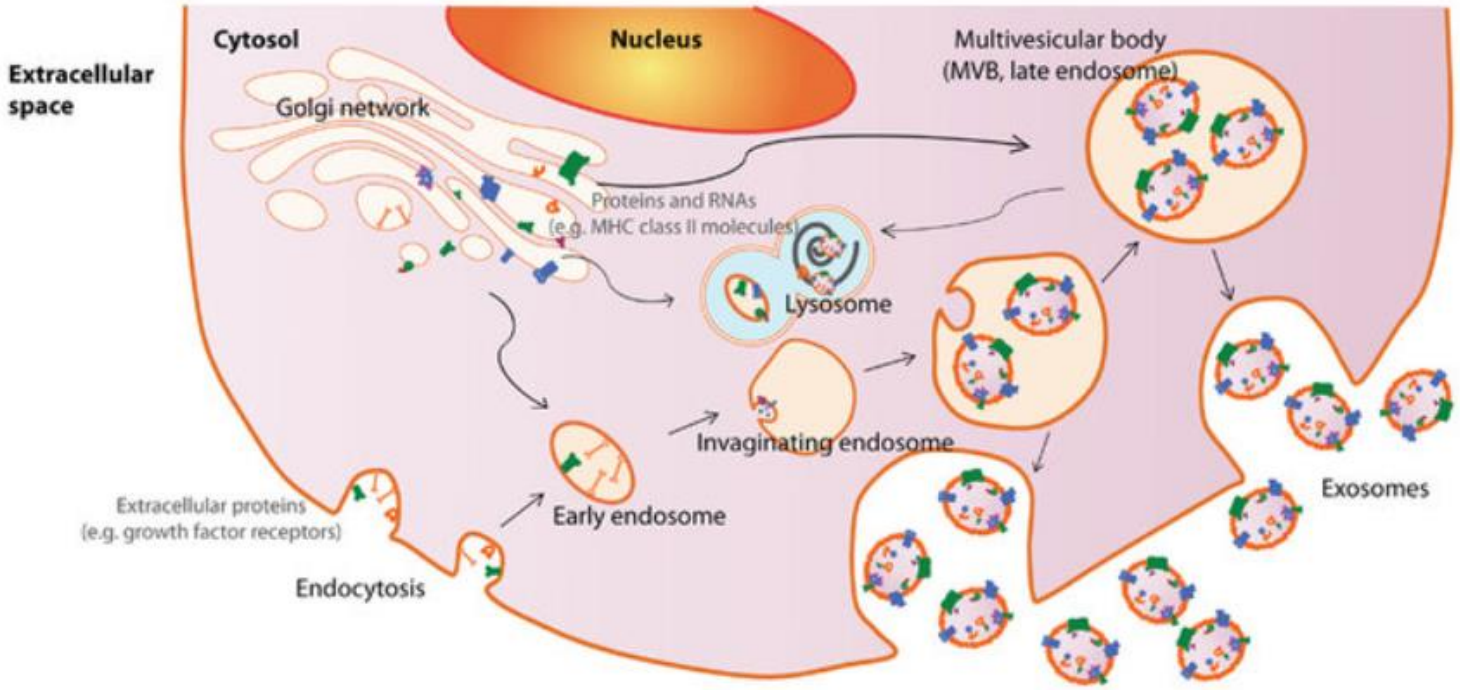


Figure 1: Exosome biogenesis and secretion. Exosomes are released by cells when intracellular organelles called multivesicular bodies (MVBs) fuse with the plasma membrane. MVBs are formed by invaginations of late endosomes, which contained molecules from the Golgi (e.g., MHC class II molecules) or the cell surface (e.g., growth factor receptors). Consequently, exosomes contain cytosolic materials and are enriched in endosome-associated protein markers such as the the Rab proteins, ALIX, TSG101, and MHC class II molecules or endocytic proteins, such as transferrin receptors and clathrins. This figure was modified from Lai et al. (169).

DOI: 10.3389/fimmu.2014.00518



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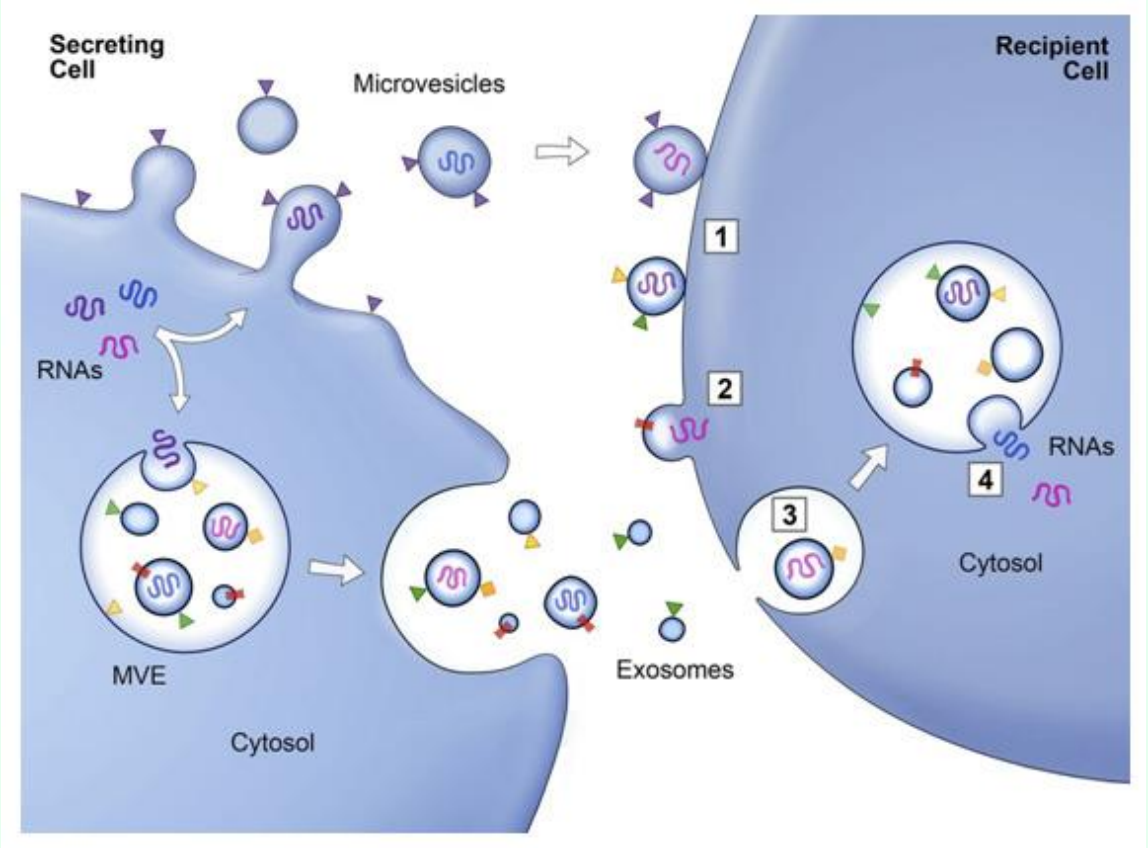
# Exosomes – cellular dustmen

- Vesicles that help remove the waste products of cellular metabolism
- They are formed by the fusion of the cell membrane and the internal parts of the cell
- **Exosomes are part of intracellular communication**



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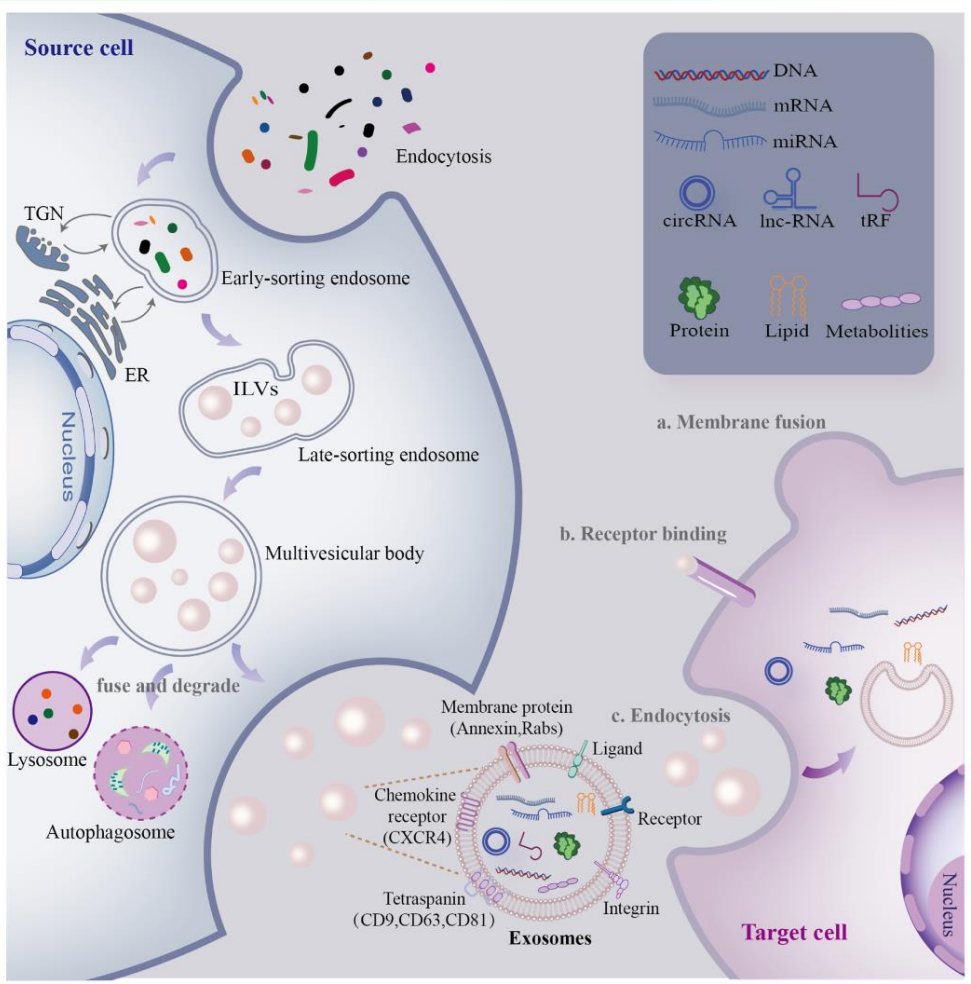
# New functions of exosomes

- They can transport proteins, nucleic acids, lipids and metabolites between cells
- antigen presenting cells share pathogens that are captured in exosomes = amplification of immune response
- some exosomes, for example, display Fas ligand on their surface, which, after binding to the Fas receptor (also known as the "death receptor"), initiates apoptosis
- mRNA carried by the exosome can be translated into a polypeptide in the target cell




Biogenesis and secretion of exosomes. The secretion of exosomes involves two invaginations of the plasma membrane. Intercellular communication mediated by circulating exosomes occurs through endocytosis, ligand–receptor interaction, and membrane fusion. Components such as proteins, nucleic acids, lipids, and metabolites are delivered by exosomes from the source to target cells [33]. Proteins located in the plasma membrane, including CD63, CD9, CD81, TSG101, and Alix, are commonly used as markers for exosomes [26].

https://www.mdpi.com/2073-4409/12/2/311

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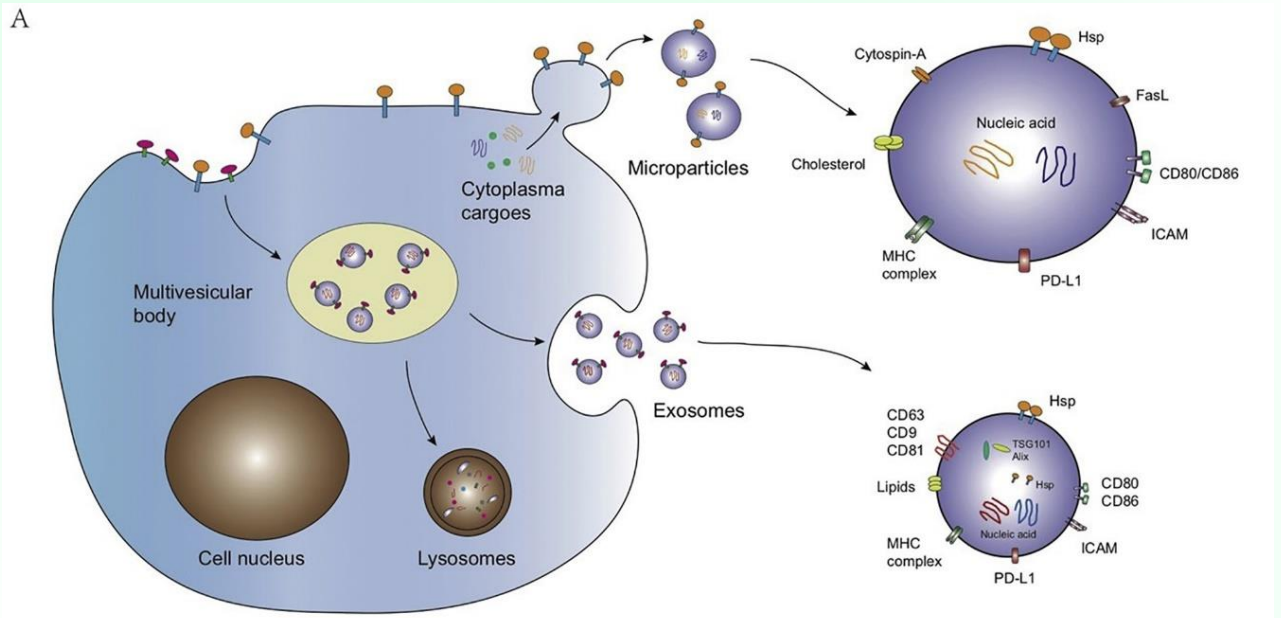
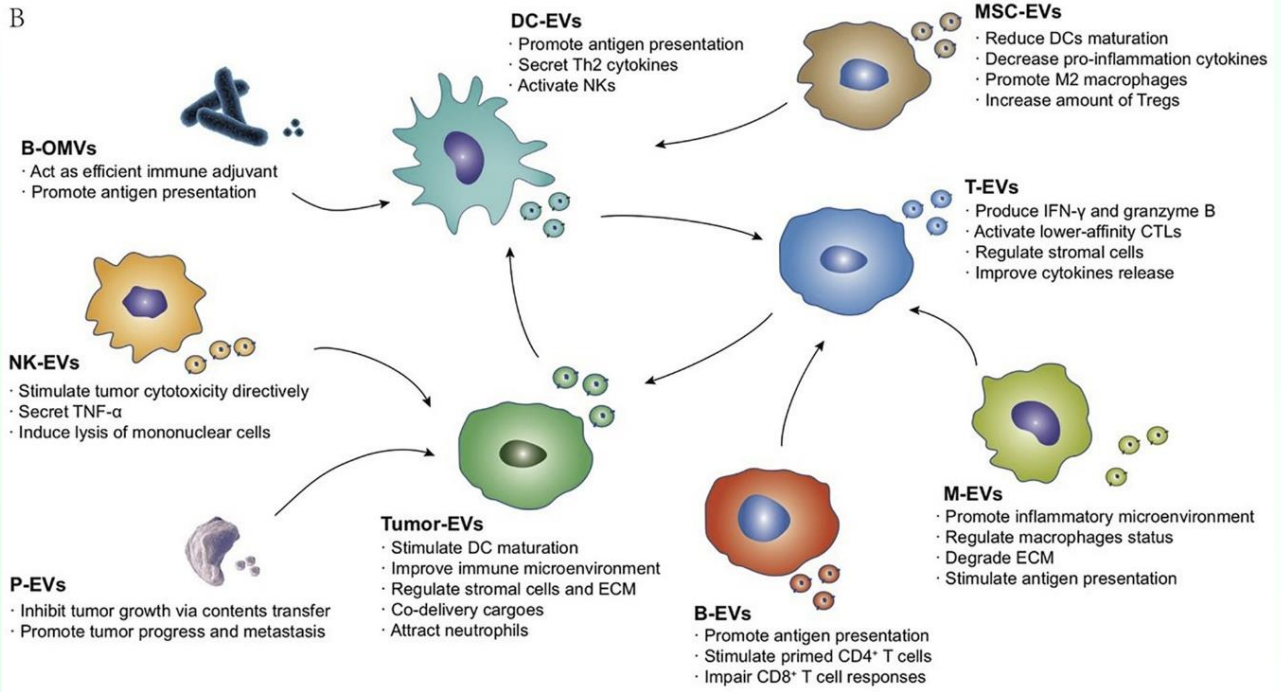
# Exosomes as drug carriers for tumor immunotherapy

- Extracellular exosomes and microparticles of immune cells can influence tumor progression




## Highlights

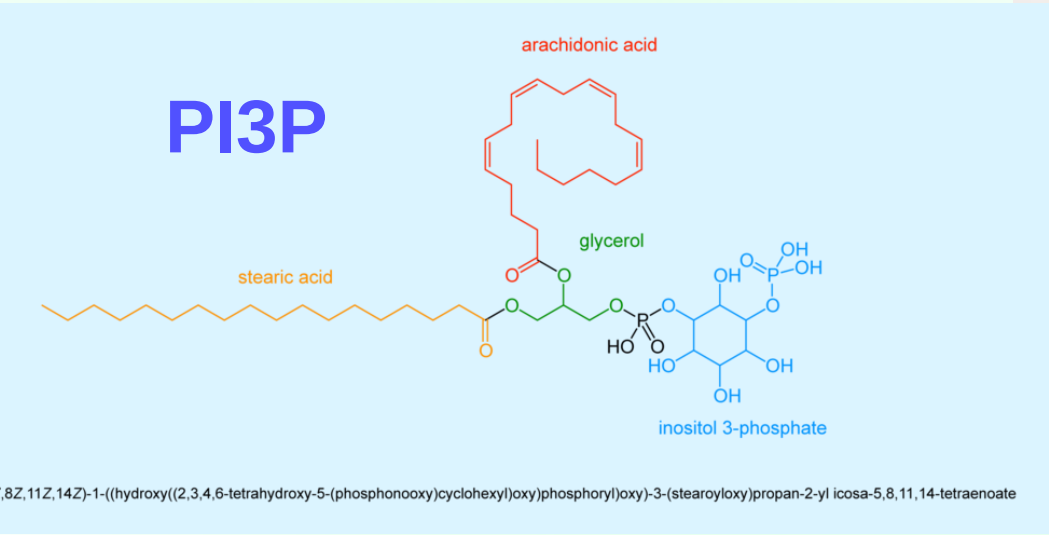
- Extracellular vesicles derived from diverse types of cells possess significant immunomodulation properties.
- Mechanisms of extracellular vesicles regulating tumor immune microenvironment contribute to excellent anti-tumor efficacy.
- Engineering modification of extracellular vesicles is an excellent approach for enhanced therapeutic effects.



https://doi.org/10.1016/j.jconrel.2020.09.028

# Recycling of membrane proteins

- Plasma membrane phospholipids and membrane proteins can be recycled
- In the **endosome**, phospholipids are modified, which serve as markers for recycling/degradation




https://doi.org/10.1038/nature16868

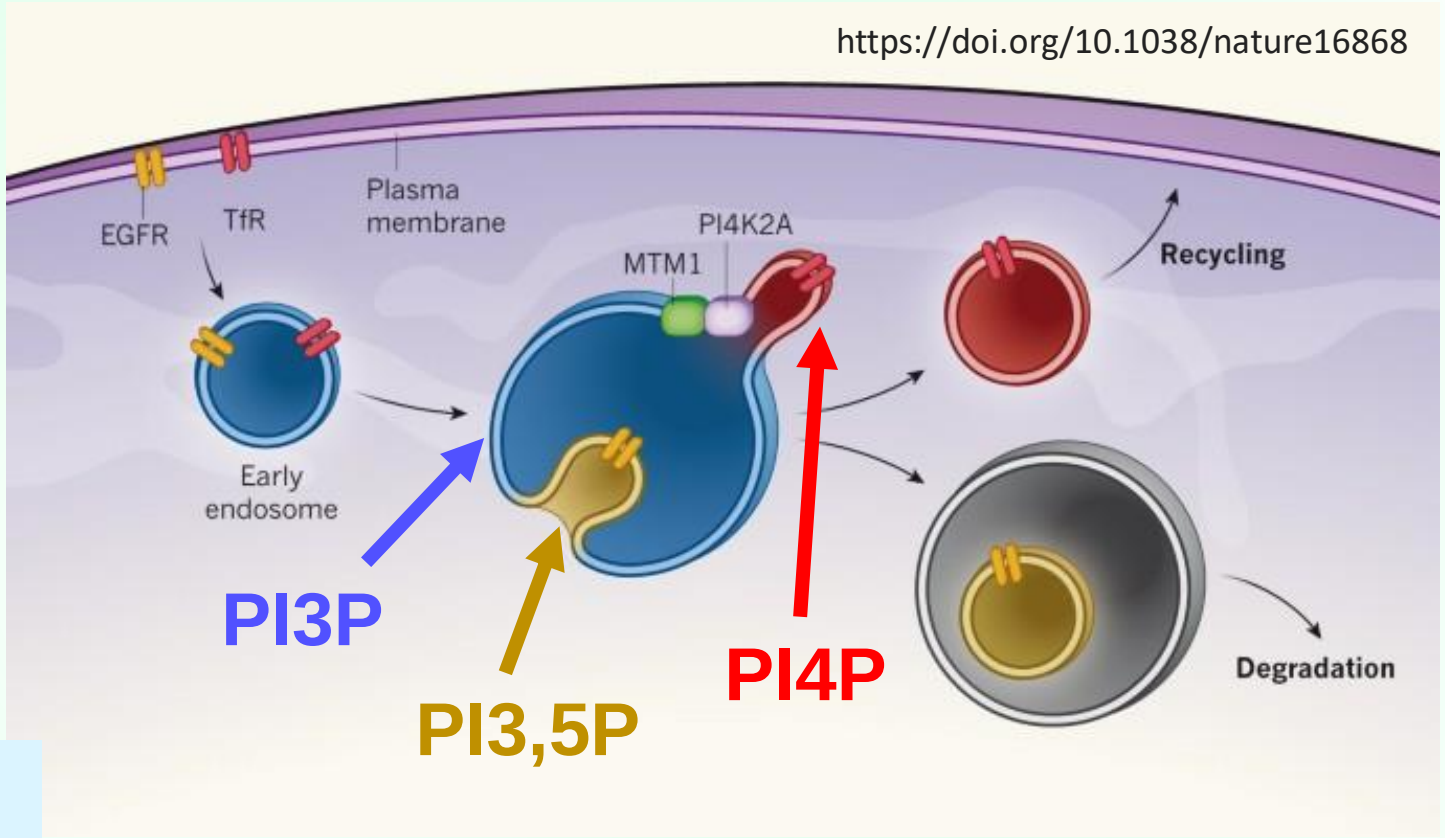
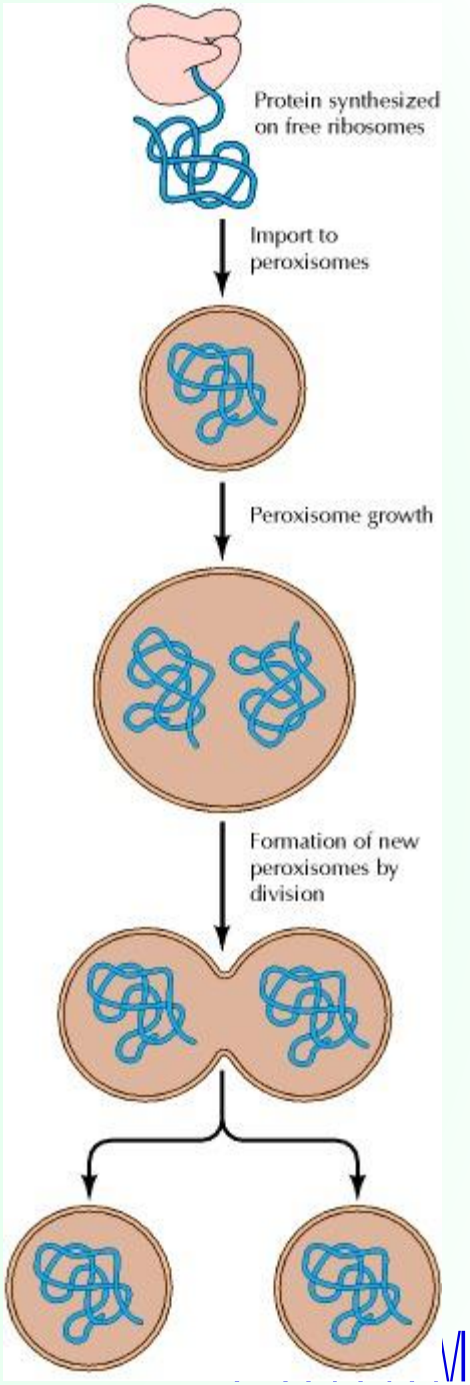



**Figure 1 | Phospholipids direct membrane sorting.** The proteins epidermal growth factor receptor (EGFR) and transferrin receptor (TfR) are removed from the cell surface in membranous structures called endosomes. The membranes of early endosomes contain PI3P (PI3P-containing membranes are indicated in blue) — a phospholipid of the phosphoinositide family that is tagged with a phosphate group at 'position 3'. As they mature, endosomes are sorted to determine the fate of the proteins they contain. In membrane regions such as those harbouring EGFR, PI3P is converted to $PI(3,5)P_2$ (yellow membranes), marking the region for degradation (the lipids present in the outer membrane of endosomes destined for degradation remain unknown). Ketel *et al.*[1] report that regions destined for recycling, such as those harbouring TfR, are modified by the sequential action of two enzymes. First, MTM1 removes the phosphate group from PI3P, then PI4K2A adds a phosphate group to position 4, generating PI4P (red membranes). The presence of PI4P directs the endosome back to the plasma membrane so that the proteins can be reused.

# Peroxisomes

- Simple organelles capable of "dividing" themselves
- Proteins enter the peroxisomes from the cytoplasm, where they are formed by free ribosomes
- Functions:

  - Oxidation of various substrates → inactivation of toxins, **beta-oxidation of fatty acids**
  - Detoxification of oxygen radicals (hydrogen peroxide, superoxides and epoxides) → **catalase**
  - The first steps in the synthesis of glycerolipids or plasmalogens
  - **Formation of bile acids,** dolichol, **and cholesterol**




https://www.ncbi.nlm.nih.gov/books/NBK9930/