11

Cytology

Doctor 2019 | Medicine | JU

◉ Sheet ○ Slides

Done By

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Contributed in the Scientific Correction

Contributed in the Grammatical Correction

Doctor

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12.5: Membrane Biosynthesis in the Endoplasmic Reticulum

- Membranes do not arise de novo that is, as new entities from pools of proteins and lipids that mixed together. Instead, they arise from pre-existing membranes.

- To clarify …membrane grow by addition of proteins & lipids into existing membranes in the ER.

- Each compartment has unique membranes due to :

Membrane components move from the ER to all other cell compartment;
while membrane moving through compartments his proteins & lipids are modified by enzymes (that reside in the cell's various organelles); so lead to unique composition & distinct identity. for each membrane compartment.

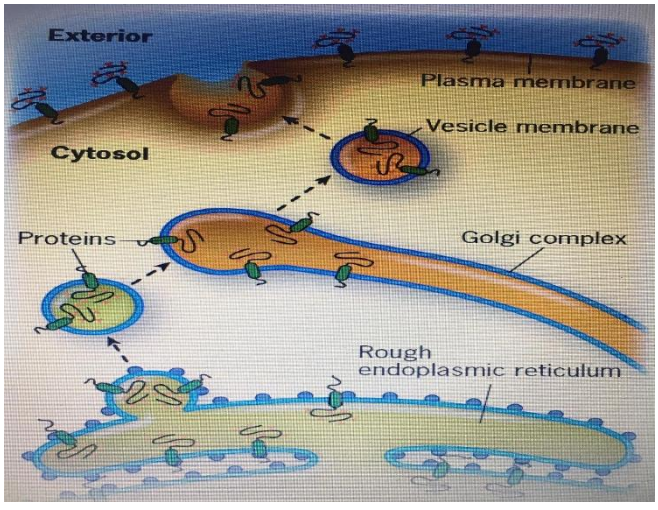
- Not only the difference found in various membrane compartment but also in *the 2 phospholipid layers (leaflets)*
- Cellular membranes is asymmetric (why??)

1. *the 2 phospholipid layers (leaflets)* have different compositions, & this <u>asymmetry is established initially in the ER</u>

Asymmetry is maintained as membrane carriers bud from one compartment & fuse to the next. How?

1. Thus, domains located at the ER membrane cytosolic surface can be identified on the cytosolic surfaces of transport vesicles & Golgi cisternae & the internal (cytoplasmic) surface of the plasma membrane
2. Similarly, domains situated at the luminal surface of the ER membrane maintain their orientation & are found at the external (exoplasmic) surface of the plasma membrane like: sugar.

Important: What we find in cytosol remain in cytosol but what found in lumen stay in the lumen so then will be in cell surface(away from cytosol)



Maintenance of membrane asymmetry. As each protein is synthesized in the rough ER, it becomes inserted into the lipid bilayer in a predictable orientation determined by its amino acid sequence. This orientation is maintained throughout its travels in the endomembrane system, as illustrated in this figure. The carbohydrate chains, which are first added in the ER, provide a convenient way to assess membrane sidedness because they are always present on the cisternal side of the cytoplasmic membranes, which becomes the exoplasmic side of the plasma membrane following the fusion of vesicles with the plasma membrane.

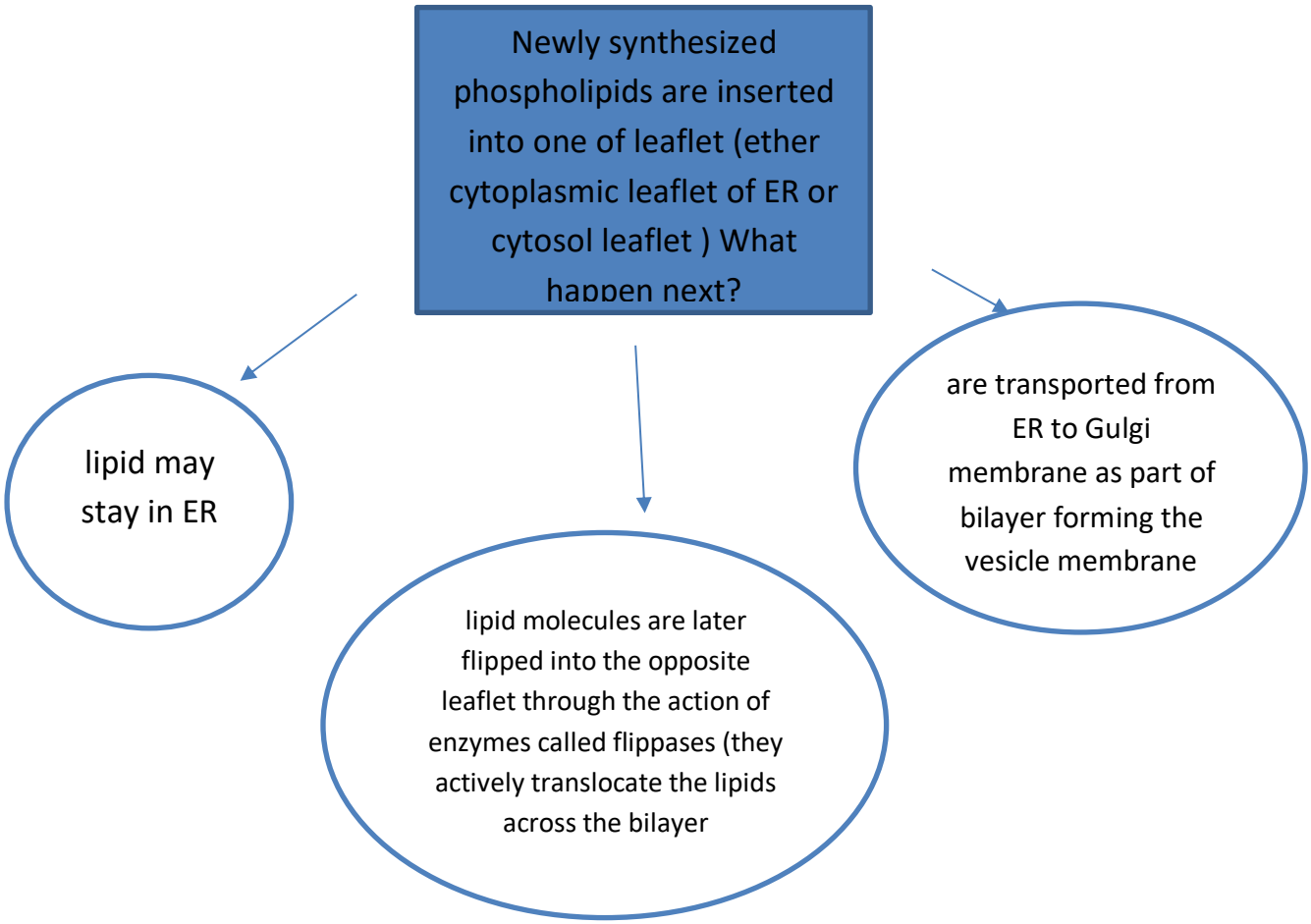
- The ER lumen (as well as other secretory pathway compartments) is a lot like the extracellular space. because of its high calcium concentration & abundance of proteins with disulfide bonds & carbohydrate chains

- All lipid membrane are synthesized entirely within the ER membrane with the following exceptions：

1.phingomyelin & glycolipids, whose synthesis starts in the ER & is completed in the Golgi complex .

2.Some of the unique mitochondrial & chloroplast membrane lipids (synthesized by enzymes residing in those membrane.

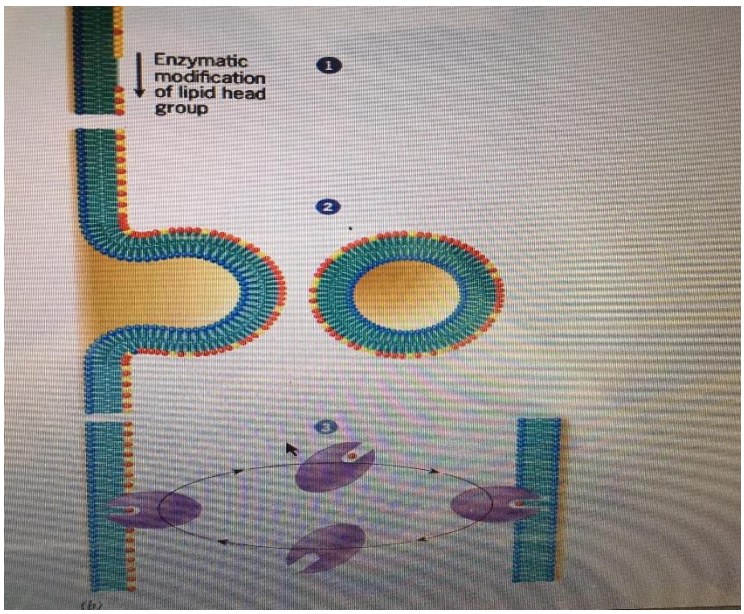
- Integral ER membrane enzymes with their active sites facing the cytosol are the same enzyme that involved in phospholipid synthesis .



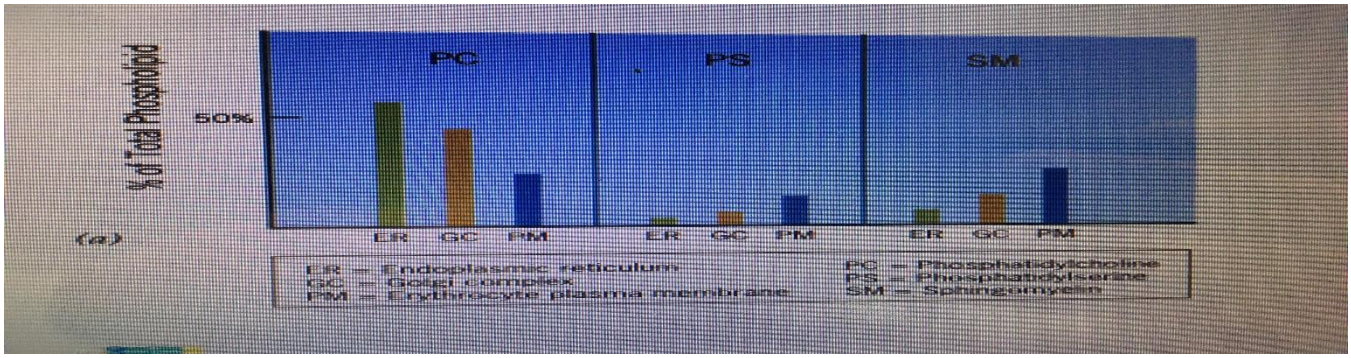
- Why the lipid differ from one organelle to other ??

1. Conversion of one type of phospholipid to another - most membranous organelles have enzymes that modify lipids already present in the membrane (example – phosphatidylserine to phosphatidylcholine)
2. When vesicles bud from a compartment, some types of phospholipids may be preferentially included within the membrane of the forming vesicle, while other types may be left behind
3. Cells contain **lipid-transfer proteins** that can bind & transport lipids *through the aqueous cytosol* from one membrane compartment to another.

- These proteins facilitate the movement of specific lipids from the ER to other organelles without the involvement of transport vesicles .This process occur in site where ER become close to the outer membrane of other organelle .



Modifying the lipid composition of membranes.
(a) Histogram indicating percentage of each of three phospholipids (phosphatidylcholine, phosphatidylserine, and sphingomyelin) in three different cellular membranes (ER, Golgi complex, and plasma membrane). The percentage of each lipid changes gradually as membrane flows from the ER to the Golgi to the plasma membrane
. (*b*) Schematic diagram showing three distinct mechanisms that might explain how the phospholipid composition of one membrane in the Endomembrane system can be different from another membrane in the system, even though the membranous compartments are spatially and temporally continuous. (1) The head groups of phospholipids of the bilayer are modified enzymatically ; (2) the membrane of a forming vesicle contains a different phospholipid composition from the membrane it buds from; (3) lipids can be removed from one membrane and inserted into another membrane by lipid-transfer proteins.



PS and SMبس بصورة النسب انتبهوا على اماكن وجود الليبد ومين اعلى واقل يعني مثلاً نفس التوزيع PCبس عكسهم تماماً

12.6 Glycosylation in the Rough Endoplasmic Reticulum

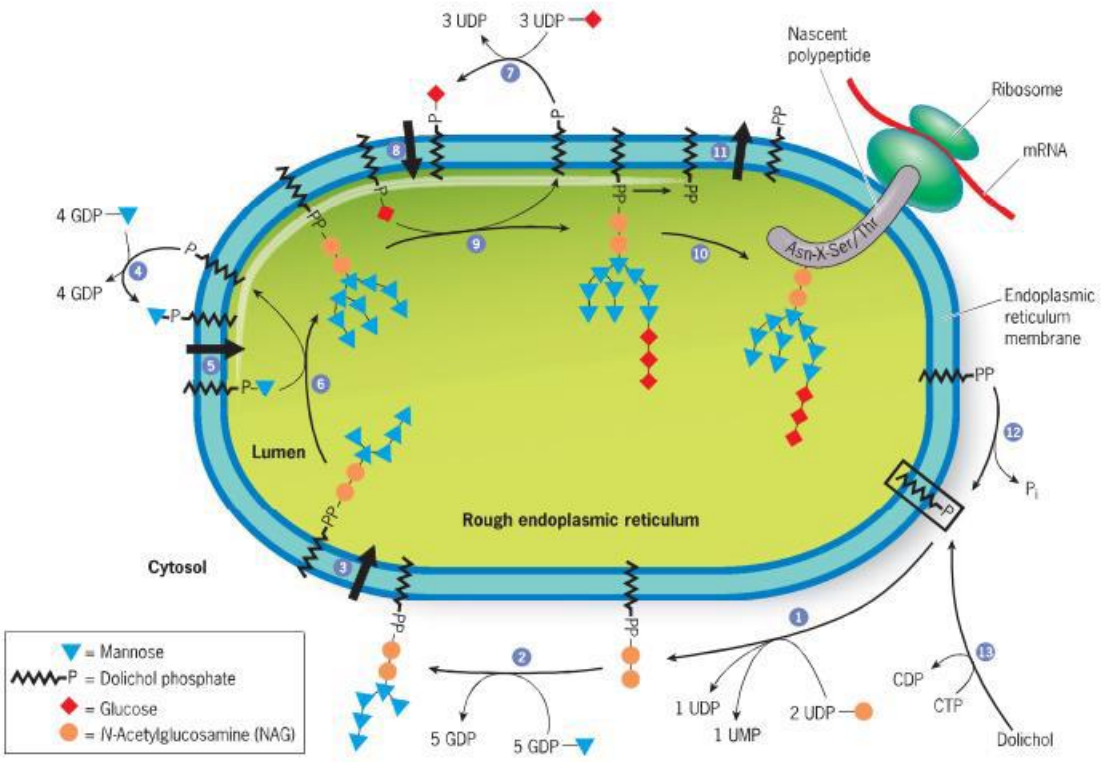


FIGURE 12.16 **Steps in the synthesis of the core portion of an *N*-linked oligosaccharide in the rough ER.** The first seven sugars (five mannose and two NAG residues) are transferred one at a time to the dolichol-PP on the cytosolic side of the ER membrane (steps 1 and 2). At this stage, the dolichol with its attached oligosaccharide is then flipped across the membrane (step 3), and the remaining sugars (four mannose and three glucose residues) are attached on the luminal side of the membrane. These latter sugars are attached one at a time on the cytosolic side of the membrane to the end of a dolichol phosphate molecule (as in steps 4 and 7), which then flips across the membrane (steps 5 and 8) and donates its sugar to the growing end of the oligosaccharide chain (steps 6 and 9). Once the oligosaccharide is completely assembled, it is transferred enzymatically to an asparagine residue (within the sequence N-X-S/T) of the nascent polypeptide (step 10). The dolichol-PP is flipped back across the membrane (step 11) and is ready to begin accepting sugars again (steps 12 and 13).

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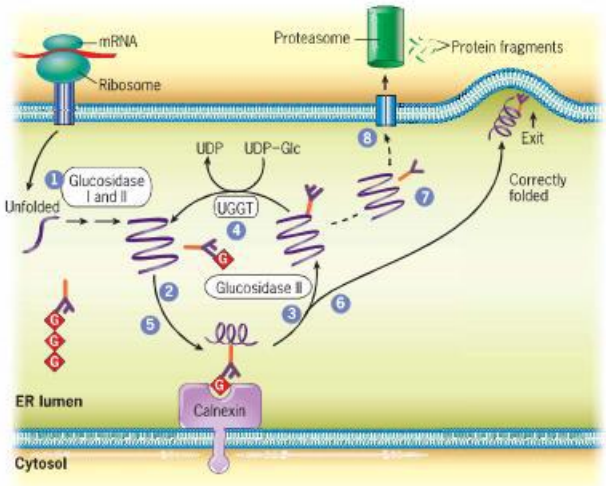


FIGURE 12.17 **Quality control: ensuring that misfolded proteins do not proceed forward.** Based on this proposed mechanism, misfolded proteins are recognized by a glucosyltransferase (UGGT) which adds a glucose to the end of the oligosaccharide chains. Glycoproteins containing monoglucosylated oligosaccharides are recognized by the membrane-bound chaperone calnexin and given an opportunity to achieve their correctly folded (native) state. If that does not occur after repeated attempts, the protein is dislocated to the cytosol and destroyed. The steps are described in the text. A soluble chaperone (calreticulin) participates in this same quality-control pathway.

SOURCE: L. Ellgaard et al., *Science* 286:984, 1999; copyright 1999, reprinted with permission from AAAS.

I. Most proteins made on membrane-bound ribosomes are glycosylated & thus become glycoproteins, whether they are integral components of the membrane, soluble lysosomal or vacuolar enzymes or parts of the ECM

A. Carbohydrate groups roles in the function of many glycoproteins ：

1.particularly as binding sites in their interactions with other macromolecules .

2 .They also aid in the proper folding & stabilization of the protein to which they are attached

3. The sugar sequences that comprise)contain (glycoprotein oligosaccharides are highly specific

So if the oligosaccharides are isolated from glycoprotein from a given type of cell, their sequence is consistent & predictable. How ?

The addition of sugars to an oligosaccharide chain is catalyzed by a family of membrane-bound enzymes (**glycosyltransferases)**<<<which transfers a specific monosaccharide from a nucleotide sugar to the growing end of the chain

- The donor <<<< a nucleotide sugar - GDP-mannose, GDP-fucose, UDP-galactose, UDP-*N*-acetylglucosamine
- The acceptor of the transferred sugar <<<< the growing end of carbohydrate chain

- The sequence of sugar transferred depends on the sequence of action of glycosyltransferases participating in the process
- Glycosyltransferases depend on location of specific enzymes within the various secretory pathway membranes
- Sugar arrangement in the oligosaccharide chains depends on the spatial localization of particular enzymes .

II. Carbohydrate chains are attached to protein by N-linkages (an asparagine N atom) or O-linkages (to serine or threonine O atom or to a collagen hydroxylysine residue) of both soluble & integral membrane proteins

A. These oligosaccharides differ in average size, sugar composition & path of synthesis & also share properties like their high specificity

B. The N-linked basal (core) segment of each carbohydrate chain is not assembled on the protein itself, but put together independently on a lipid carrier

1. The carbohydrate chain is then transferred, as a block, to specific asparagine residues of the polypeptide

2. .The lipid carrier is **dolichol phosphate** ;it is embedded in the ER membrane

(A Dolichol phosphate is a hydrophobic molecule built from 20< isoprene units)

3. Sugars are added to the dolichol phosphate molecule one at a time by membrane-bound glycosyltransferases; this part of the glycosylation process is essentially invariant

4. This preassembled block of 14 sugars is then transferred by the enzyme oligosaccharyltransferase from dolichol phosphate to

certain asparagines in the nascent polypeptide .This happens as the polypeptide is being translocated into the ER lumen

1. Mutations that lead to the total absence of *N*-glycosylation cause the death of embryos prior to implantation
2. However, mutations leading to partial glycosylation pathway disruption in the ER also are responsible for serious inherited disorders affecting nearly every organ system

B. These diseases are called Congenital Diseases of Glycosylation (CDGs) & they are usually identified through blood tests that detect abnormal glycosylation of serum proteins

C. Example: One of these diseases, CDG1b can be managed through a remarkably simple treatment

.1CDG1b results from the deficiency of the enzyme phosphomannose isomerase (it catalyzes conversion of fructose-6-phosphate to mannose-6-phosphate)

a. This reaction is a crucial reaction in the pathway that makes mannose available for incorporation into oligosaccharides

.2The disease can be managed by giving patients oral supplements of mannose

IV. Shortly after it is transferred to the nascent polypeptide, the oligosaccharide chain undergoes a gradual process of modification

A. This modification begins in the ER with the enzymatic removal of 2 of the 3 terminal glucose residues by glucosidases (Step 1)

B. This sets the stage for an important event in a newly made glycoprotein's life

1. At this time, the glycoprotein is screened by a system of **quality control** that determines whether or not it is fit to move on to the next compartment of the biosynthetic pathway
2. The screening process begins with each glycoprotein, which at this stage contains a single remaining glucose, binding to an ER chaperone (calnexin or calreticulin; Step 3)

3 .Removal of the remaining glucose by glucosidase II leads to the release of the glycoprotein from the chaperone (Step 3)

C. If the protein's folding is incomplete or if the protein is misfolded, it is recognized by a conformation-sensing enzyme (called UGGT)

1 .UGGT adds a single glucose residue back to one of the mannose residues at the exposed end of the recently trimmed oligosaccharide (Step 4)

2 .UGGT recognizes incompletely folded or misfolded proteins because they display exposed hydrophobic residues that are absent from properly folded proteins

3 .Once the glucose residue has been added, the "tagged" glycoprotein is recognized by the same ER chaperones, which give the protein another chance to fold properly (Step 5)

4 .After some time with the chaperone, the added glucose residue is removed & the conformation-sensing UGGT checks the protein again to see if it has achieved its proper 3D structure

a. If the 3D structure is right, the protein continues on its way (Step 6)
b. If the 3D structure is still partially folded or misfolded, another glucose residue is added & the process repeats until, eventually, the glycoprotein folds correctly or it remains misfolded & is destroyed

5 .Studies suggest the "decision" to destroy the defective protein is governed by a slow-acting enzyme in the ER

a. It trims a mannose residue from an exposed end of the oligosaccharide of a protein that has been in the ER for an extended period
b. Once one or more of these mannose residues has been removed (Step 7), the protein can no longer be recycled ,& instead, is sentenced to degradation (step 8)

6 .The oligosaccharide assembled in the ER is enlarged as it passes through the Golgi complex on its journey through the biosynthetic pathway .

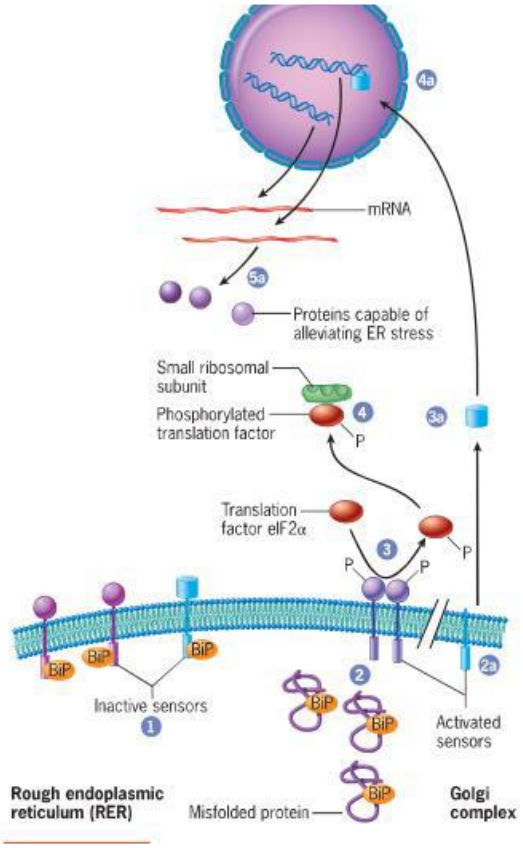
12.7 Mechanisms That Ensure the Destruction of Misfolded Proteins

I. Misfolded proteins are not destroyed in the ER, but are instead transported into the cytosol by a process of *dislocation* (there is some debate about this mechanism)

1. This process, known as *ER-associated degradation*) *ERAD* ,(ensures that aberrant proteins are not transported to other parts of cell, but it can have negative consequences
When misfolded protein reach cytosol ,the oligosaccharide chains are removed & the misfolded proteins are destroyed in proteasomes, which are protein-degrading machines see the figure below
60<2.human diseases, including cystic fibrosis, are attributed to the ERAD pathway
a. In most patients with cystic fibrosis, the plasma membrane of epithelial cells is lacking the abnormal protein encoded by the cystic fibrosis gene
b. In these cases, the mutant protein, which often would be functional if allowed sufficient time to fold, is destroyed by the quality-control process & thus fails to reach the cell surface

II. Under certain circumstances, misfolded proteins can be generated in the ER at a rate faster than they can be exported to the cytoplasm

A. The accumulation of misfolded proteins, which is potentially lethal) kill (to cells, triggers a comprehensive "plan of action" within the cell known as the **unfolded protein response**) **UPR** (
B. The ER contains protein sensors that monitor the concentration of unfolded or misfolded proteins in the ER lumen



A model of the mammalian unfolded protein response (UPR). The ER contains transmembrane proteins that function as sensors of stressful events that occur within the ER lumen.
Under normal conditions, these sensors are present in an inactive state as the result of their association with chaperones, particularly BiP (step1). If the number of unfolded or misfolded proteins should increase to a high level, the chaperones are recruited to aid in protein folding,which leaves the sensors in their unbound, activated state and capable of initiating a UPR. At least three distinct UPR pathways have been identified in mammalian cells, each activated by a different proteinsensor. Two of these pathways are depicted in this illustration. In one of these pathways, the release of the inhibitory BiP protein leads to thedimerization of a sensor (called PERK) (step 2). In its dimeric state, PERK becomes an activated protein kinase that phosphorylates a protein (eIF2) that is required for the initiation of protein synthesis (step 3). This translation factor is inactive in the phosphorylated state, which stops the cell from synthesizing additional proteins in the ER (step 4), giving the cell more time to process those proteins already present in the ER lumen. In the second pathway depicted here, release of the inhibitory BiP protein allows the sensor (called ATF6) to move on to the Golgi complex where the cytosolic domain of the protein is cleaved away from its transmembrane domain (step 2a). The cytosolic portion of the sensor diffuses through the cytosol (step 3a) and into the nucleus (step 4a), where it stimulates the expression of genes whose encoded proteins can alleviate the stress in the ER (step 5a). These include chaperones, coat proteins that form on transport vesicles, and
proteins of the quality-control machinery.

1 .The prevailing model) common (suggests that the sensors are normally kept in an inactive state by molecular chaperones, particularly BiP .
2.If circumstances should lead to an accumulation of misfolded proteins,
the BiP molecules in the ER lumen are called into service as chaperones for the misfolded proteins

a. This make them) BiP molecules) incapable of inhibiting the sensors & ,the sensors are thus activated
C. Activation of the sensors leads to a multitude of signals that are transmitted into both the nucleus & cytosol & results in :

1 .The expression of hundreds of different genes whose encoded proteins have the potential to reduce stressful conditions within the ER; these include genes that encode :
a. ER-based molecular chaperones that can help misfolded proteins reach the native state
b. Proteins involved in the transport of the proteins out of the ER
c. Proteins involved in the selective destruction of abnormal proteins as described above

2.Phosphorylation of a key protein) eIFα (required for protein synthesis

a. This modification inhibits protein synthesis & decreases the flow of newly synthesized proteins into the ER
b. This gives the cell an opportunity to remove those proteins that are already present in the ER lumen

D. the UPR is more than a cell-survival mechanism; it also includes the activation of a pathway that leads to the death of the cell

1. It is presumed that the UPR gives the cell an opportunity to relieve itself of the stressful conditions
2. If these corrective measures are unsuccessful, the cell-death pathway is triggered & the cell is destroyed .

The Golgi Complex (12.9)

- It has a characteristic morphology – primarily flattened, disk-like, membranous cisternae with dilated rims & associated vesicles & tubules (it has smooth membranes so it is found with smooth microsomes).
- Cisternae (typically 0.5 - 1.0 µm diameter (are arranged in an orderly stack .And curved look like shallow bowl) slightly deep.(
  - in plants, a single Golgi stack is sometimes called a *dictyosome*
- Typically 8> ,cisternae are present per stack. one cell contain many stack) few 1000 distinct stack per cell) like :Mammalian cell Golgi stacks form a single, large ribbonlike complex typically situated adjacent to the cell's nucleus
- Vesicles seem to bud from a peripheral tubular domain of each cisterna; many of these vesicles seem to have a distinct protein coat seen in the EM
- Golgi cisternae polarized - *cis* face (entry face closest to ER) ;*trans* face (exit face at the opposite end of the stack; closer to the plasma membrane)

A. Golgi complex is divided into several functionally distinct compartments arranged along a *cis*-*trans* axis; new materials enter the *cis* face & pass to the *trans* face, where they exit the Golgi complex

1. The *cis*-most face of the organelle is composed of an interconnected network of tubules (the ***cis* Golgi network** ;**CGN**(
   a. The CGN seems to function primarily as a sorting station that distinguishes between proteins to be shipped back to the ER & those that are allowed to proceed to the next Golgi station
   b. The bulk of the Golgi complex consists of a series of large, flattened cisternae divided into 3 regions: the ***cis*** ,***medial*** & ,***trans*** **cisternae**
2. The *trans*-most face has a distinct network of tubules & vesicles) ***trans*** **Golgi network** ;**TGN**(

A. The TGN is a sorting station, where proteins are segregated into different types of vesicles heading either to the plasma membrane or to various intracellular destinations

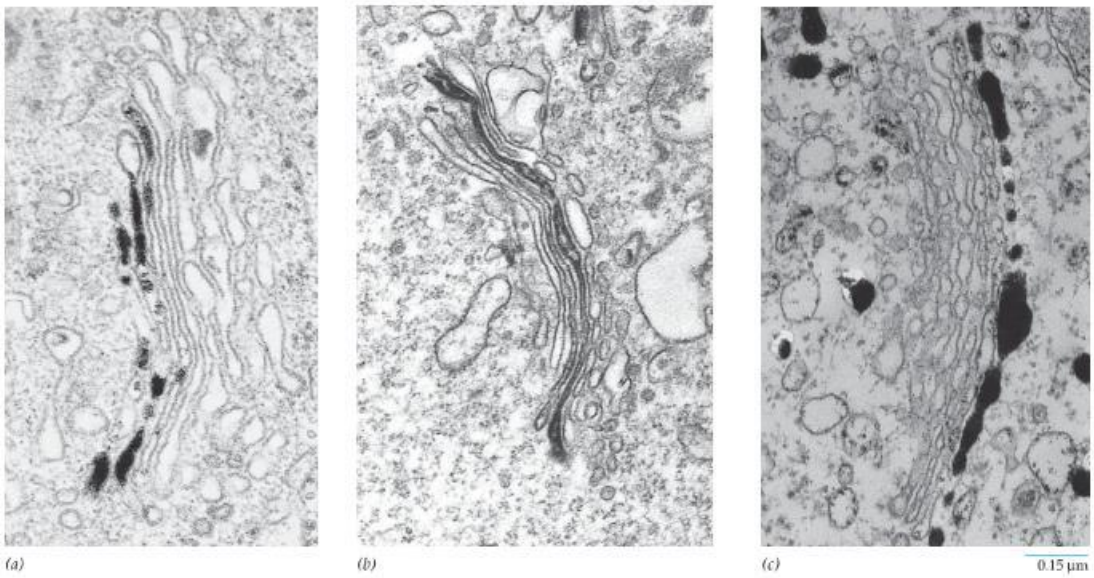
B. The membranous elements of the Golgi complex are thought to be supported mechanically by a peripheral membrane skeleton or a scaffold composed of a variety of proteins, including) :details is from book but doctors didn't say it 1-2(3-

1. Members of the spectrin ,ankyrin & ,actin families (these proteins are also present as part of the plasma membrane skeleton)

2 .The Golgi scaffold may be physically linked with motor proteins that direct the movement of vesicles & tubules entering & exiting the Golgi complex

3. A separate group of fibrous proteins are thought to form a Golgi "matrix" that plays a key role in the disassembly & reassembly of the Golgi complex during mitosis

- Differences in the composition of the membrane compartments from the *cis* -to the *trans*-face so Golgi complex is not uniform in composition from one end to the other
  - The membrane protein is leave ER and go to cis face of Golgi then trans face.



Protein synthesized in ER are modified in Golgi) more specifically carb attached to protein(

Golgi shape in EM

Regional differences in membrane composition across the Golgi stack. (*a*) Reduced osmium tetroxide preferentially impregnates the *cis* cisternae of the Golgi complex. (*b*) The enzyme mannosidase II, which is involved in trimming the mannose residues from the core oligosaccharide as described in the text, is preferentially localized in the *medial* cisternae. (*c*) The enzyme nucleoside diphosphatase, which splits dinucleotides (e.g., UDP) after they have donated their sugar, is preferentially localized in the *trans* cisternae.

IV. Glycosylation in Golgi complex – Golgi plays a key role in glycoprotein/glycolipid CHO assembly; synthesis site of most of cell's complex polysaccharides

the synthesis of *N*-linked CHO chains in the ER, glucose residues had just been removed from the ends of the core oligosaccharide of the *N*-linked carbohydrate chains

1 .As newly synthesized soluble & membrane glycoproteins pass though the *cis* & *medial* Golgi cisternae ,most of the mannose residues are also removed from the core oligosaccharides

2.Other sugars are added sequentially by various **glycosyltransferases**

a. The Golgi complex produces carbohydrate domains of remarkable sequence diversity the *N*-linked oligosaccharides <<<<synthesis starts in the ER, oligosaccharides attached to proteins by *O*-linkages are assembled entirely within <<<<the Golgi complex

B. In the Golgi, as in the RER, the sequence in which sugars are inserted into oligosaccharides is determined by the spatial arrangement of specific glycosyltransferases that contact new proteins as they pass through

.1Sialyltransferase) puts sialic acid at chain terminal position in animal cells) is found in Golgi stack *Trans* end; as would be expected if new glycoproteins were constantly moving toward this part of organelle

glycosylation steps can be quite varied for Golgi complex from the ER, where a single core oligosaccharide is assembled

C. The Golgi complex is also the site of synthesis of most of a cell's complex polysaccharides, including the glycosaminoglycan chains of proteoglycans & the pectins & hemicellulose found in plant cell walls

V. That materials move through various Golgi complex compartments has long been established; however, 2 model explain this

A .*Cisternal maturation model* – it was generally accepted, that cisternae were transient structures

.1It was supposed that Golgi cisternae were formed at the stack's *cis* face by fusion of membranous carriers from the ER & ERGIC & that each cisterna physically moved from the *cis* to *trans* face of the stack

a. As they moved through the stack, the cisternae supposedly changed in composition

.2According to the model, each cisterna "matures" into the next cisterna along the stack (origin of name)

B .the *vesicular transport model* so the maturation model of Golgi movement was largely abandoned & replaced by an alternate model.

.1This model proposed that the cisternae of the Golgi stack remain in place as stable compartments

.2Cargo (secretory, lysosomal & ,membrane proteins) is shuttled through Golgi stack from the CGN to the TGN in vesicles

a. These vesicles bud from one membrane compartment & fuse with a neighboring compartment farther along the stack

The acceptance of vesicular transport model was based largely on the following observations :A. Each of the various Golgi cisternae in a stack has a distinct resident enzyme population; how could the various cisternae have such different properties if each gave rise to the next in line as stated by the other model?

B. Large numbers of vesicles are seen in electron micrographs to bud from the rims of Golgi cisternae

.1Using cell-free preparations of Golgi membranes, they showed that transport vesicles could bud from one Golgi cisterna & fuse with another Golgi cisterna *in vitro*

.2This landmark experiment formed the basis for a hypothesis suggesting that inside the cell, cargo-bearing vesicles budded from *cis* cisternae & fused with cisternae situated at a more *trans* position in the stack

the cisternal maturation model is the best ;several major reasons for this:

A. The cisternal maturation (CM) model say that there a highly dynamic Golgi complex in which the major elements of the organelle, the cisternae, are continually being formed at the *cis* face & dispersed at the *trans* face

.1According to this view, the very existence of the Golgi complex itself depends on the continual influx of transport carriers from the ER & ERGIC

.2As the CM model predicts, when formation of transport carriers from the ER is blocked by cell treatment with specific drugs or the use of temperature-sensitive mutants, the Golgi complex simply disappears

.3When the drugs are removed or the mutant cells are returned to the permissive temperature, the Golgi complex rapidly reassembles as ER-to-Golgi transport is renewed

B. New evidence for CM model - certain materials that are produced in the ER & travel through the Golgi complex can be shown to stay in Golgi cisternae & never appear within Golgi-associated transport vesicles(doctor don't say 1)

.1fibroblast studies – large complex of procollagen molecules (extracellular collagen precursors) move from *cis* cisternae to the *trans* cisternae without ever leaving the cisternal lumen

C.it was assumed that transport vesicles always moved in forward) **anterograde** (direction, from a *cis* origin to a more *trans* destination, but a large body of new evidence indicates that……

.1Vesicles can move in a "backward) "**retrograde** (direction from a *trans* donor to a *cis* acceptor membrane

D. Studies on live budding yeast cells containing fluorescently labeled Golgi proteins have shown directly that the composition of an individual Golgi cisterna can change over time

.1A cisterna can change from one that contains early) *cis* (Golgi resident proteins to one that contains late) *trans* (Golgi resident proteins

.2The results of this experiment are not compatible with the vesicular transport model

.3Whether these results on yeast can be extrapolated to a mammalian Golgi complex, which has a more complex, stacked structure, remains to be determine

A current version of the cisternal maturation model acknowledges a role for transport vesicles, which have been clearly shown to bud from Golgi membranes

A. In this model, transport vesicles do not shuttle cargo in an anterograde direction, but instead carry resident Golgi enzymes in a retrograde direction

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.1Instead, it is the Golgi cisternae themselves that serve as the primary anterograde Golgi carriers. the scientist find this by electron micrograph from mammalian cells that were cut from a frozen block.

.2In both cases, frozen sections were treated with antibodies that were linked to gold particles prior to examination in the EM; the antibodies were made against a cargo protein (the viral protein VSVG protein)

.3The VSVG molecules were present within cisternae, but absent from nearby vesicles, suggesting that cargo is carried in an anterograde direction within maturing cisternae but not in small transport vesicles

B. In another experiment, sections were treated with gold-labeled antibodies that bind to a Golgi resident protein (the processing enzyme mannosidase II) <— it was seen in both the cisternae & the associated vesicles

.1This strongly supports the proposal that these vesicles are utilized to carry Golgi-resident enzymes in a retrograde direction

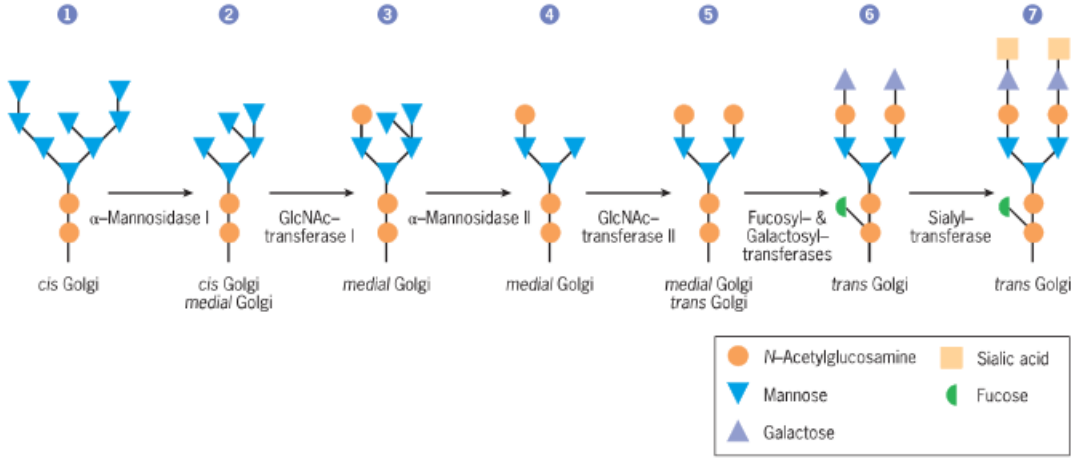
.2Golgi-resident proteins may also move in a retrograde direction through tubules that have been seen to connect different Golgi cisternae

C. The revised cisternal maturation model explains how different Golgi cisternae in a stack can have a unique identity

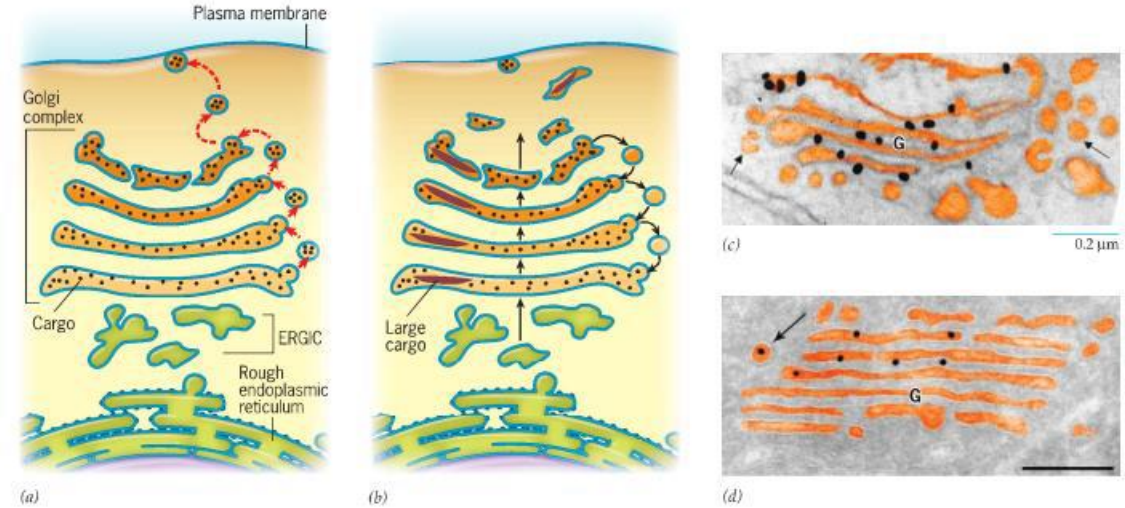
.1Mannosidase II is an enzyme that removes mannose residues from oligosaccharides & is largely restricted to the <u>*medial* cisternae</u>

.2It can be recycled backward in transport vesicles as each cisterna moves toward the *trans* end of the stack

D. It should be noted that some prominent researchers still argue, based on other experimental results, that cargo can be carried by transport vesicles between Golgi cisternae in an anterograde direction



Steps in the glycosylation of a typical mammalian *N*-linked oligosaccharide in the Golgi complex. Following the removal of
the three glucose residues, various mannose residues are subsequently removed, while a variety of sugars (*N*-acetylglucosamine, galactose, fucose,
and sialic acid) are added to the oligosaccharide by specific glycosyltransferases. These enzymes are integral membrane proteins whose active sites
face the lumen of the Golgi cisternae. This is only one of numerous glycosylation pathways.



The dynamics of transport through the Golgi complex. (*a*) In the vesicular transport model, cargo (black dots) is carried in an anterograde direction by transport vesicles, while the cisternae themselves remain as stable elements. (*b*) In the cisternal maturation model, the
cisternae progress gradually from a *cis* to a *trans* position and then disperse at the TGN. Transport vesicles carry resident Golgi enzymes (indicated by
the colored vesicles) in a retrograde direction. The red lens-shaped objects represent large cargo materials, such as procollagen complexes of
fibroblasts. (*c*) Electron micrograph of an area of Golgi complex in a thin frozen section of a cell that had been infected with vesicular stomatitis virus
(VSV). The black dots are nanosized gold particles bound by means of antibodies to VSVG protein, an anterograde cargo molecule. The cargo is

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عارفين انه الشيت شوي طويل بس انتم قدها
كل التوفيق
فالكم_A#