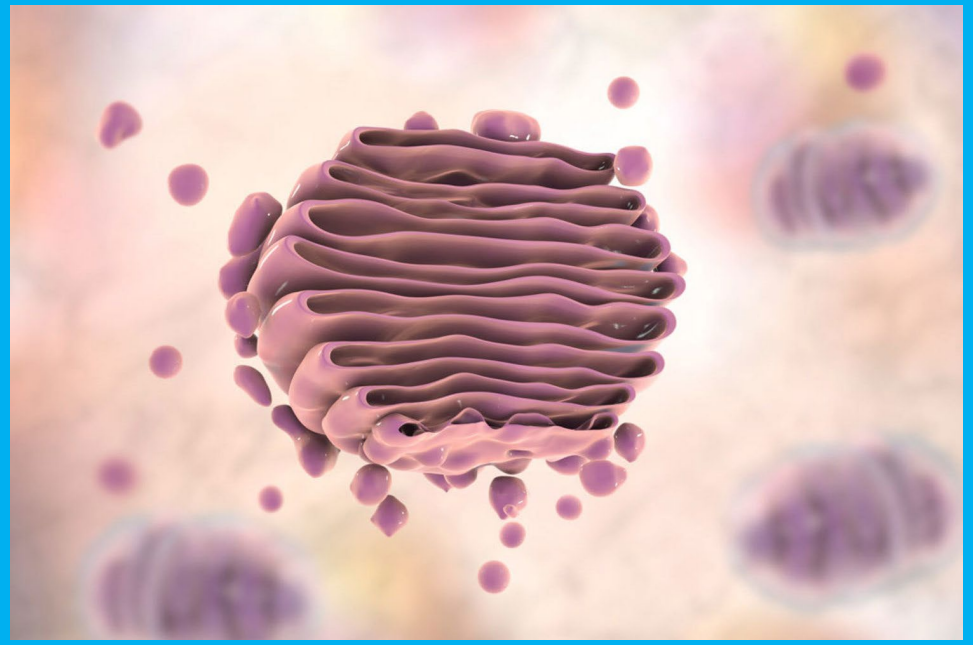
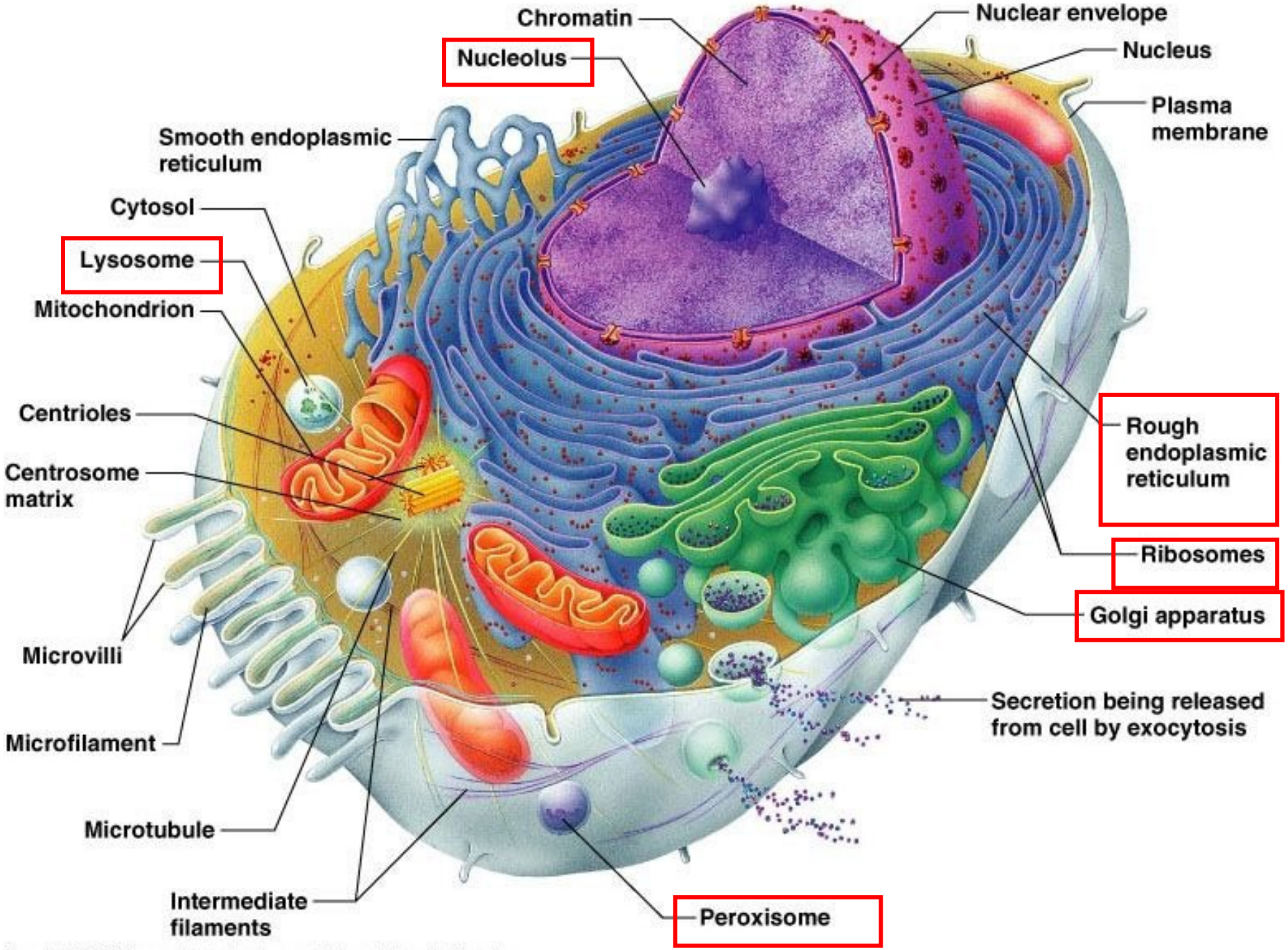
Protein Synthesis and Digestion: ER, Golgi and Vesicles



Marjorie D. Shaw, Ph.D.

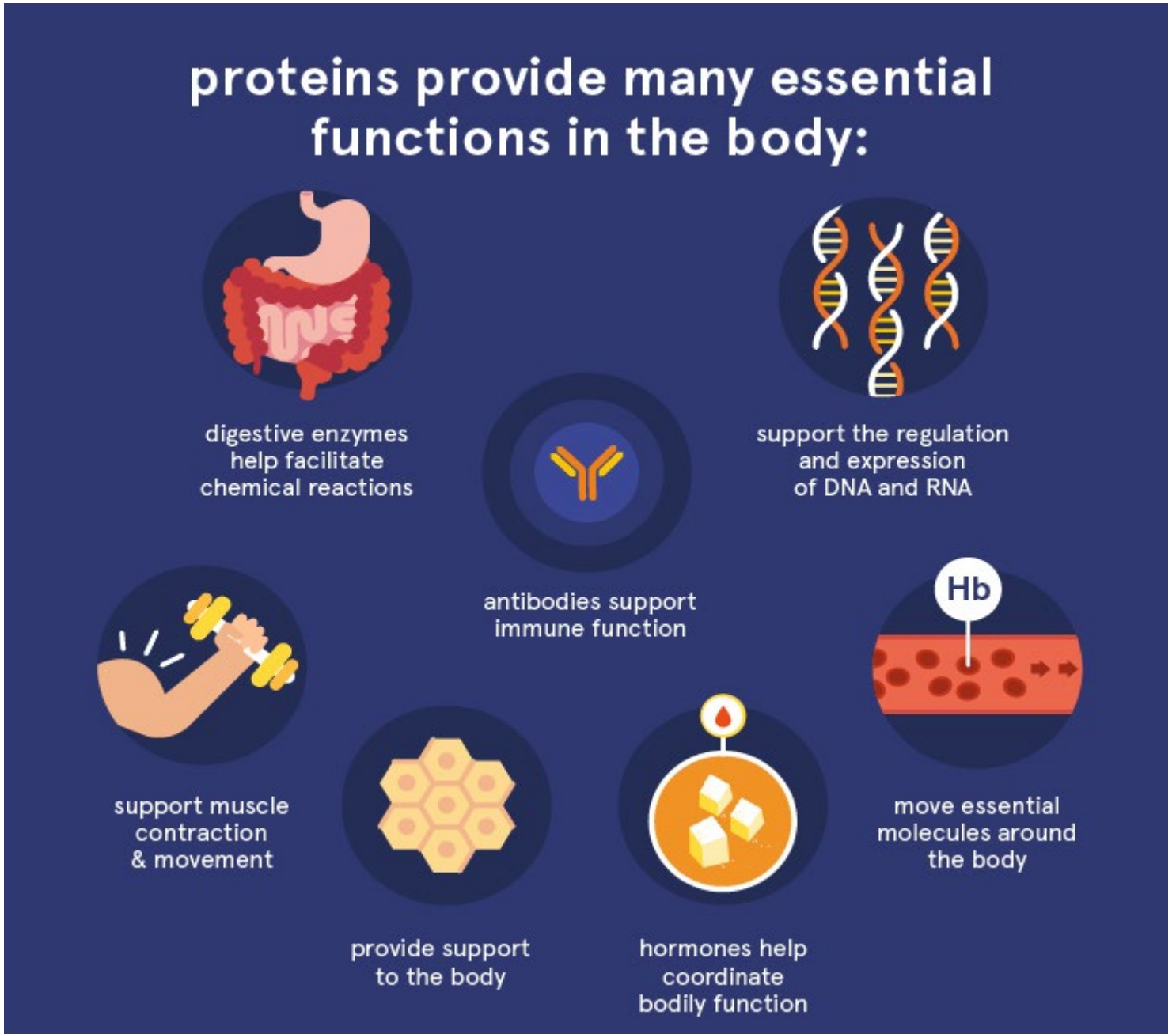
OLLI Fall 2023

Study Group : 426



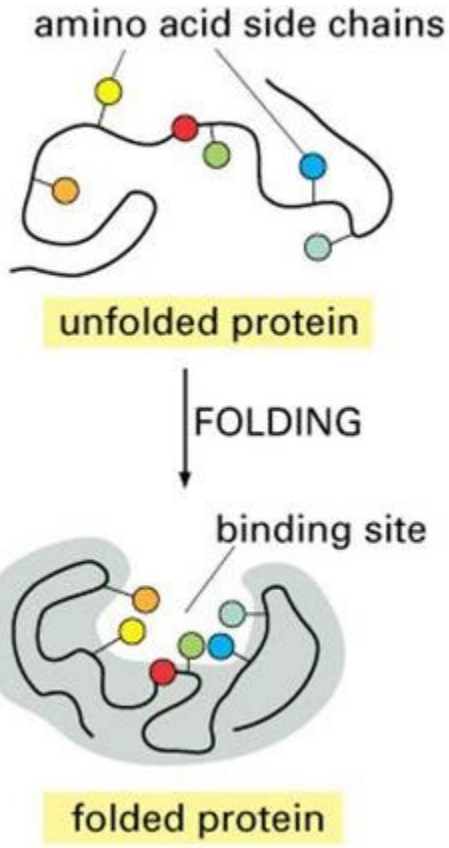
Protein Functions

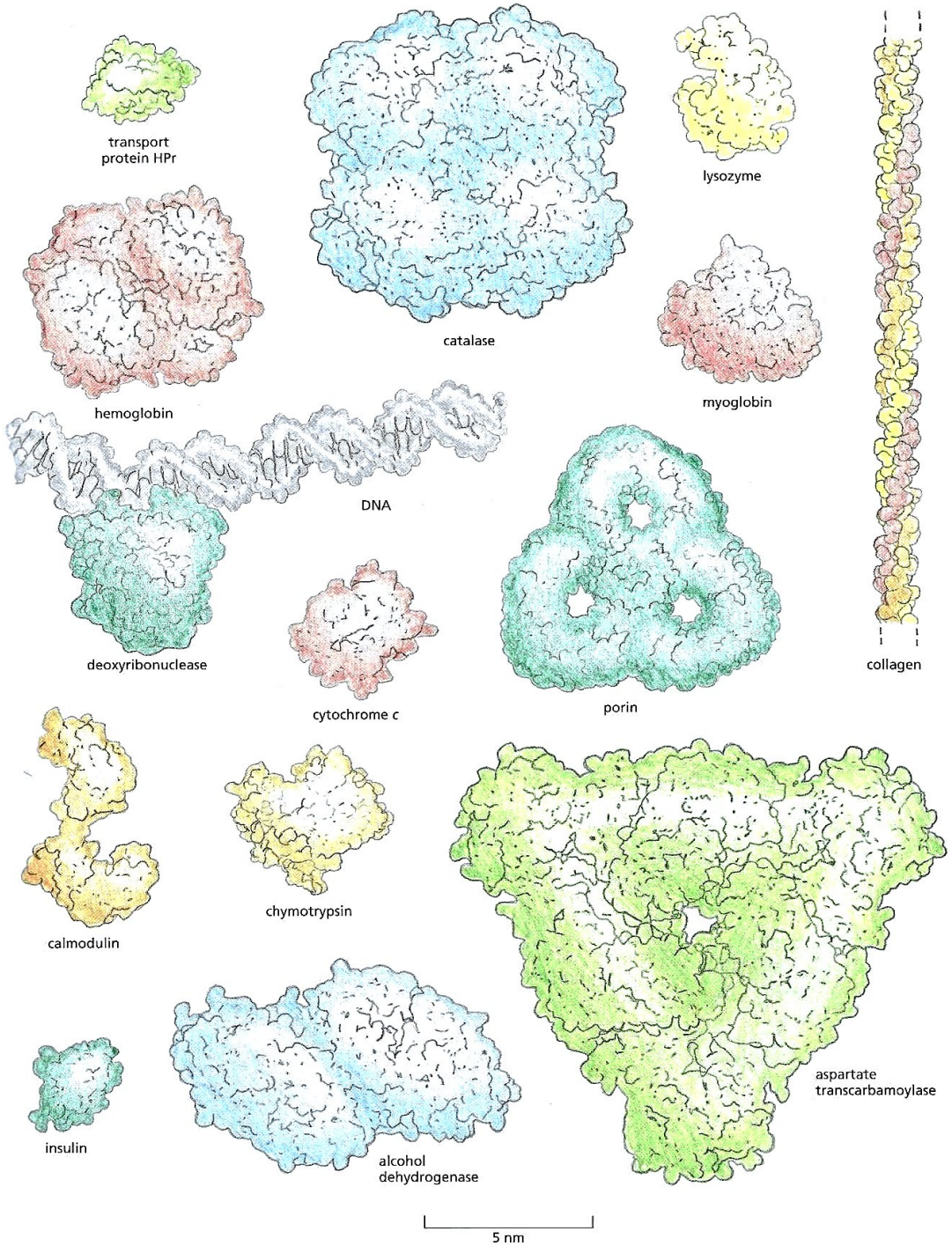
Provide structure and execute most functions.
Enzymes : facilitate reactions
Channels: transport across membranes
Receptors: for signals
Motors: along microtubules
Messages: between cells and within
Regulators: control DNA transcription
Carriers: of oxygen, iron…



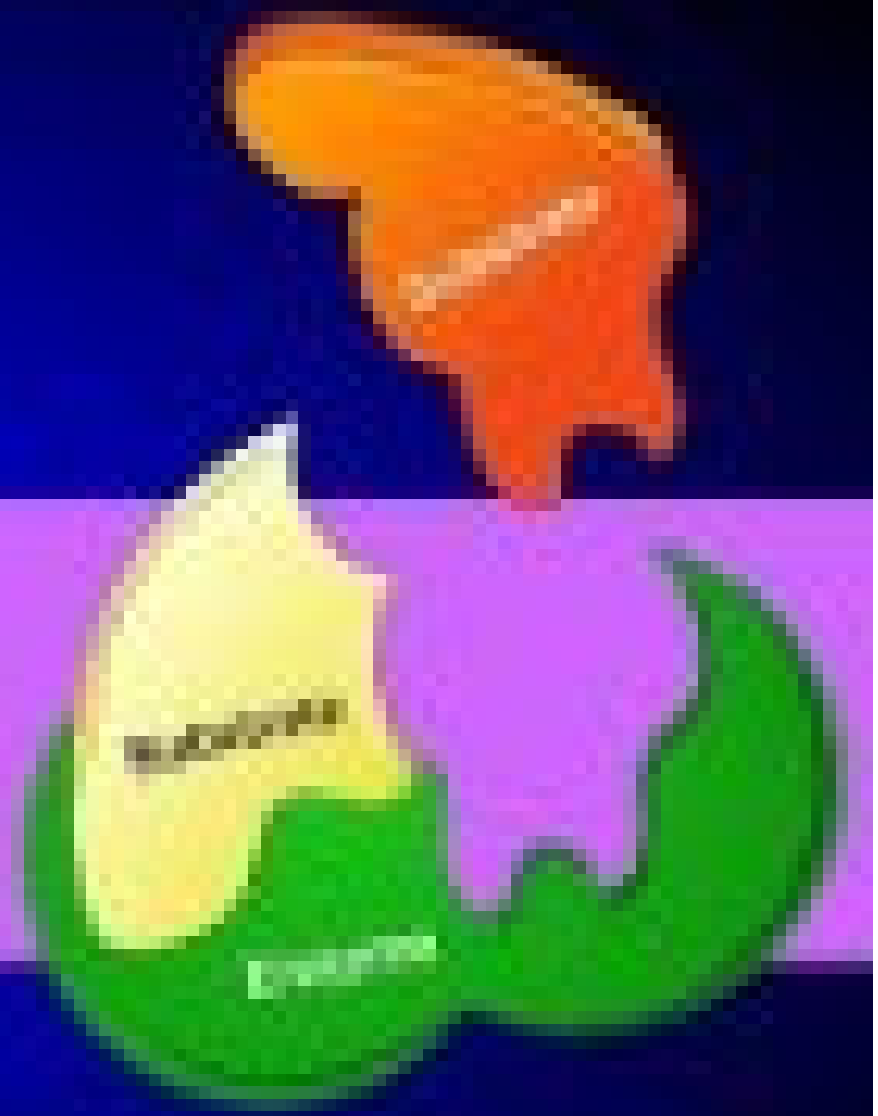
Function determined by shape

The shape coordinates the chemical interactions of molecules associate with it. Only interacts with specific molecules. How is the shape determined?



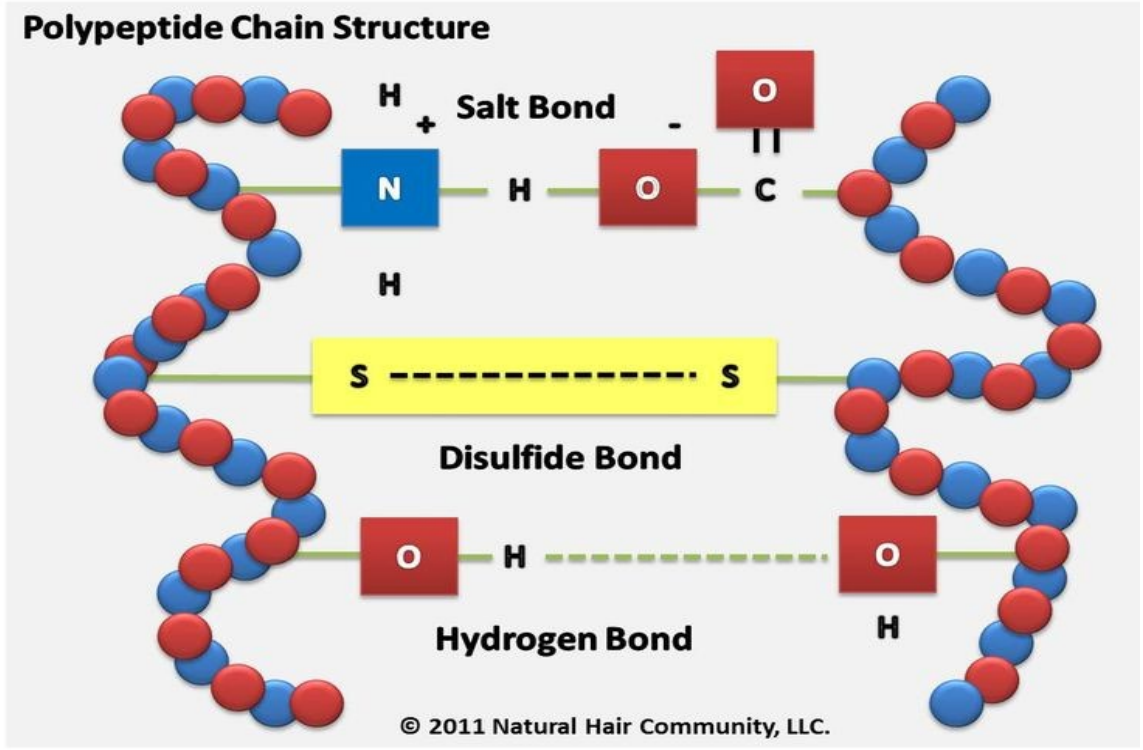


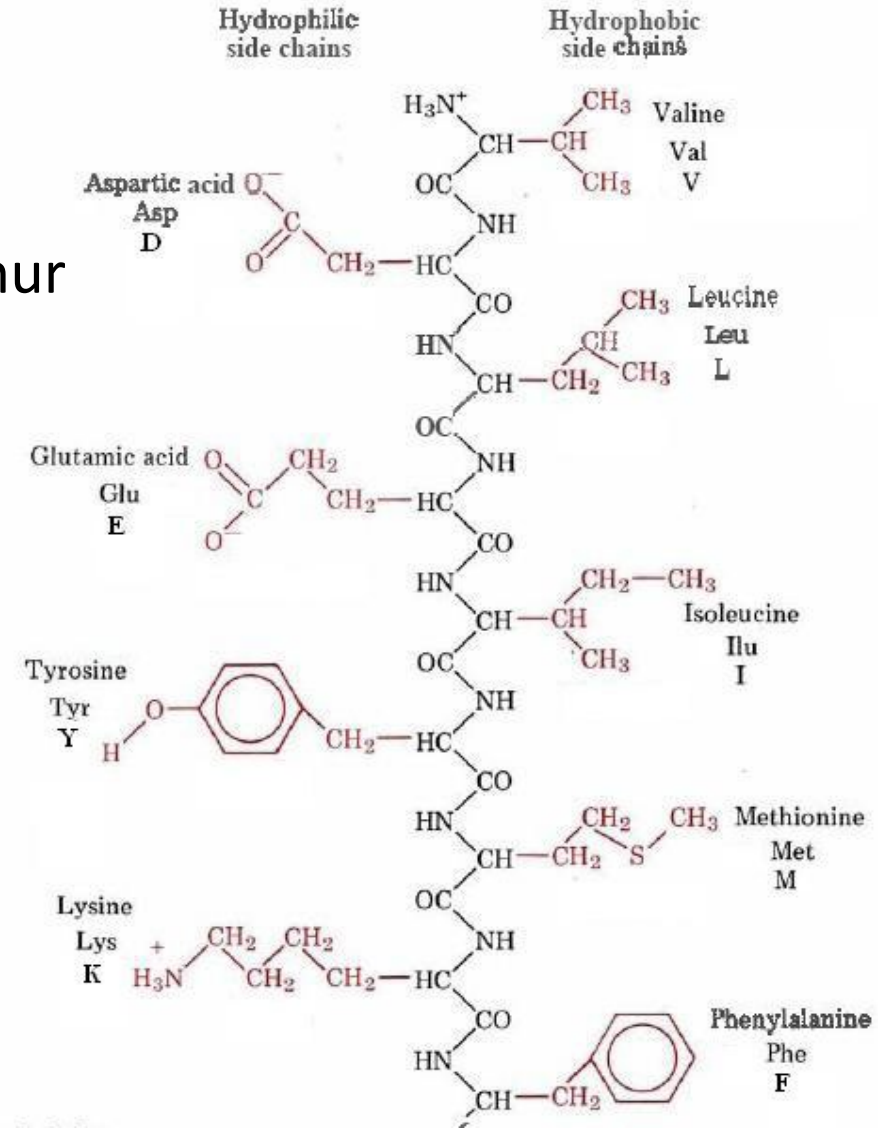
How Enzymes Work



Amino Acid Sequence

Proteins are strings of amino acids (peptides). 20 common amino acids used in human proteins. Every protein has a unique amino acid sequence. Although all amino acids have same basic backbone, they have different side chains that react with other **side chains**: hydrophobic, hydrophilic, sulphur bonding, hydrogen binding etc.





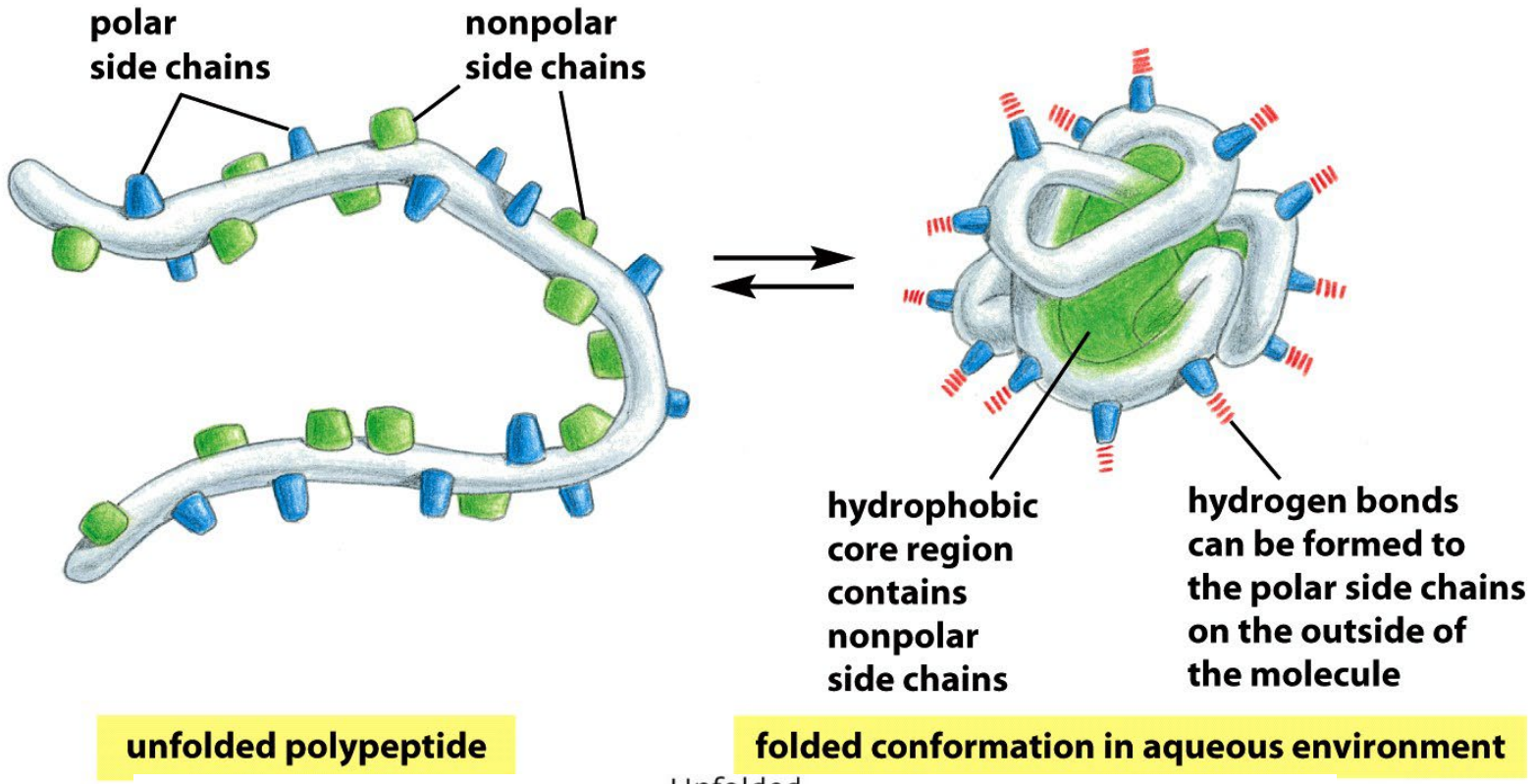
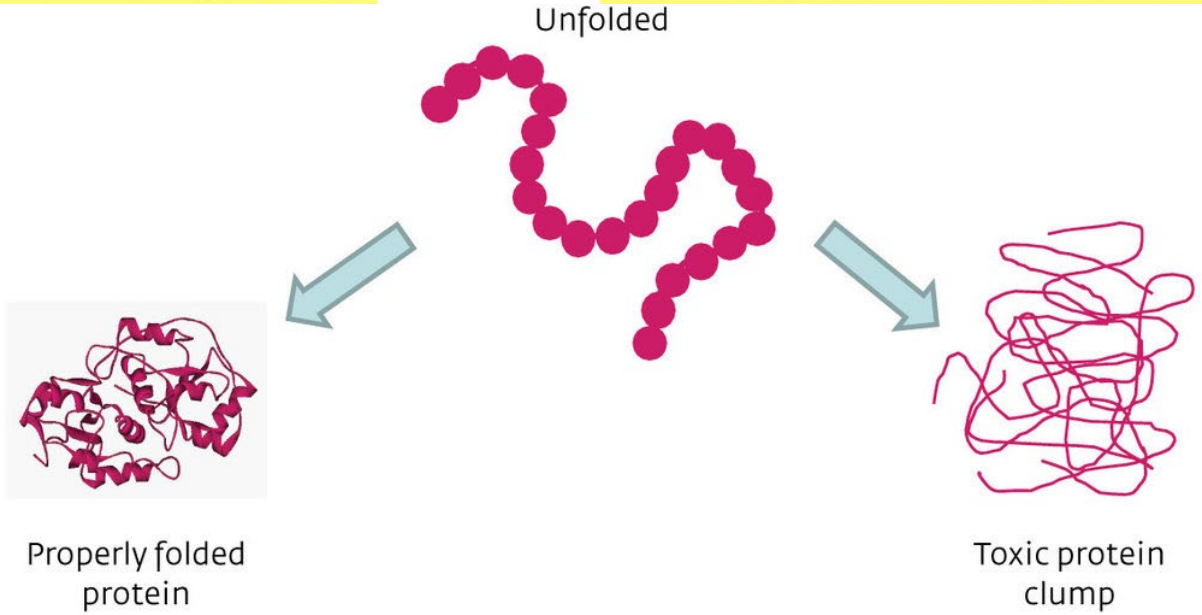


Figure 4-5 Ess

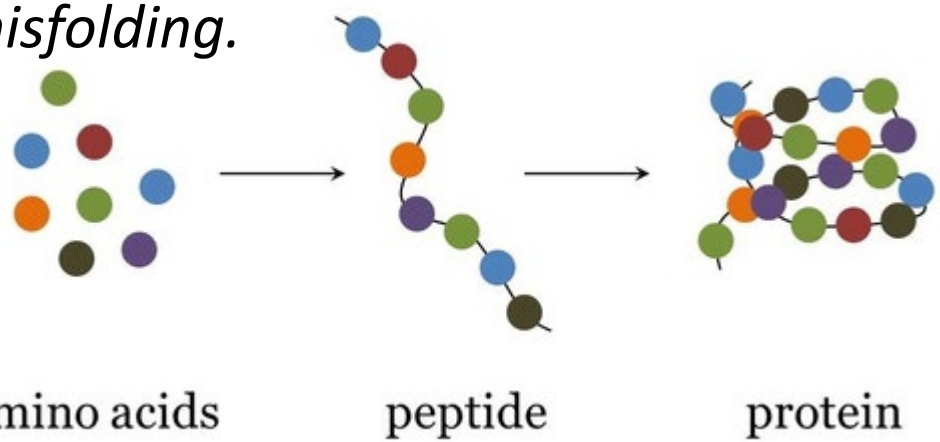


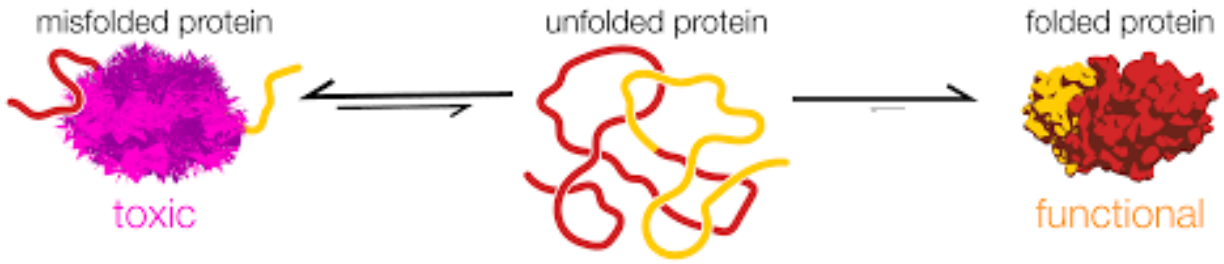
Shape is crucial to function

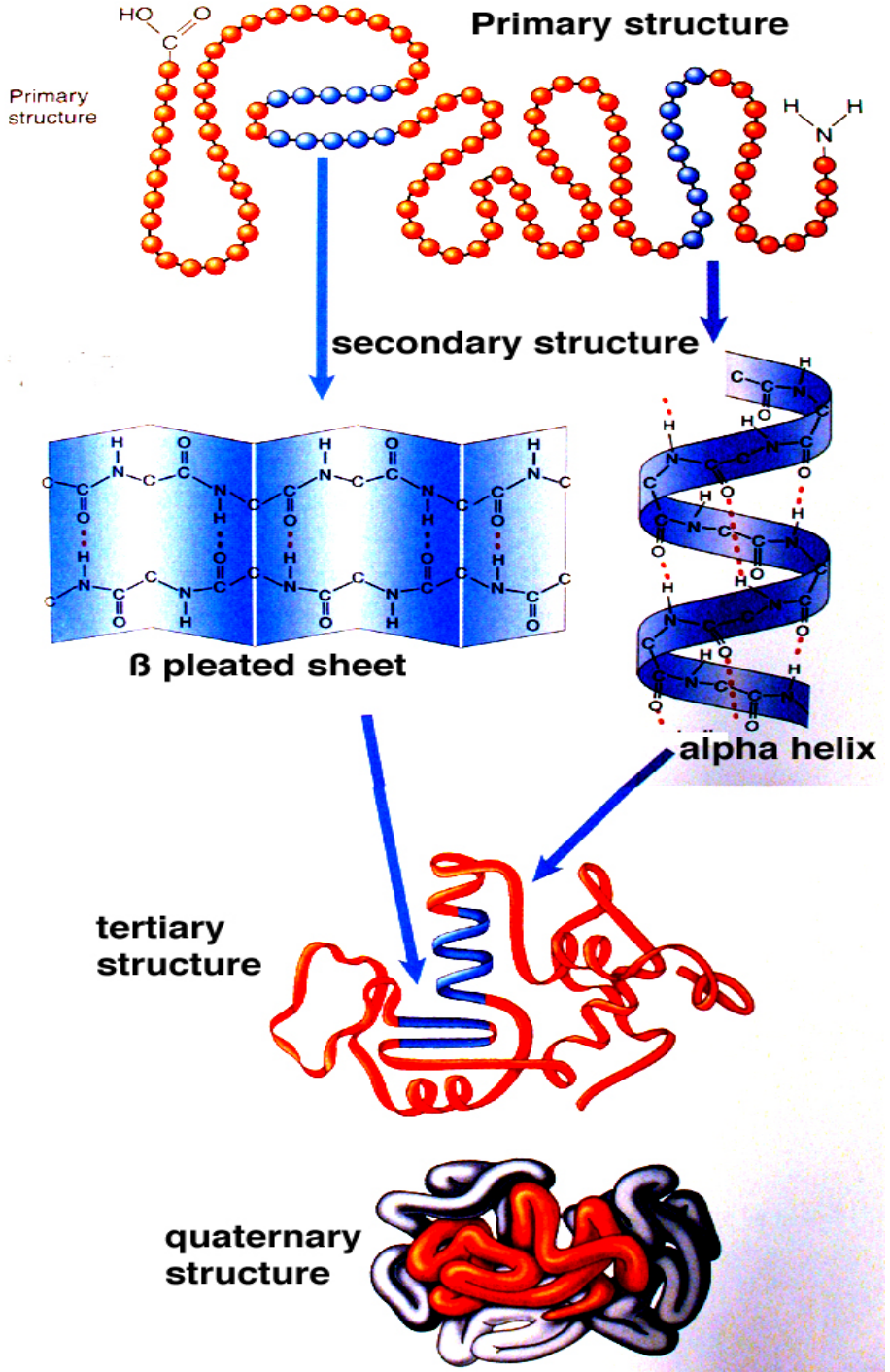
An improperly folded protein can be toxic, so folding may be facilitated by **chaperone proteins** (eg misfolded membrane transport protein in cystic fibrosis, amyloid in Alzheimer's, Parkinson's and Huntington's, prions in mad-cow)

Amino acids make proteins

The order of the amino acids in the peptide creates folding in specific ways, which is crucial to its function. *Mutations cause misfolding.*

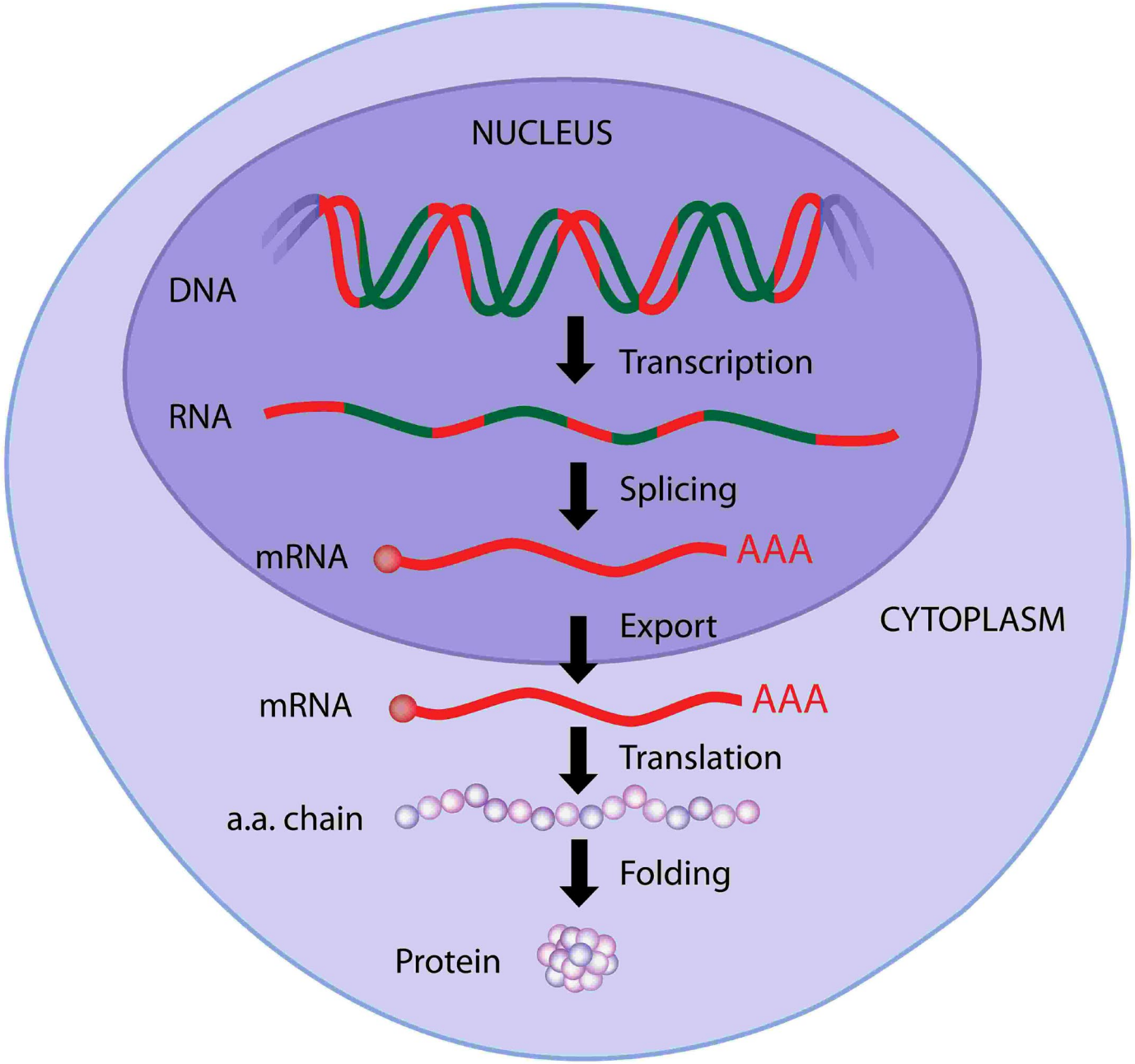






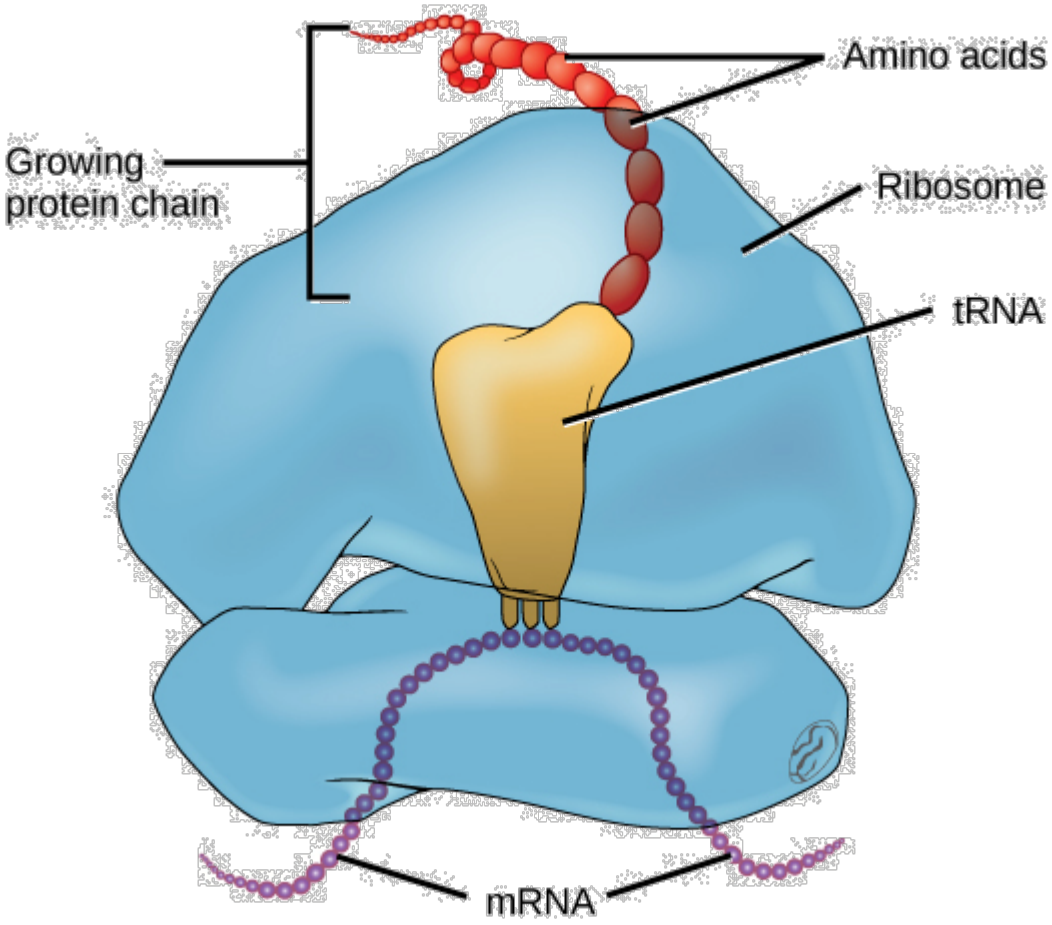
Protein synthesis

Active genes are transcribed into RNA in the nucleus, spliced to assemble just the exons into messenger RNA. The mRNA leaves the nucleus through the pores. In the cytoplasm, the mRNA must attach to a **ribosome** to start being *translated* into amino acid chains, which fold into proteins.

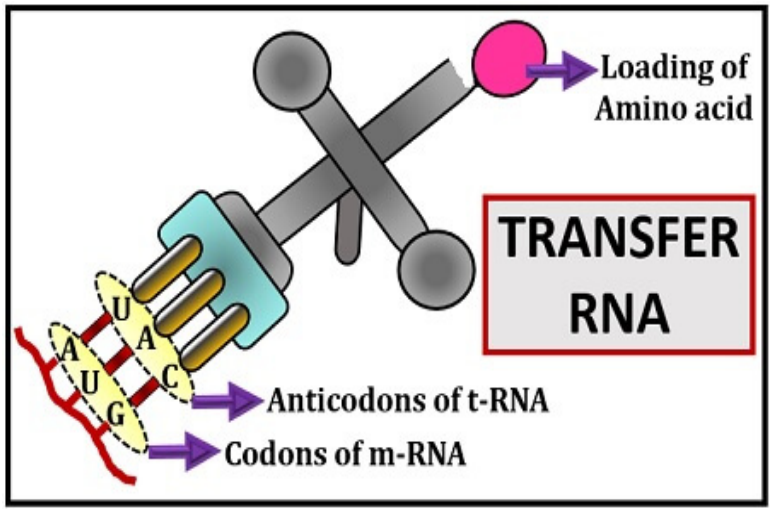


Ribosomes

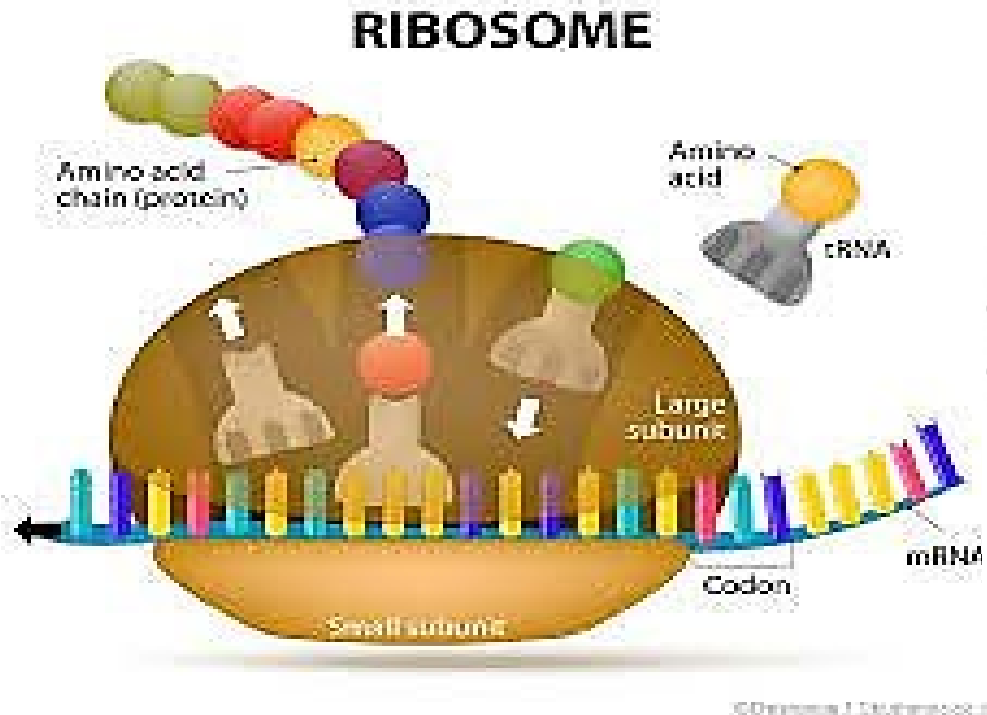
Ribosome offers a platform where **transfer RNAs** (tRNA) can align with mRNA. Ribosomes are assembled in the cytoplasm from ribosomal RNA subunits transcribed in **nucleolus**.



Transfer RNA



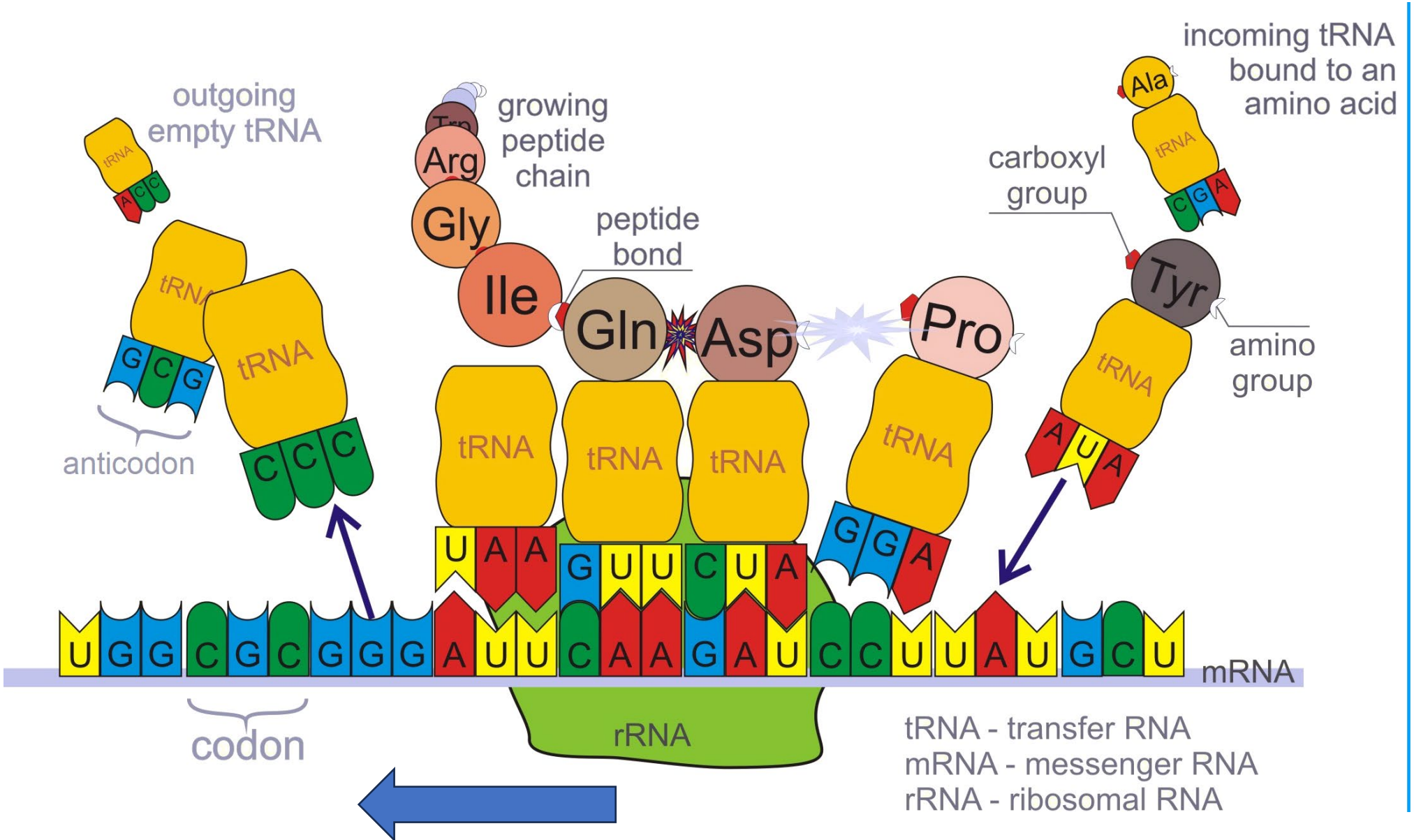
The mRNA has **codons** (sets of 3 bases) that match with *anti-codons* on the tRNA. **Each different 3 letter anti-codon carries a distinct amino acid**. So, the order of codons in mRNA directs the order of the amino acids.



Second letter

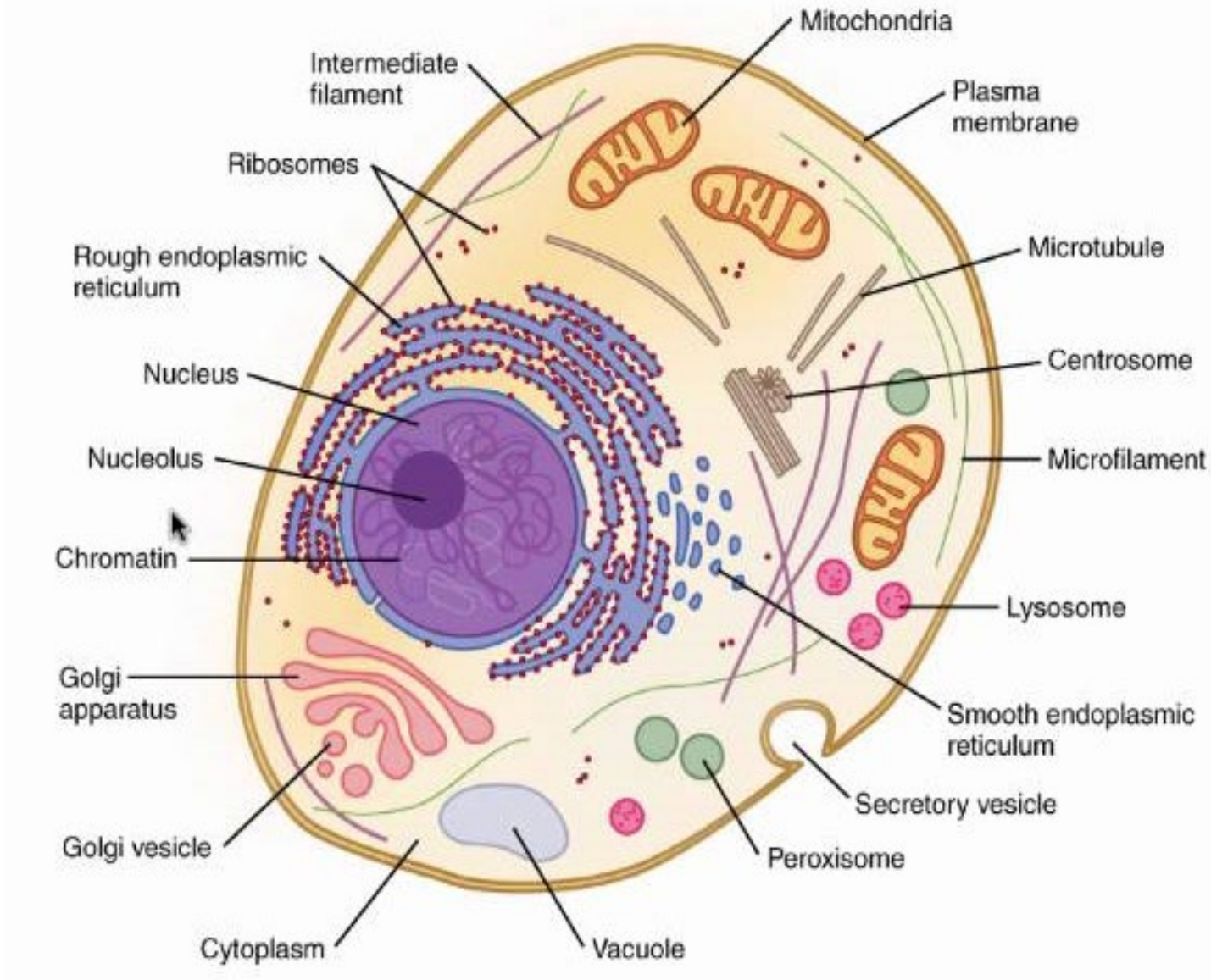
First letter	U	C	A	G	Third letter
U	UUU, UUC } Phe UUA, UUG } Leu	UCU, UCC, UCA, UCG } Ser	UAU, UAC } Tyr UAA Stop UAG Stop	UGU, UGC } Cys UGA Stop UGG Trp	U C A G
C	CUU, CUC, CUA, CUG } Leu	CCU, CCC, CCA, CCG } Pro	CAU, CAC } His CAA, CAG } Gln	CGU, CGC, CGA, CGG } Arg	U C A G
A	AUU, AUC, AUA } Ile AUG Met	ACU, ACC, ACA, ACG } Thr	AAU, AAC } Asn AAA, AAG } Lys	AGU, AGC } Ser AGA, AGG } Arg	U C A G
G	GUU, GUC, GUA, GUG } Val	GCU, GCC, GCA, GCG } Ala	GAU, GAC } Asp GAA, GAG } Glu	GGU, GGC, GGA, GGG } Gly	U C A G

Translation



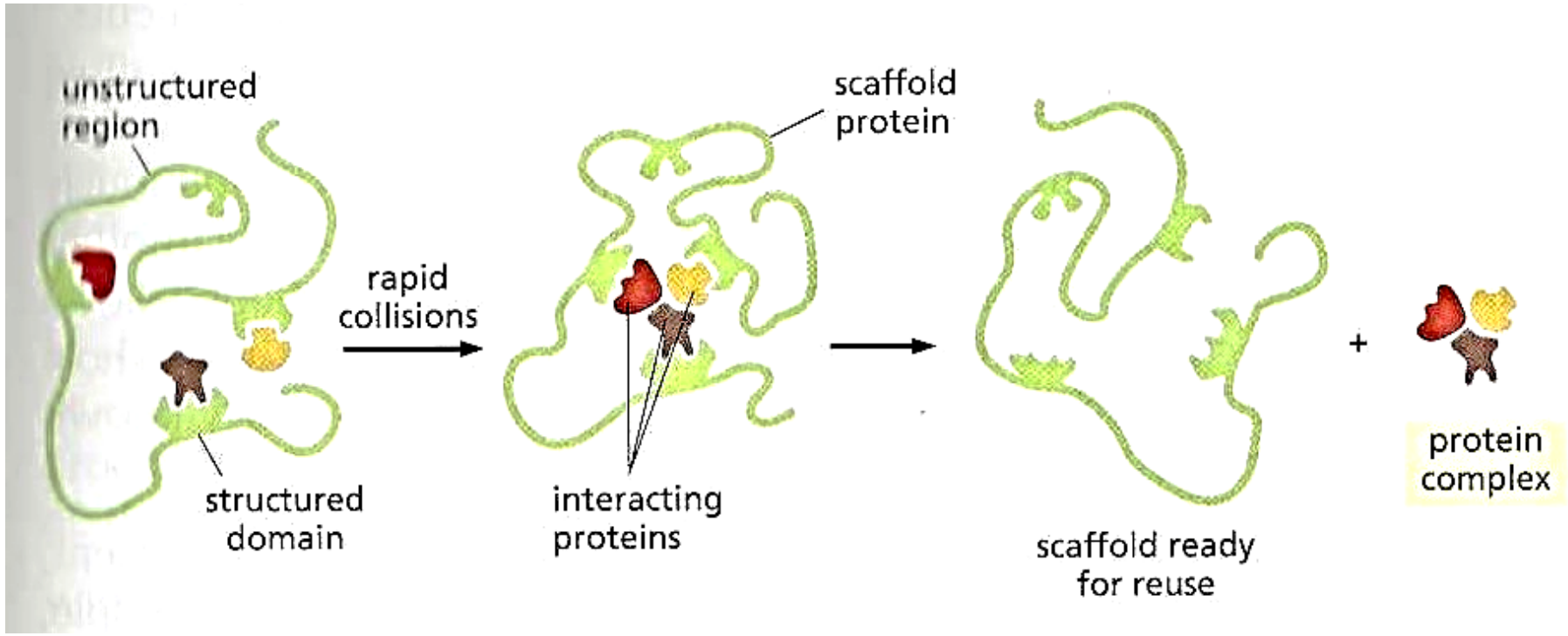
Free/bound ribosomes

Free ribosomes float free in the cytoplasm and synthesize proteins mostly for use within the cell.
Bound ribosomes on rough endoplasmic reticulum synthesize proteins for export (secretion), or to make some cell organelles or to use in lysosomes, for digestion.



Scaffolding aligns free proteins

Proteins that are translated by free ribosomes in the crowded busy cytosol may be assembled into larger structures by scaffolding proteins (chaperone proteins).



ER

A network of membranes within the cell.

Rough:

Proteins made by bound ribosomes are released inside the cisternae of the rER. There proteins are folded by chaperone proteins and modified by adding carbohydrate tags. Released in transport vesicles.

Smooth:

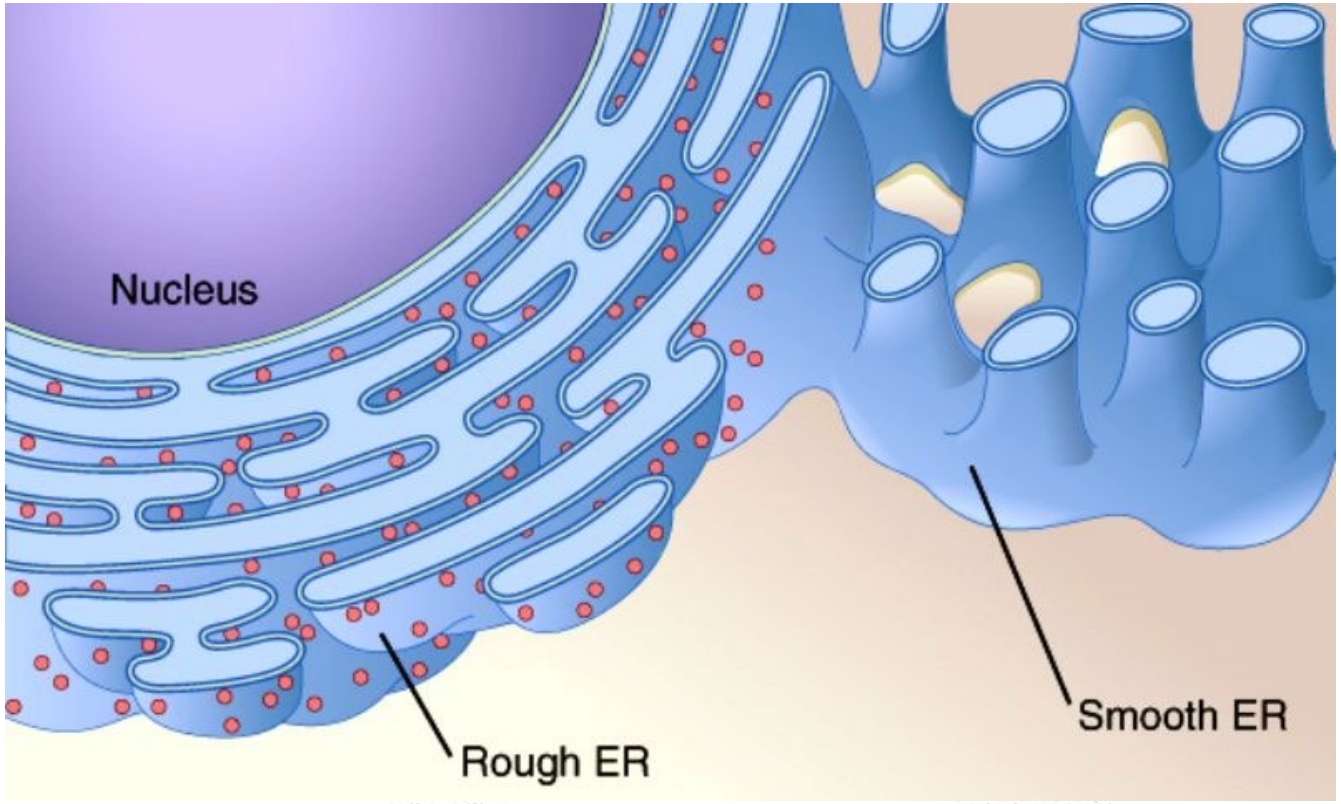
Synthesis of lipids and cholesterol for membranes

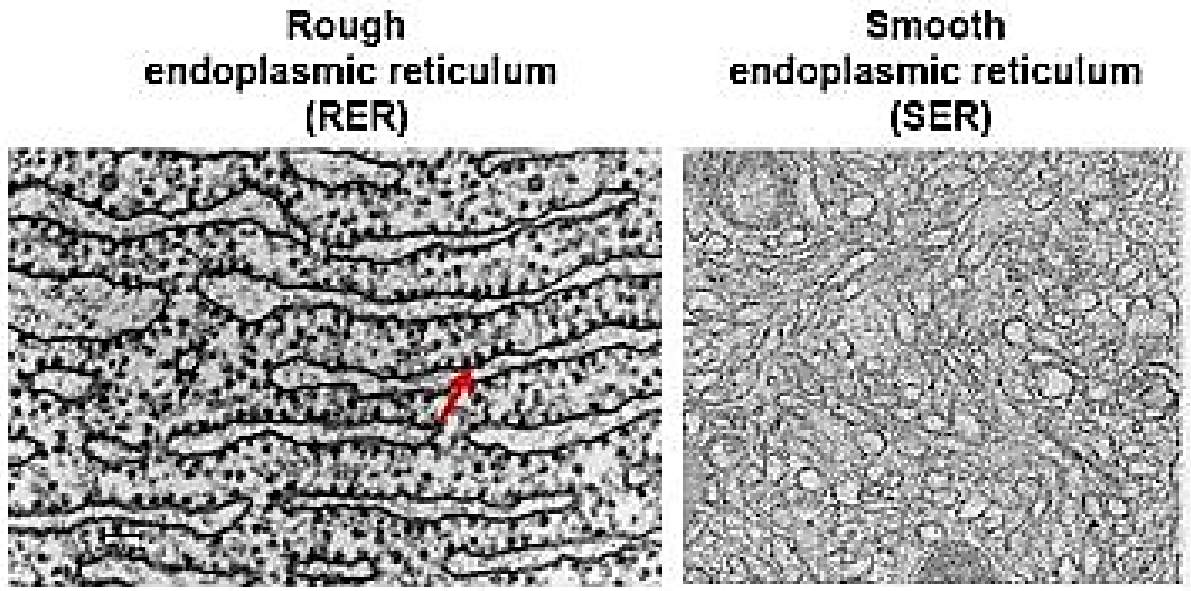
Synthesis of steroid hormones

Synthesis of glycogen (store glucose)

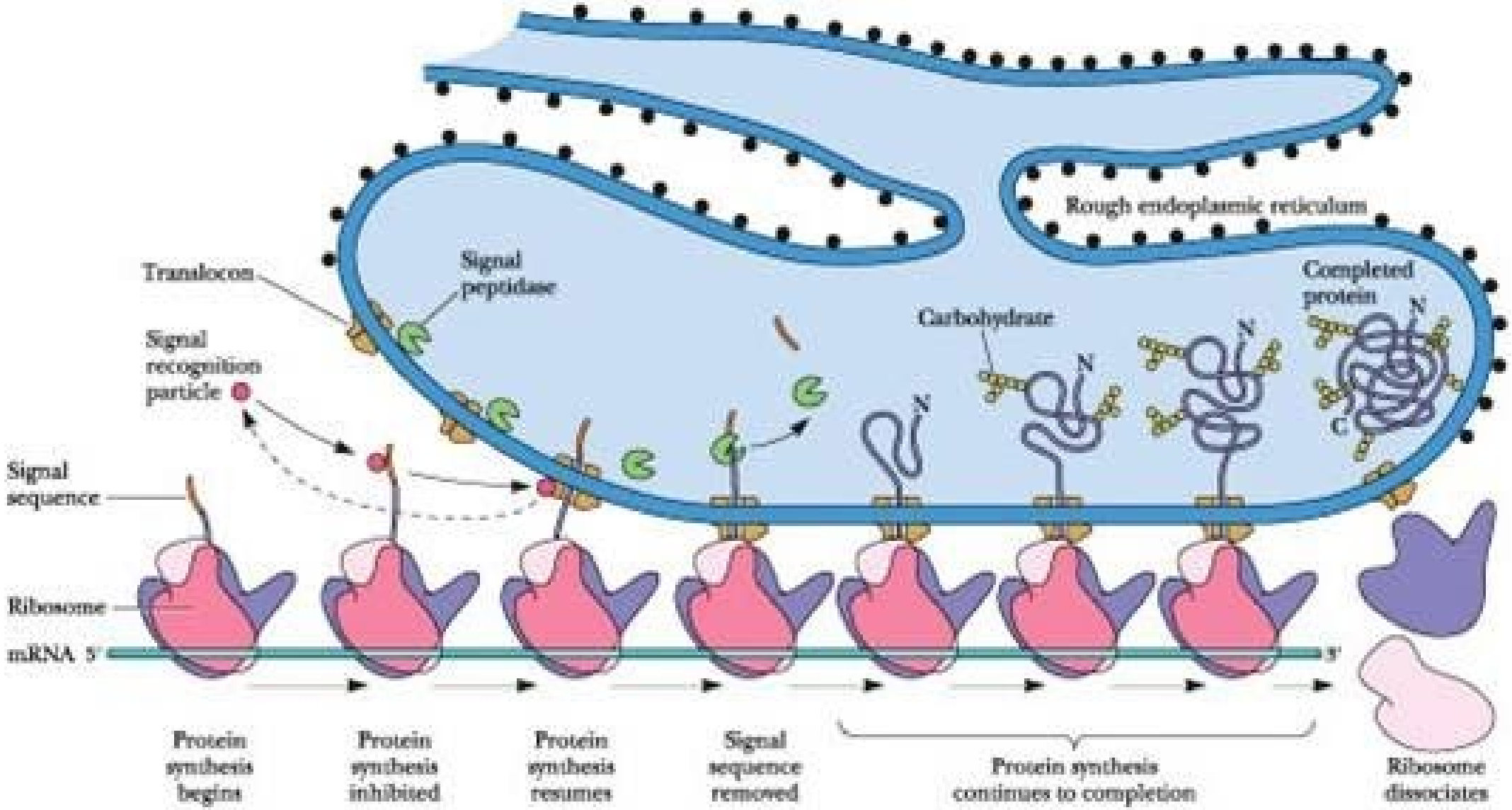
Control calcium concentrations (muscle)

Detox drugs, bilirubin (liver)



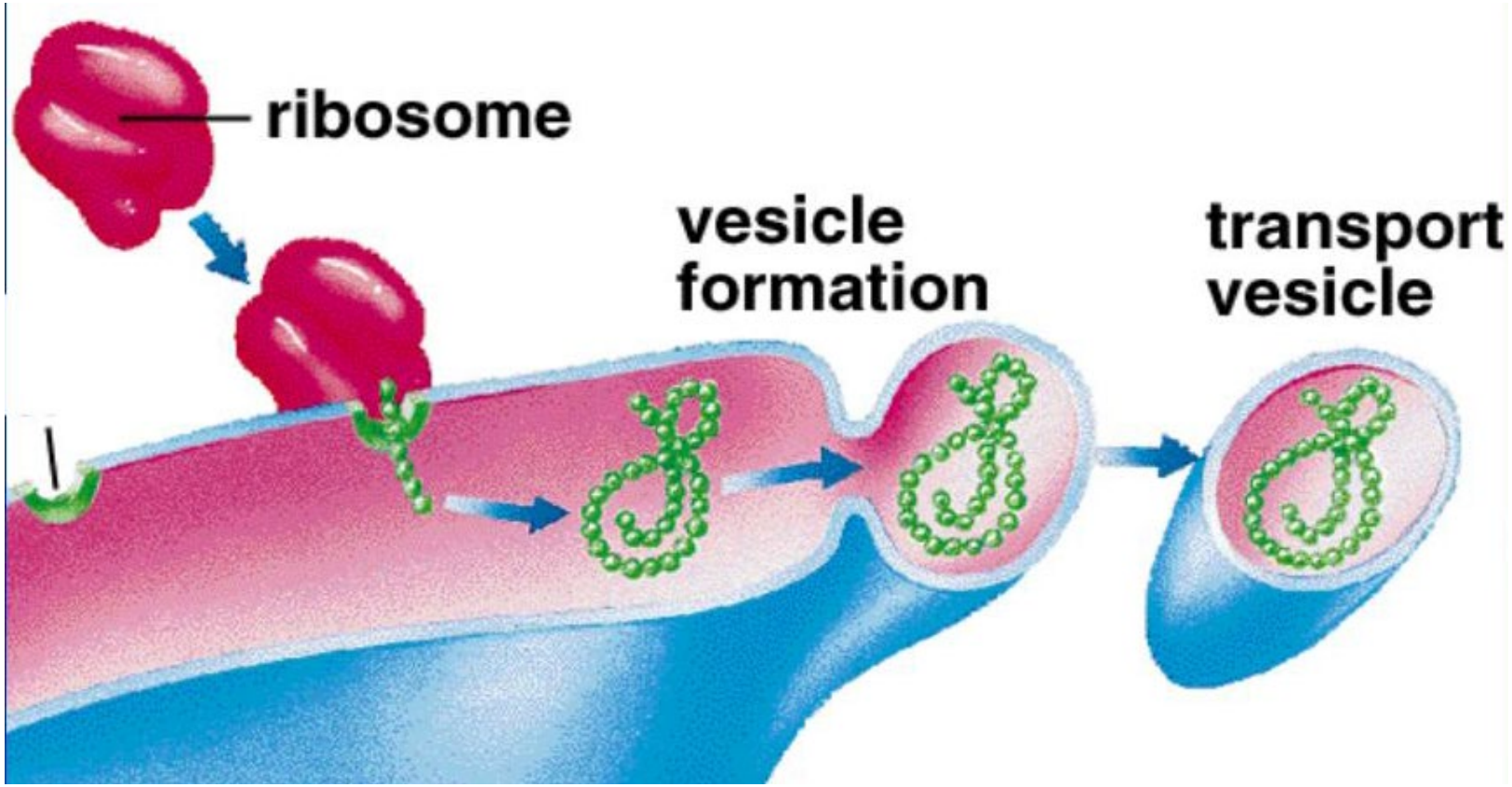


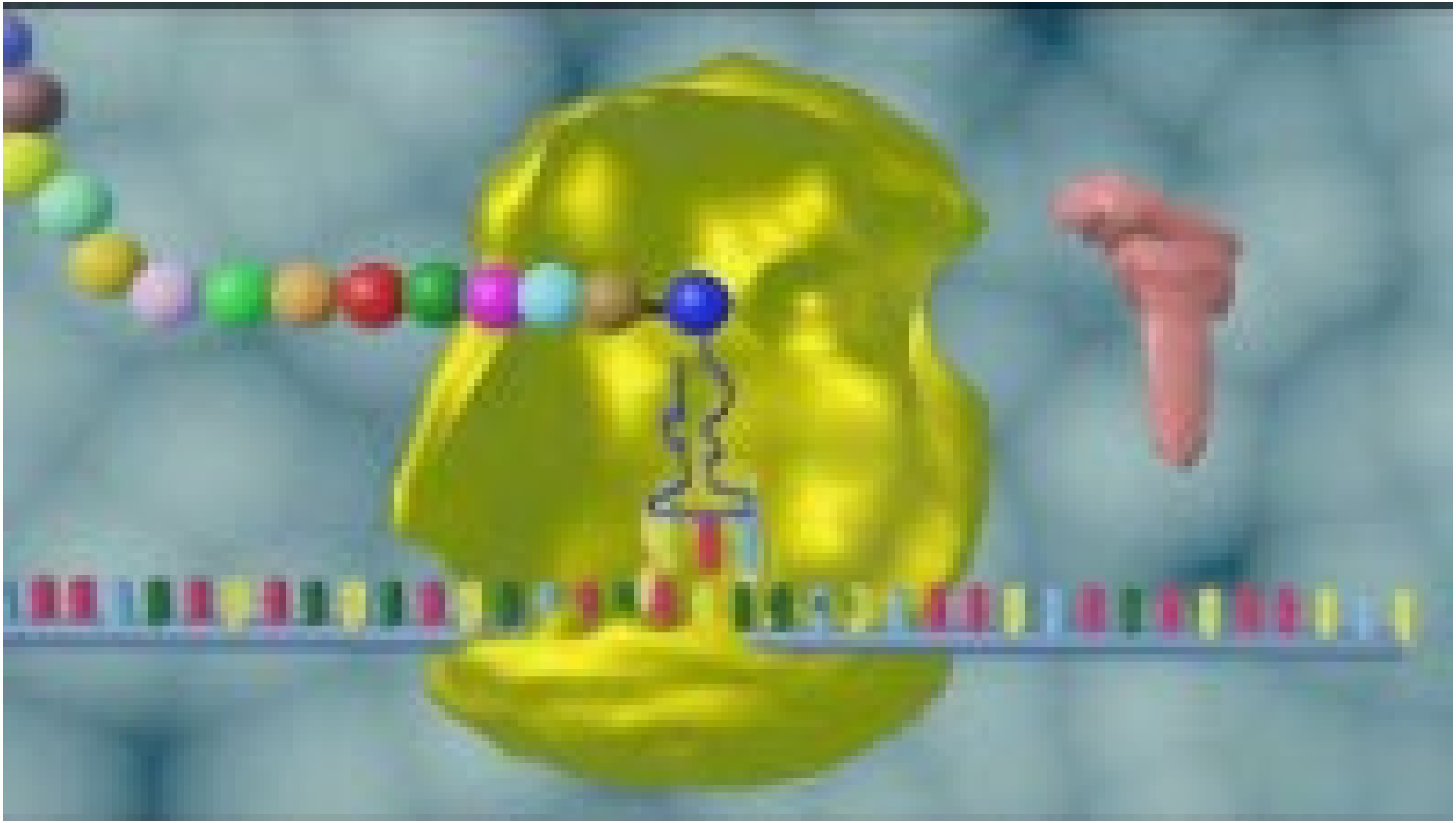
Growing protein injected into rER lumen



Rough Endoplasmic Reticulum packaging

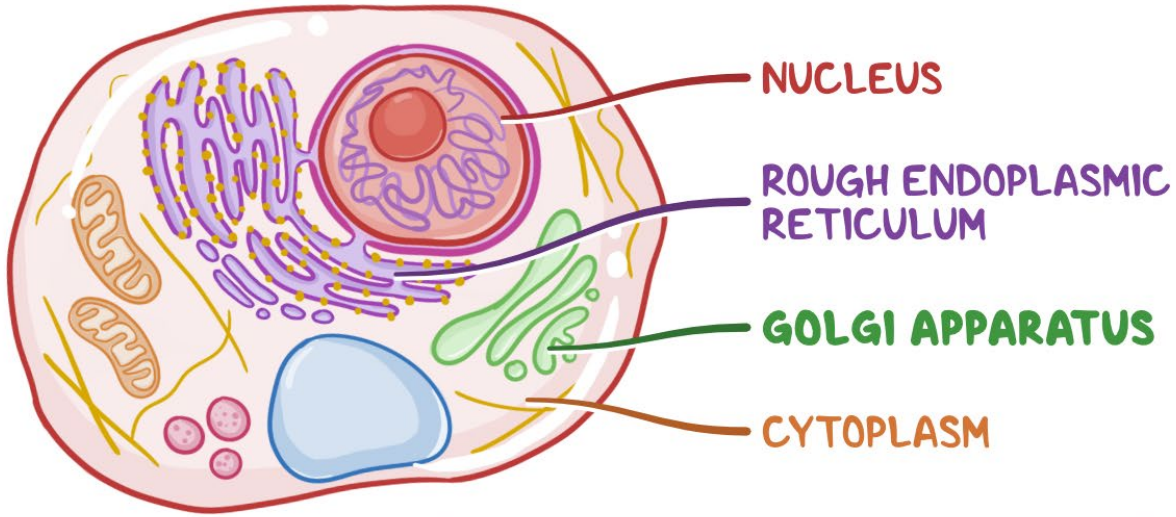
Inside the rER, add sugars (glycolipids) or phospholipids (membrane components) and packaged into vesicles.

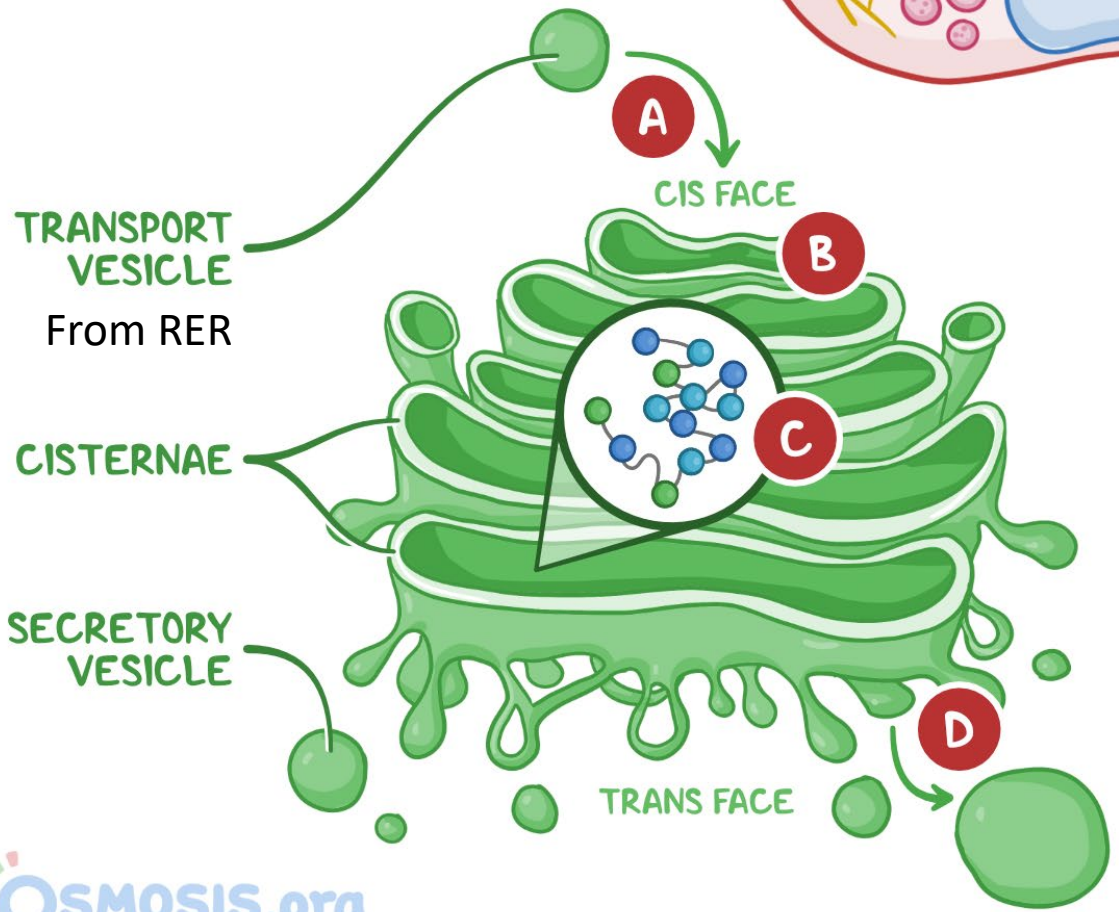




Golgi apparatus: post office

Proteins are further modified and sorted as they move through the layers of cisternae.



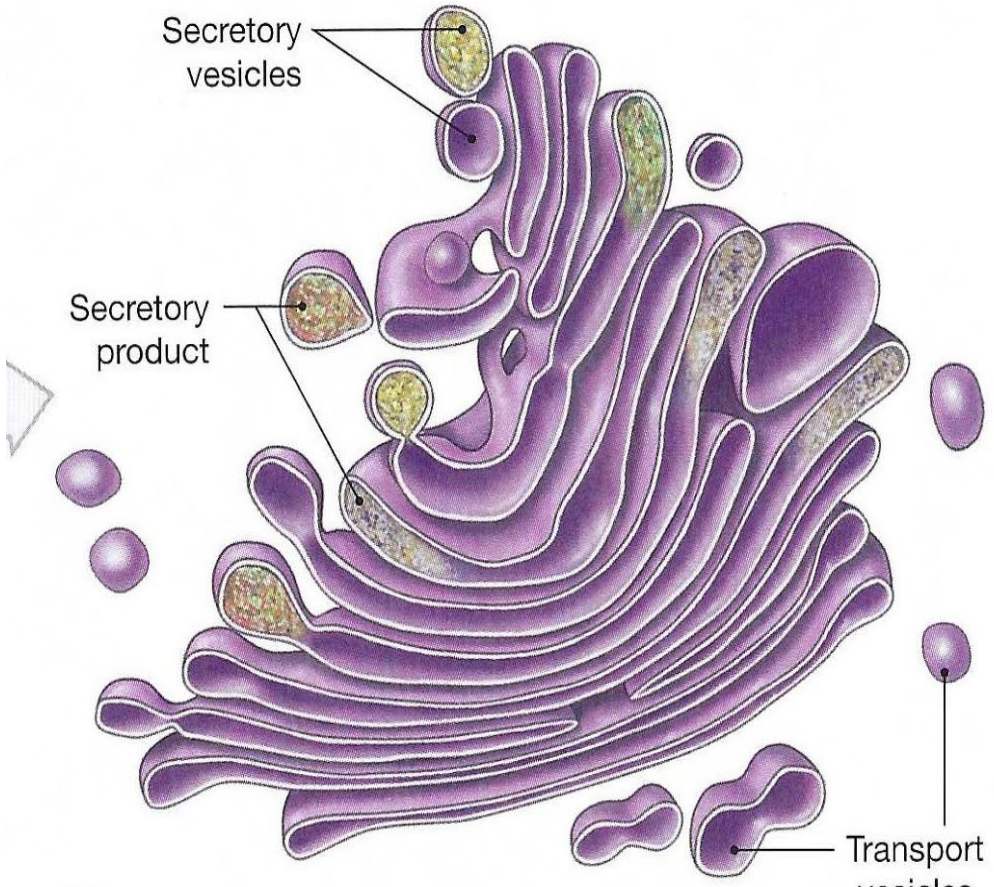


FUNCTION

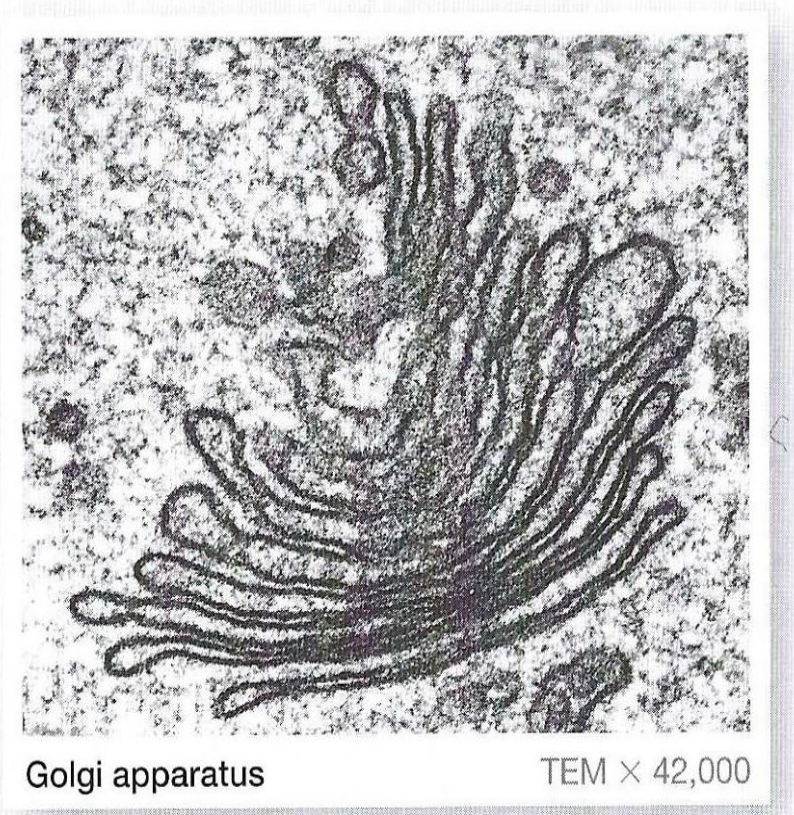
- **A** TRANSPORT VESICLES BRING MOLECULES from ROUGH ENDOPLASMIC RETICULUM
- **B** MOLECULES FUSE with MEMBRANE & are SORTED BASED on DESTINATION
- **C** MOLECULES UNDERGO REMODELING & MODIFICATIONS in CISTERNAE
- **D** MODIFIED MOLECULES are SECRETED OUT of CELL or to ANOTHER ORGANELLE

Golgi Functions

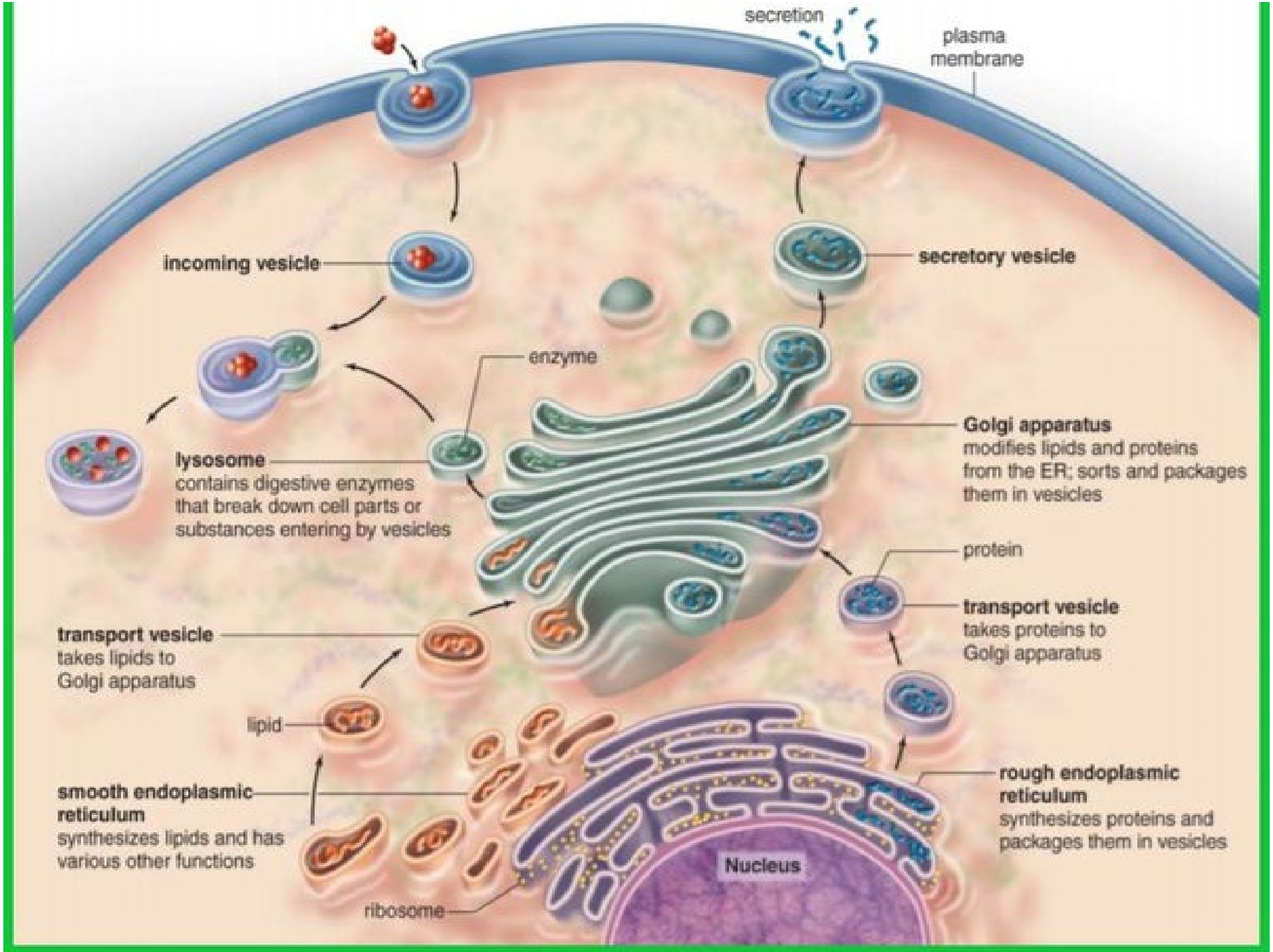
1) Packages secretions for export
2)Renews plasma membrane
3)Packages digestive enzymes for lysosomes



a Here is a three-dimensional view of the Golgi apparatus with a cut edge.

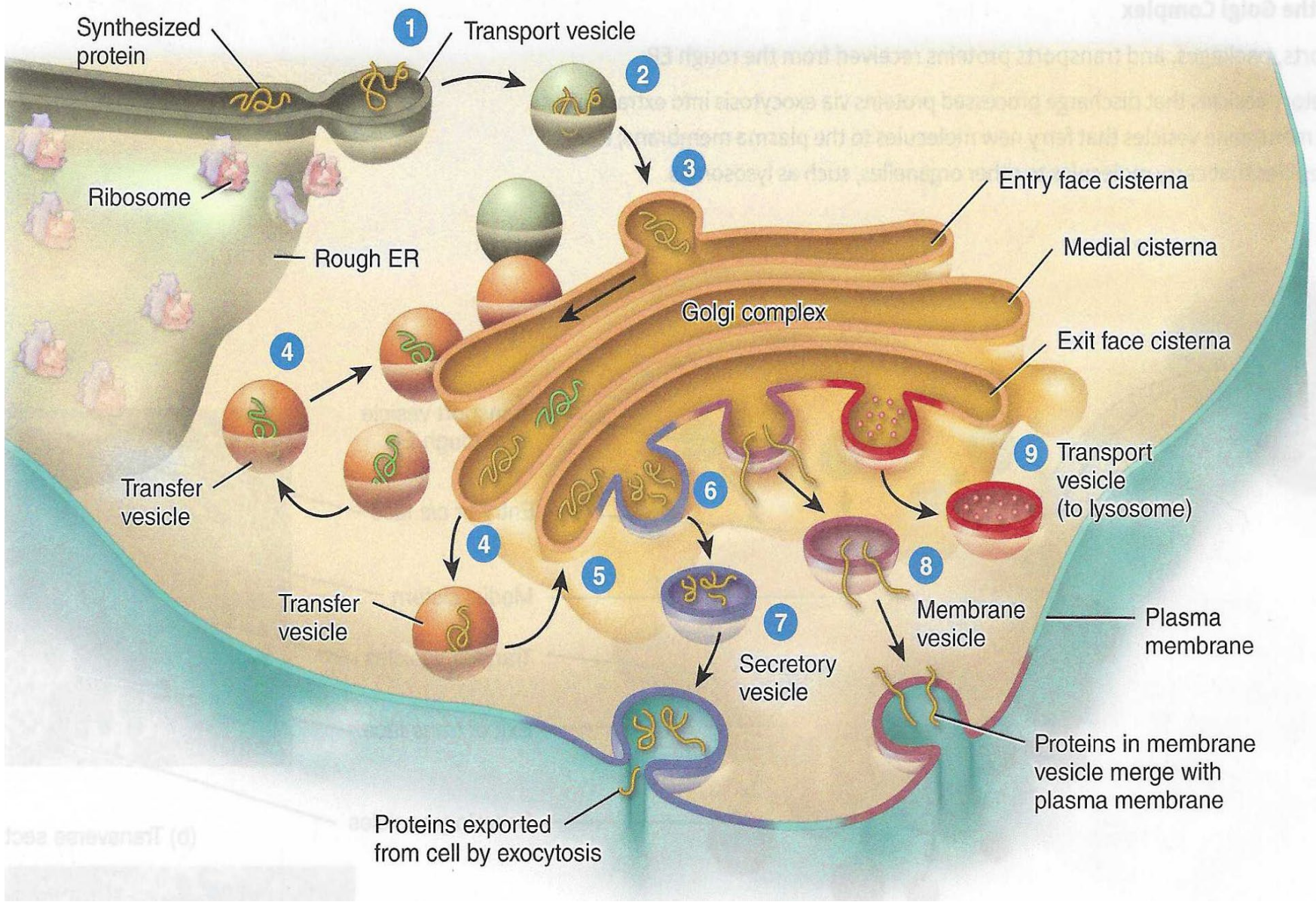


b This is a sectional view of the Golgi apparatus of an active secretory cell.


secretion
plasma membrane
incoming vesicle
secretory vesicle
enzyme
lysosome
contains digestive enzymes that break down cell parts or substances entering by vesicles
Golgi apparatus
modifies lipids and proteins from the ER; sorts and packages them in vesicles
protein
transport vesicle
takes proteins to Golgi apparatus
transport vesicle
takes lipids to Golgi apparatus
lipid
smooth endoplasmic reticulum
synthesizes lipids and has various other functions
rough endoplasmic reticulum
synthesizes proteins and packages them in vesicles
Nucleus
ribosome

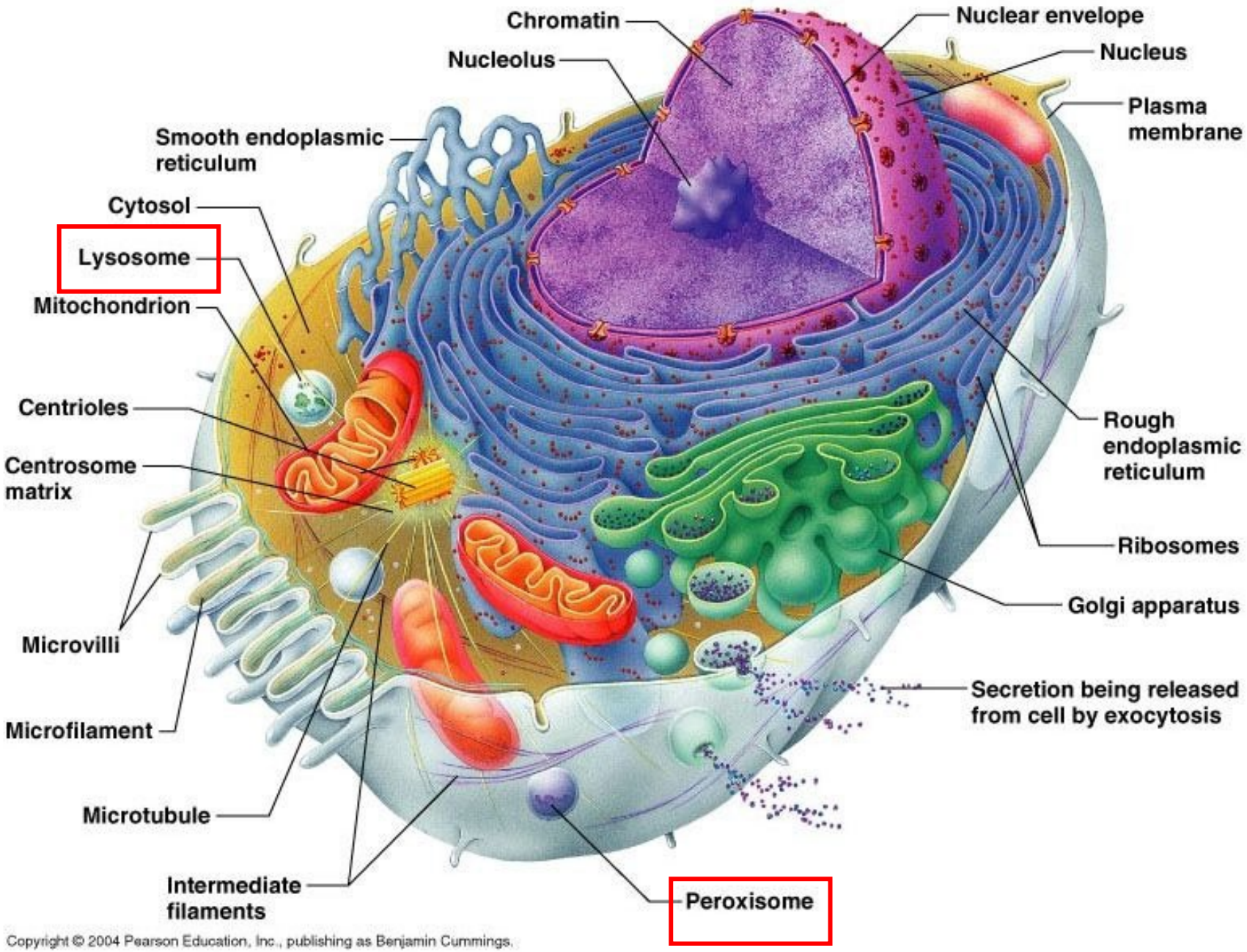
Golgi Sorting

1) Secretory (hormones, enzymes) **7**
2) Membrane components (entire cell surface replaced each hour) **8**
3) Digestive lysosomes **9**



Digestion

Lysosomes, peroxisomes and proteasomes

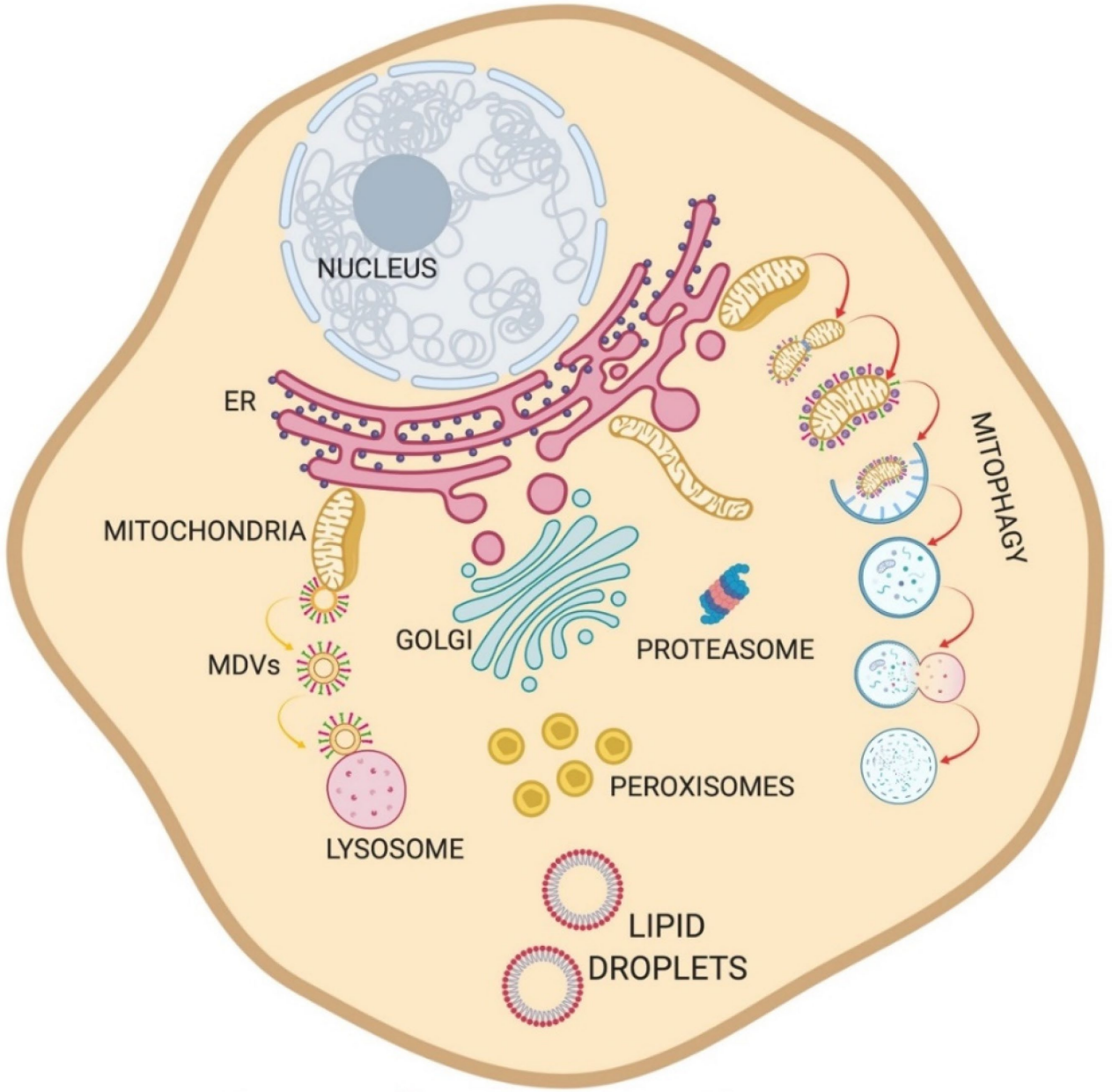


Digestion

Lysosomes: vesicles contain digestive enzymes in highly acidic environment; fuse with vesicles containing engulfed materials. Degrade old organelles (*autophagy*) or endocytosed particles. Fuel for cell.

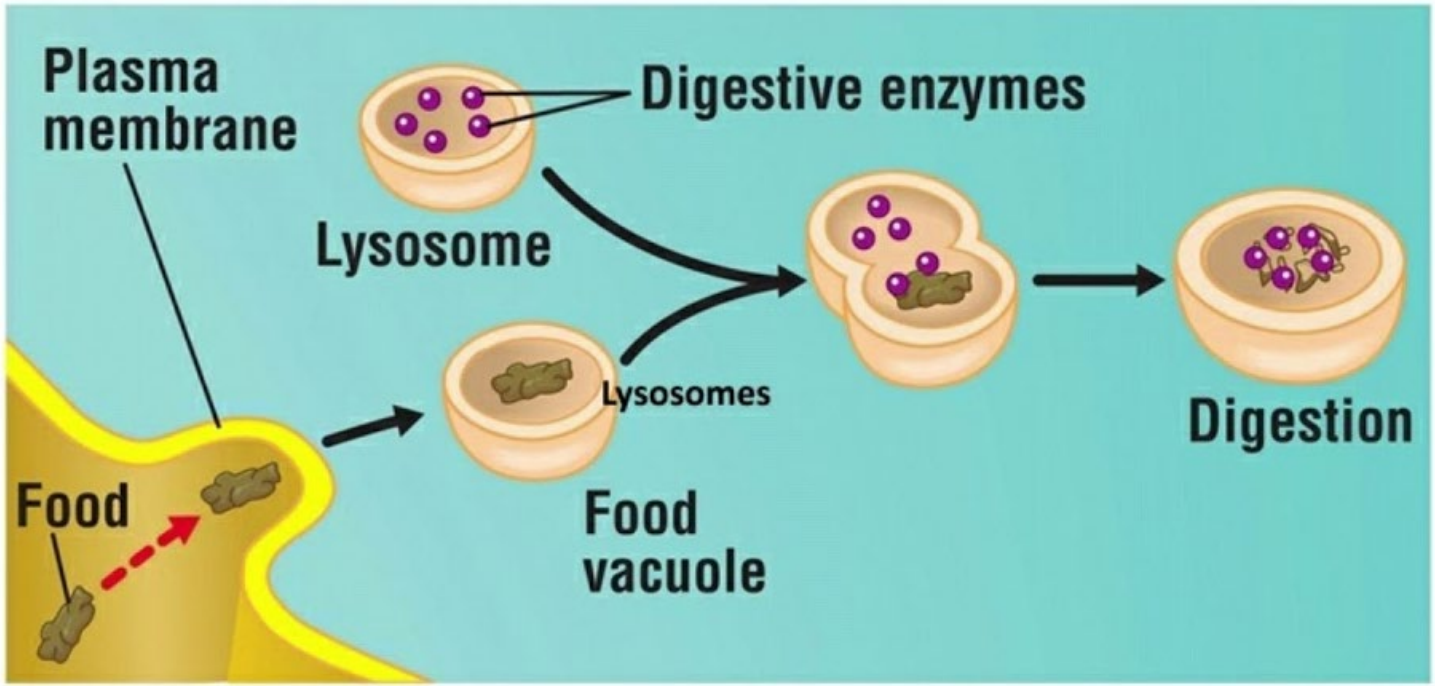
Peroxisomes : vesicles contain enzymes that breakdown fats and some drugs, using **hydrogen peroxide**. Synthesize membrane components for myelination.

Proteasomes: a protein complex, not a vesicle. Denatured proteins bound to **ubiquitin** are destroyed.

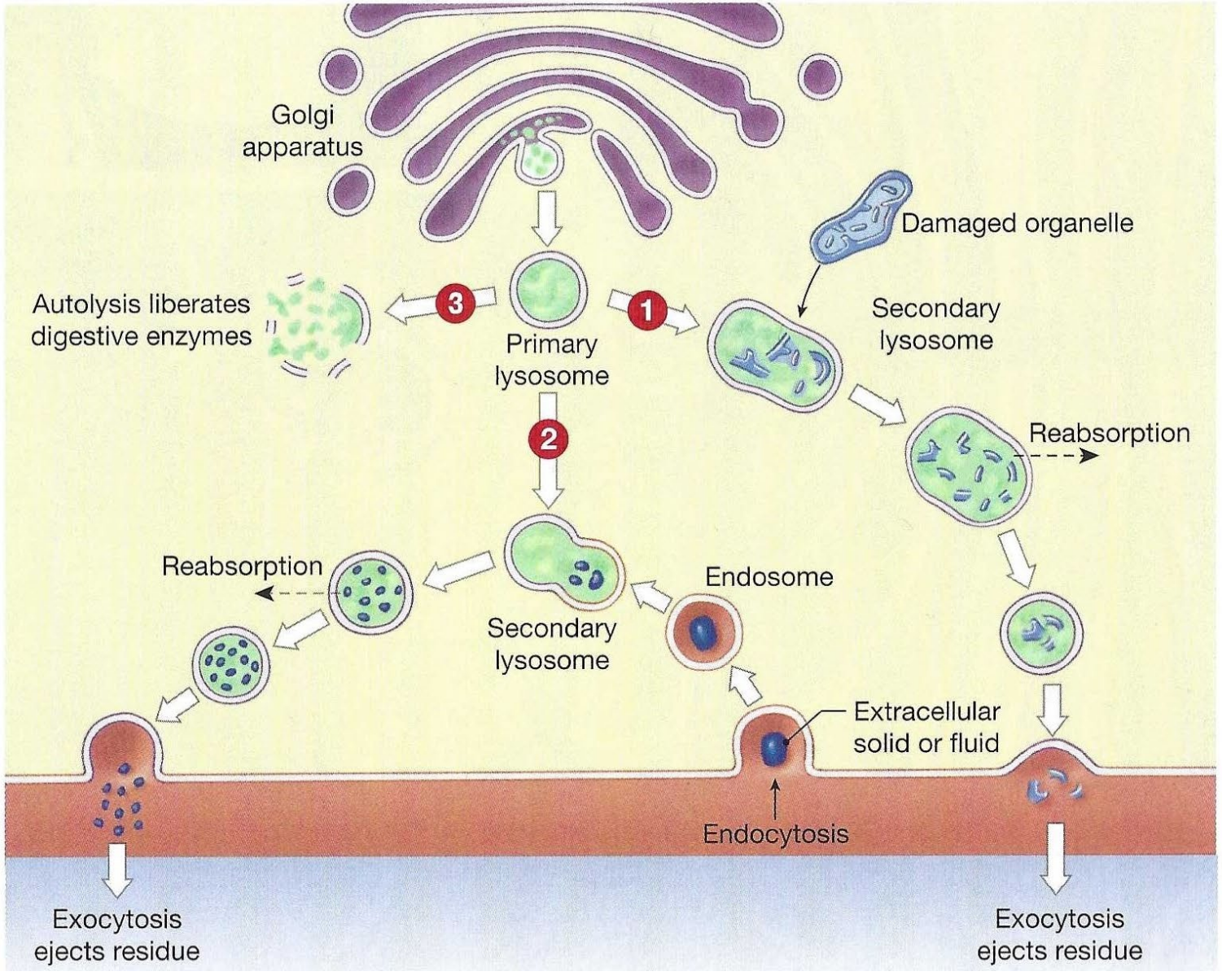


Lysosomes

1) **Digest food**: 60 kinds of powerful digestive enzymes in an acid (pH 5) environment created by active transport proton pumps. Other membrane proteins transport products of digestion (glucose, fatty acids and amino acids) from lysosome into cytosol.



2) Autophagy; 3) Autolysis (suicide)

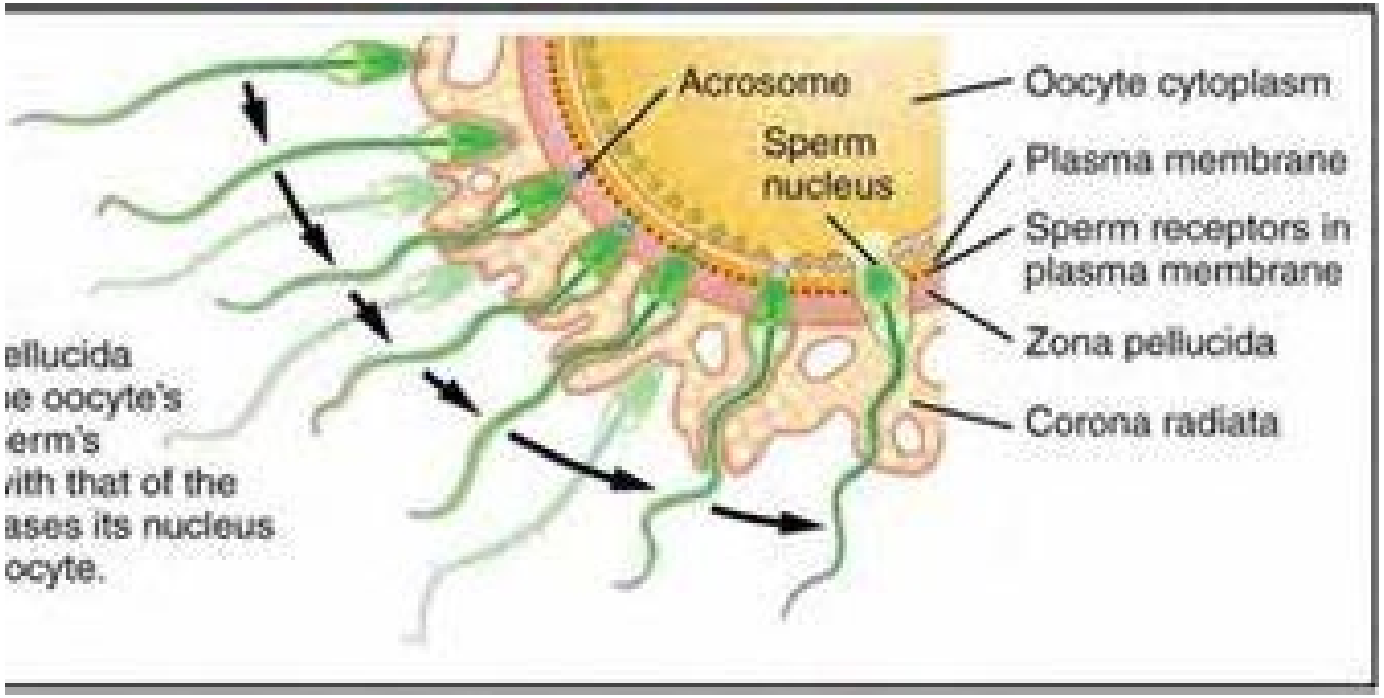


Activation of lysosomes occurs when:

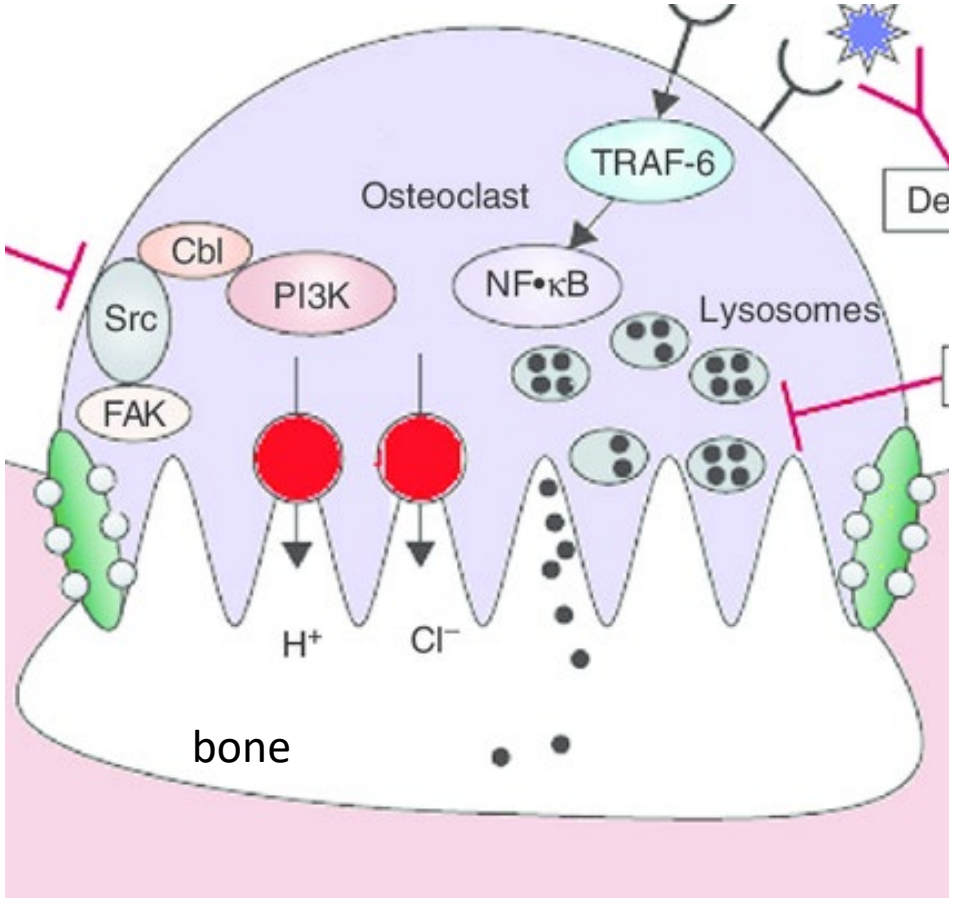
1. A primary lysosome fuses with the membrane of another organelle, such as a mitochondrion
2. A primary lysosome fuses with an endosome containing fluid or solid materials from outside the cell
3. The lysosomal membrane breaks down during autolysis following injury to, or death of, the cell

4) Extracellular digestion

Allow sperm to penetrate egg



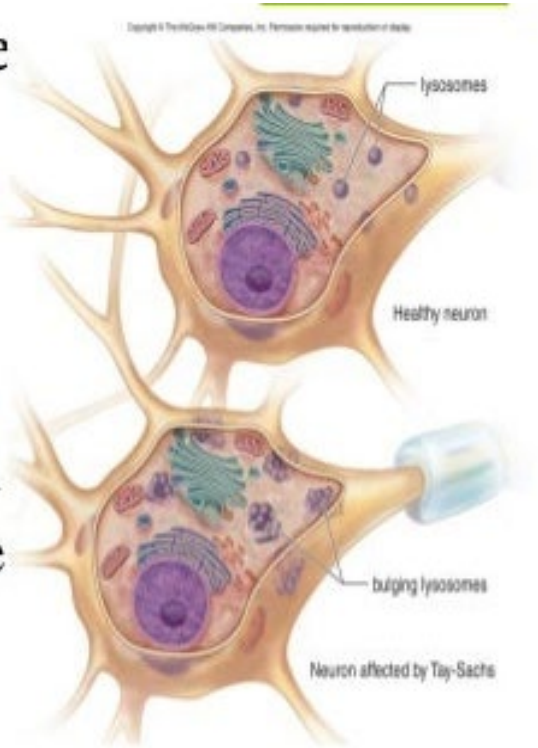
Digest and remodel bone: release acids and digestive enzymes

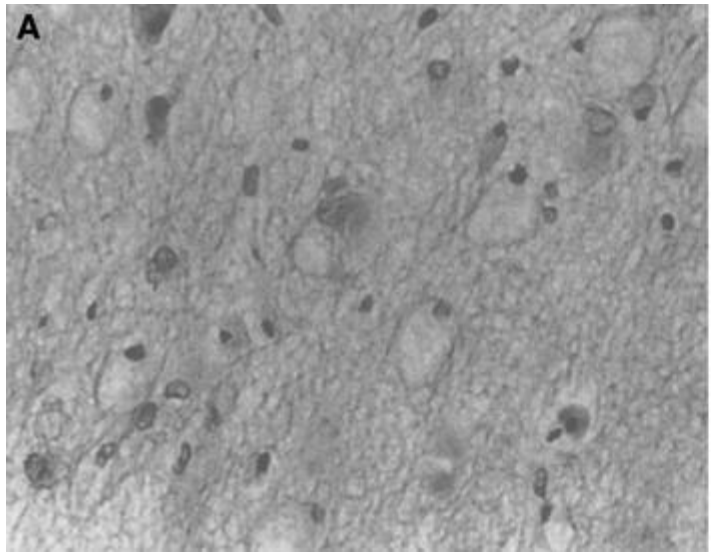


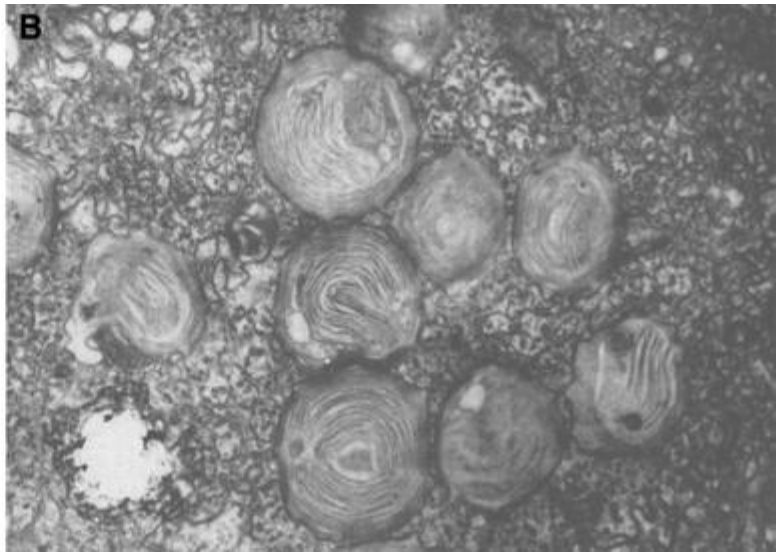
Lysosome Storage Diseases

Several lysosomal diseases, eg Tay-Sachs caused by faulty lysosomal enzymes

- Normally, β-hexosaminidase A helps to degrade a lipid called **GM2 ganglioside**
- In **Tay-Sachs** individuals, the enzyme is absent or present only in very reduced amounts, allowing excessive accumulation of the **GM2 ganglioside** in neurons.

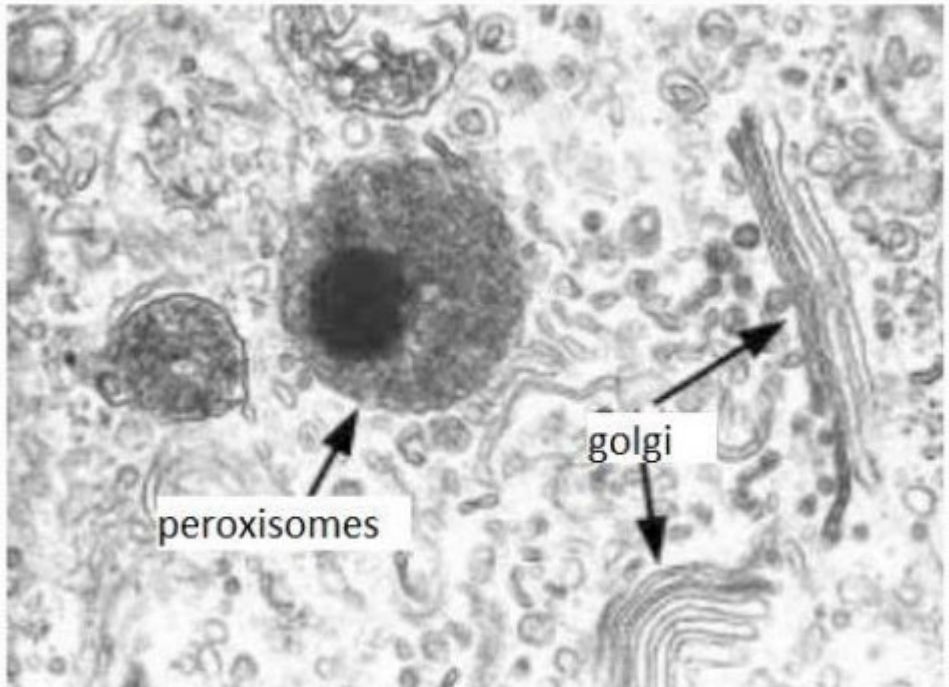


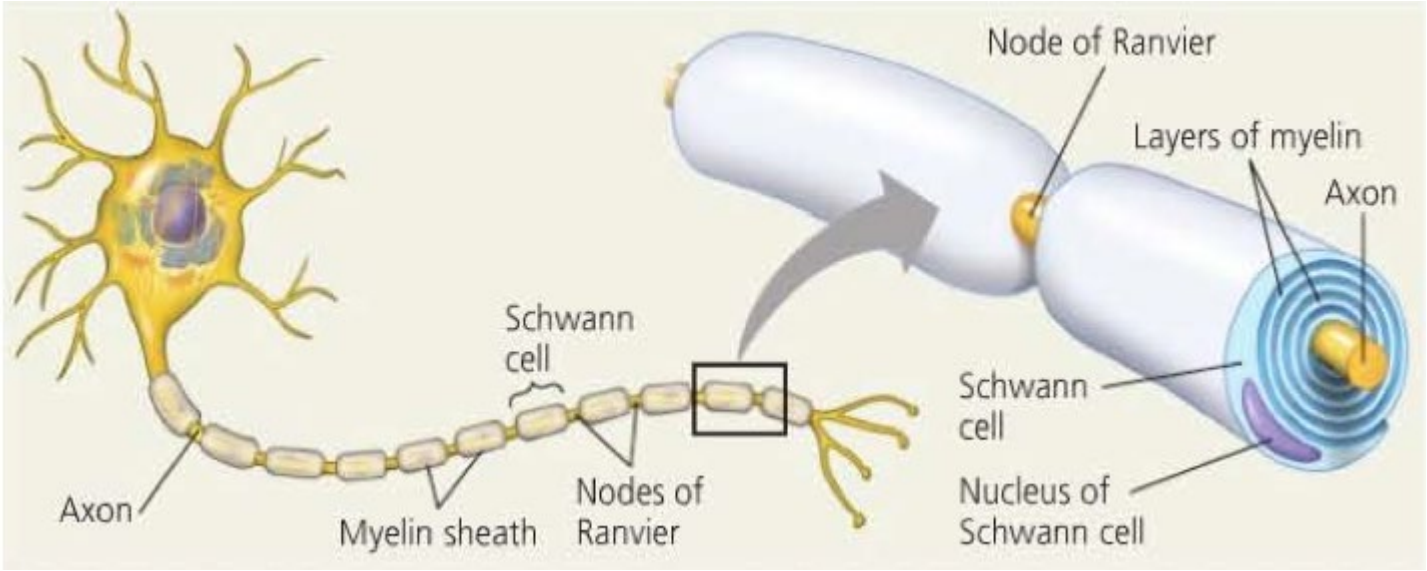




Peroxisomes

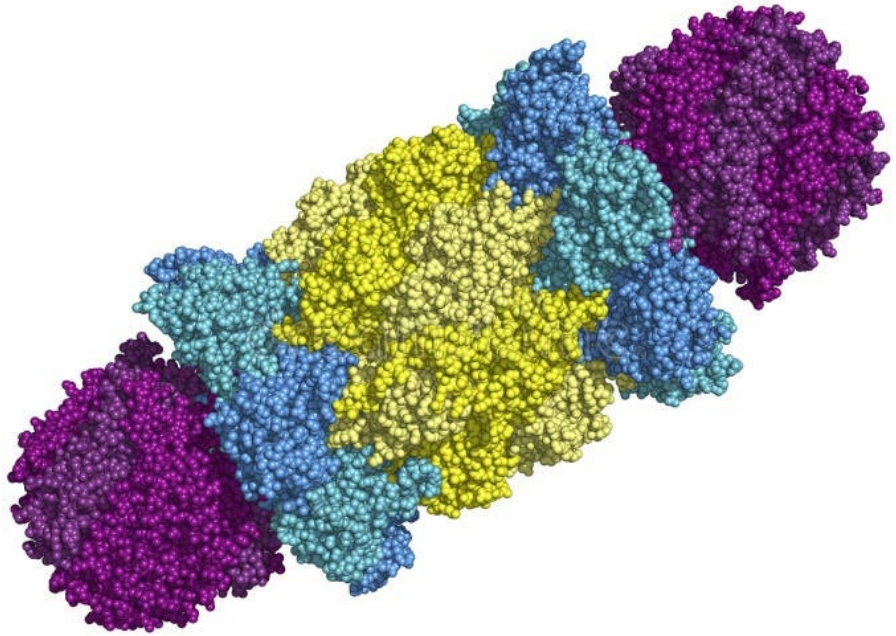
Membrane-bound organelles that contain oxidative enzymes that:
-Detoxify alcohol (prevalent in liver and kidney) and other toxic molecules
-Use H_2O_2 to breakdown fatty acids
-Help synthesize myelin, bile
Zellweger Syndrome: malfunctions of brain, liver, kidney

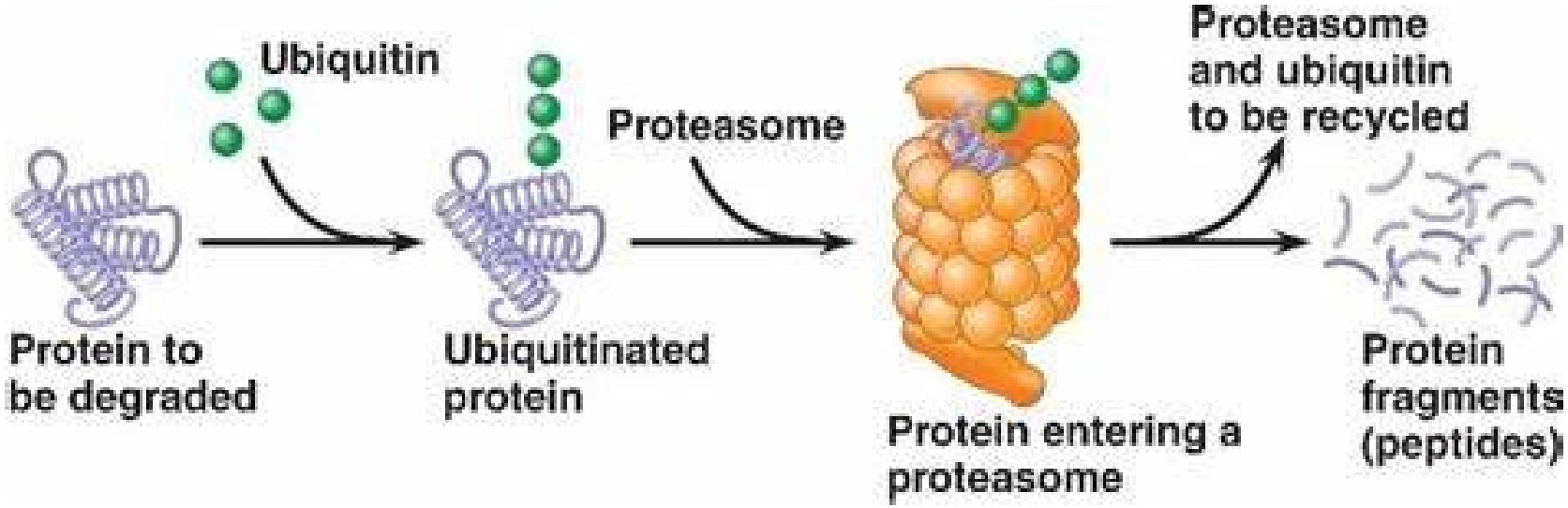




Proteasomes

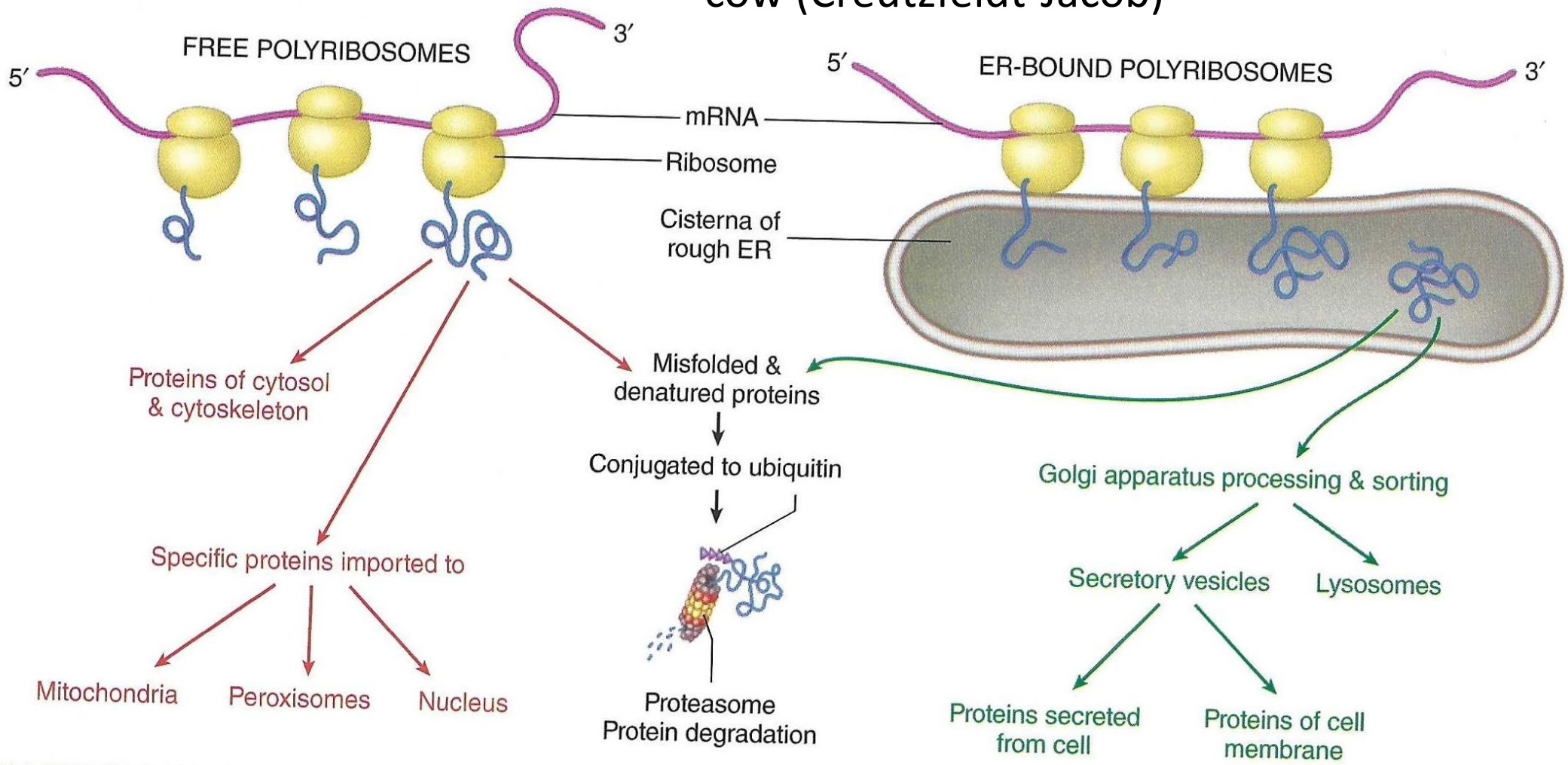
Faulty, misfolded or excess proteins are tagged with **ubiquitin** and digested.





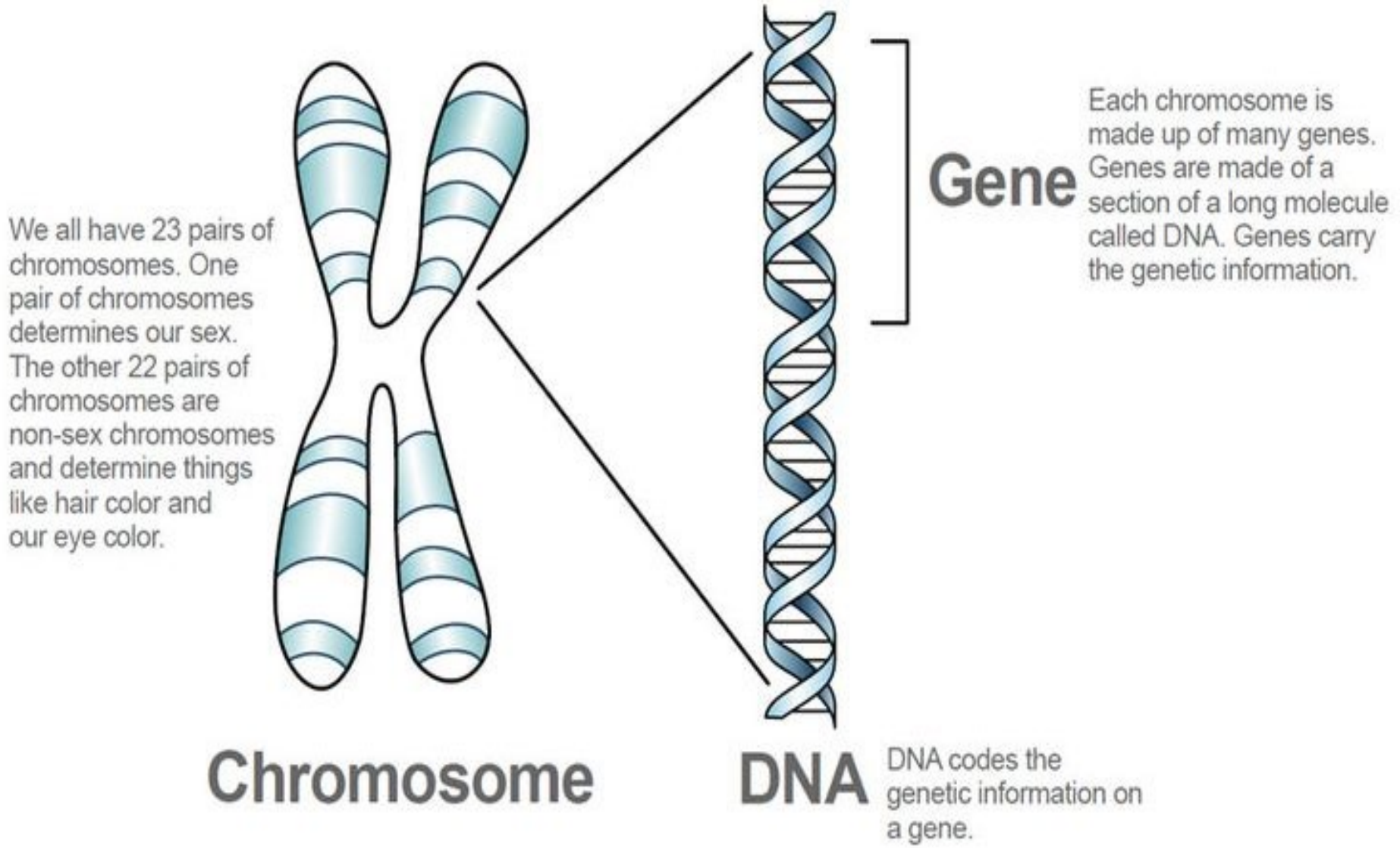
Protein Folding

Prions are misfolded proteins that can cause misfolding in other proteins : mad-cow (Creutzfeldt-Jacob)



The Great "Unknome"

Only 1.5% of the human genome codes for proteins. Only 20% of these are well studied. The other 16,000 genes, and their proteins, are unknown!



Covid Vaccine and mRNA

Knowing the amino acid sequence of the spike protein of the virus, can make mRNA that codes for that protein. MRNA is a short-lived molecule, so encase in lipid nanosphere. Injected nanosphere fuses with body cells, directs them to make virus protein. Immune system makes Ab to protein.