

✗ اختصارهم بـ GAG

Glycosaminoglycans

✗ هم عبارة عن Structural sugar or carbohydrate
يدخل بتكوين الخلية
✗ يعني لما يصنع الخلية، لازم المنتج هو

✗ يشغلوا في mucas حتى يعمل تركيب المنطقة وبمساعدة الفبرق وال MO
يبي يتعامل تقوت الجسم، وممكن يتعضوا الادمات

✗ ولما تنكسر الخلية تنكسر ماسا.

Glycosaminoglycans

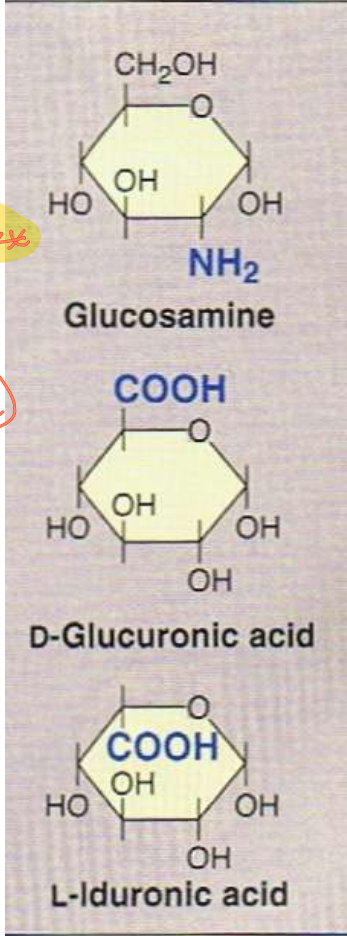
⊖
sulfate group
لا تاتي ايسلم كاسم

⊖ كاسم

- Are long, negatively charged, unbranched, heteropolysaccharide chains generally composed of a repeating disaccharide unit [acidic sugar-amino sugar]_n
- The amino sugar is either D-glucosamine or D-galactosamine in which the amino group is usually acetylated, thus eliminating its positive charge
- The amino sugar may also be sulfated on carbon 4 or 6 or on a nonacetylated nitrogen.
- The acidic sugar is either D-glucuronic acid or its carbon-5 epimer, L-iduronic acid.

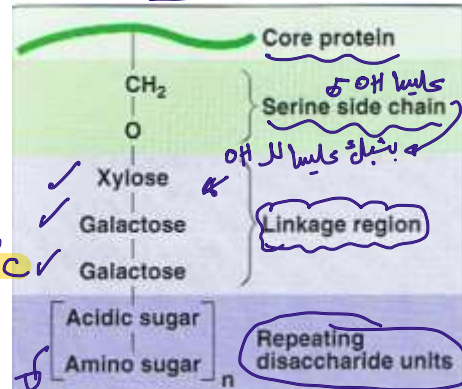
Neutral

لو بدونه يكون base ⊕
N (amide)
acylated
Neutral



Glucose عبارة عن
oxidational ويتحول الى

D-glucuronic acid → isomerization → L-iduronic acid



شوا لازم يكون عندية
كمان احون ال GAG?
لازم يكون في Core
Protein

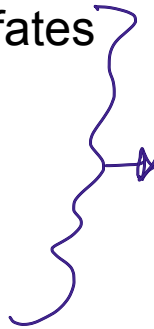
Glycosaminoglycans (GAG)

- These compounds bind large amounts of water, thereby producing the gel-like matrix that forms the basis of the body's ground substance. ↳ like Polysaccharide or mucas
- The viscous, lubricating properties of mucous secretions are also caused by the presence of glycosaminoglycans, which led to the original naming of these compounds as mucopolysaccharides. ↳ اسم ثاني ال GAG
- As essential components of cell surfaces, GAGs play an important role in mediating cell-cell signaling and adhesion

Classes of GAGs

➤ There are **six** major classes of glycosaminoglycans, including:

- chondroitin 4- and 6-sulfates
- keratan sulfate
- dermatan sulfate
- Heparin
- heparan sulfate
- hyaluronic acid.



3D واحد منسجم
disaccharide seq
متخلف عن الثاني

serine OH جزيء

بربط مع الـ GAG بربط غير تساهلي (H-bond)

➤ All of the **GAGs**, except **hyaluronic acid**, are **found covalently** attached to protein, forming **proteoglycan** monomers, which consist of a core protein to which the linear GAG chains are covalently attached

➤ The proteoglycan monomers associate with a molecule of hyaluronic acid to form proteoglycan aggregates.

اسم

Keratin

لا يوجد
IdUA & GlcUA

يمكن في تيار نخل
ترجيبة

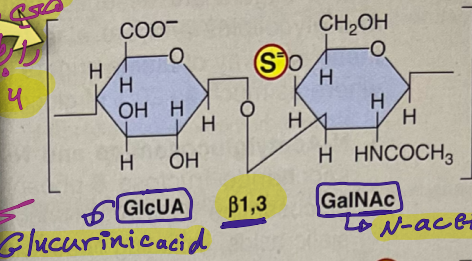
اهم واحد

لا يوجد

non-covalent bond with Protein (ionic, H-bond)
اي شيء لهم
covalent

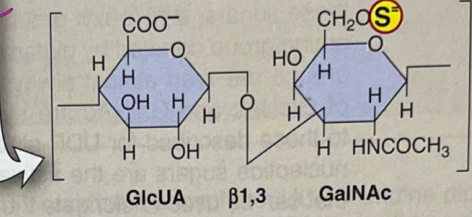
CHONDROITIN 4 AND 6 SULFATES

- Disaccharide unit: N-acetylgalactosamine with sulfate on either C 4 or C 6 and glucuronic acid
- Most abundant GAGs in the body
- Found in cartilage, tendons, ligaments, and aorta
- Form proteoglycan aggregates, often aggregating noncovalently with hyaluronic acid
- In cartilage, bind collagen and hold fibers in a tight, strong network



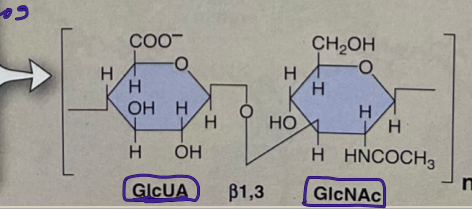
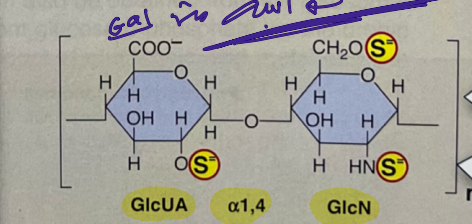
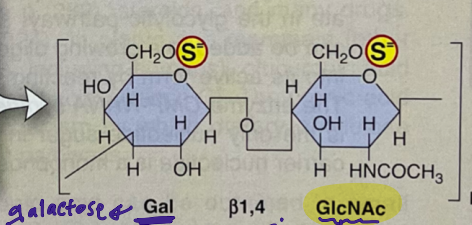
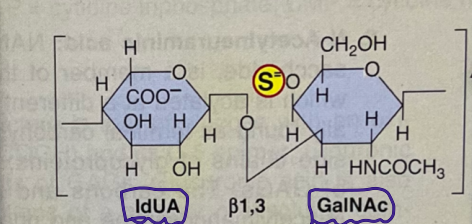
KERATAN SULFATES (KS) I and II

- Disaccharide unit: N-acetylglucosamine and galactose (no uronic acid); variable sulfate content may be present on C 6 of either sugar
- Most heterogeneous GAGs because they contain additional monosaccharides such as L-fucose, N-acetylneuraminic acid, and mannose
- KS I found in corneas; KS II found in loose connective tissue proteoglycan aggregates with chondroitin sulfate



HYALURONIC ACID (HYALURONATE)

- Disaccharide unit: N-acetylglucosamine and glucuronic acid
- Different from other GAGs: unsulfated, not covalently attached to protein, and only GAG not limited to animal tissue, but also found in bacteria
- Serves as a lubricant and shock absorber
- Found in synovial fluid of joints, vitreous humor of the eye, the umbilical cord, loose connective tissue, and cartilage



DERMATAN SULFATE

- Disaccharide unit: N-acetylgalactosamine and L-iduronic acid (with variable amounts of glucuronic acid)
- Found in skin, blood vessels, and heart valves

HEPARIN

- Disaccharide unit: Glucosamine and glucuronic or iduronic acid; most glucosamine residues are bound in sulfamide linkages; sulfate also found on C 3 or C 6 of glucosamine and C 2 of uronic acid (an average of 2.5 S per disaccharide unit)
- α -Linkage joins the sugars
- Unlike other GAGs that are extracellular compounds, heparin is an intracellular component of mast cells that line arteries, especially in liver, lungs, and skin
- Serves as an anticoagulant

HEPARAN SULFATE

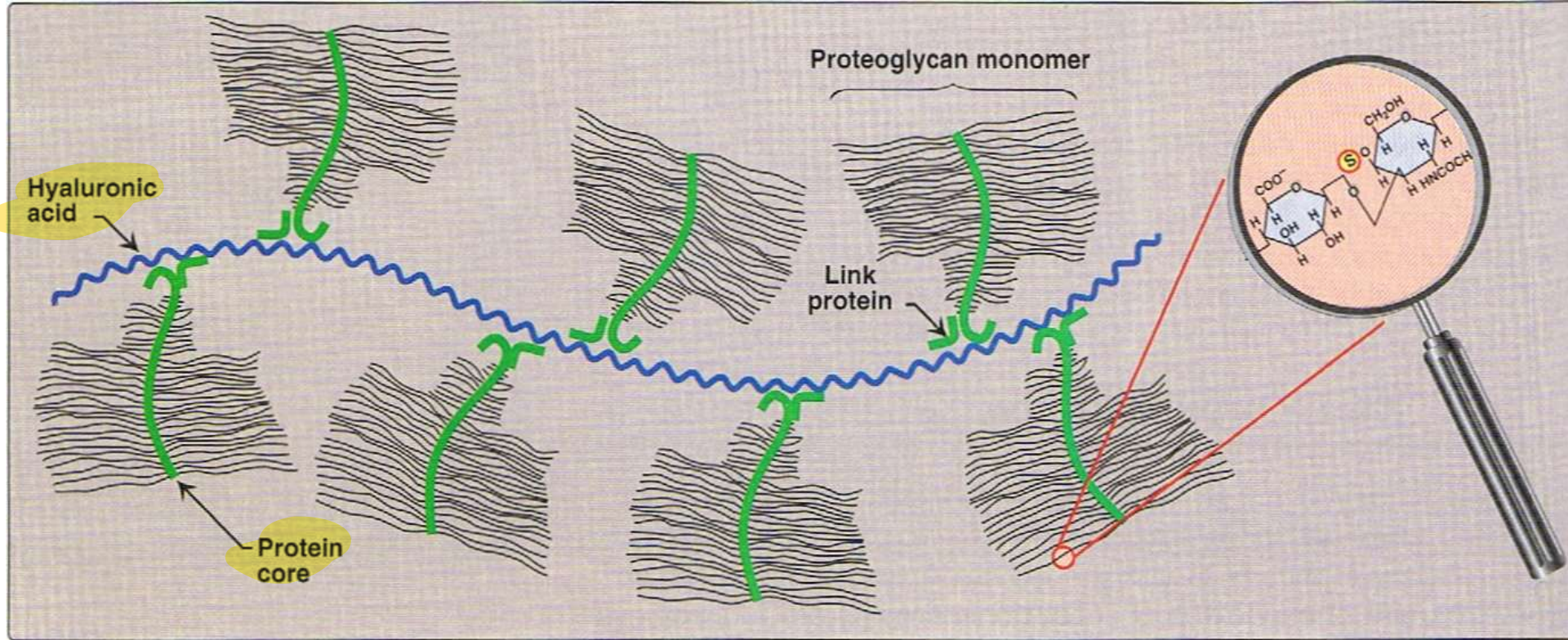
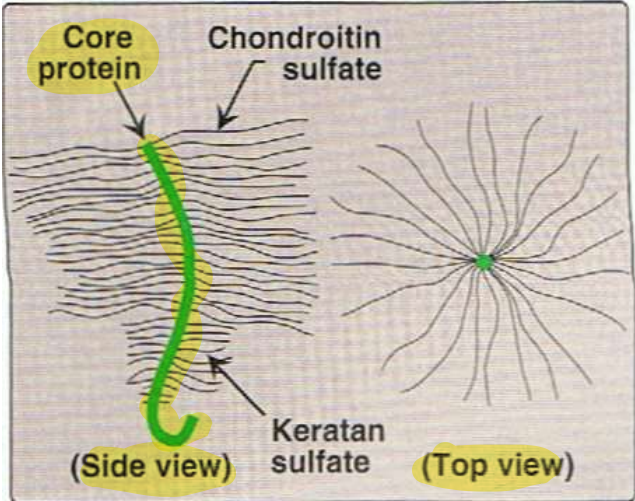
- Disaccharide unit: Same as heparin except some glucosamines are acetylated, and there are fewer sulfate groups
- Extracellular GAG found in basement membrane and as a ubiquitous component of cell surfaces

مسماة جدر

الوحيد من ال GAG يلي
داخل الخلية من خارجها
من نهاية المطاف
Intracellular - I U

بالمنزلة مقدار
sulfation كالجدر
يعني كل وحدة disacc...
فيها من 2 الي 3 S
يعني بحد 2.5 للوحدة

نفر ترجيبة ال
heparin
ولكن هذا



هو الحؤول عن عملية secretion
 الحؤول عن عملية secretion

Synthesis of Glycosaminoglycans

Golgi

بما انهم رح يتفرزوا لـ cell بالتالي لازم يكون في organism بـ secretion
 الحؤول عن عملية secretion

GAGs are synthesized in the endoplasmic reticulum and the Golgi

The polysaccharide chains are elongated by the sequential addition of alternating acidic and amino sugars, donated by their UDP-derivatives

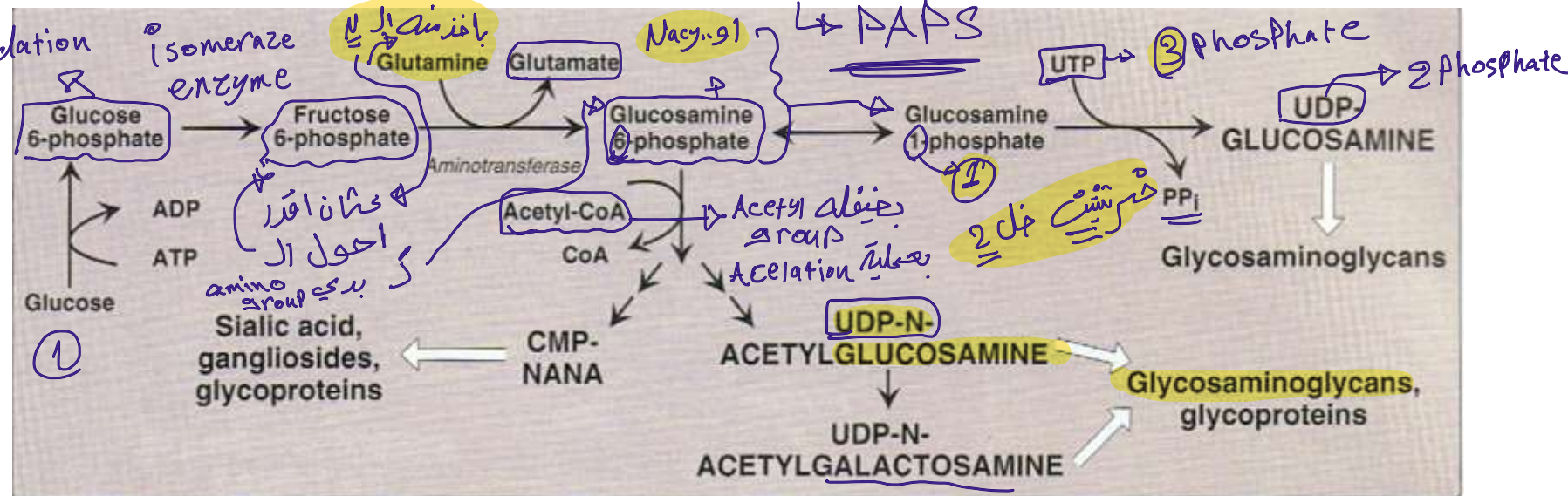
L-Gluc acid

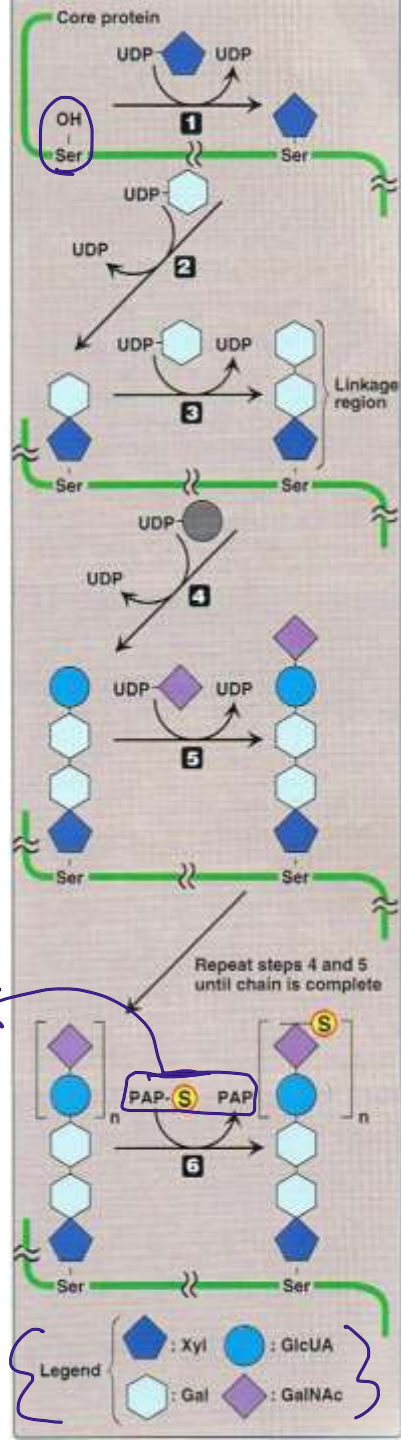
هذا يعني بعمل activation لـ sugars
 الحؤول عن عملية secretion

isomerization
 D-Gluc acid

The last step in synthesis is sulfation of some of the amino sugars. The source of the sulfate is 3'-phosphoadenosyl-5'-phosphosulfate.

oxidation





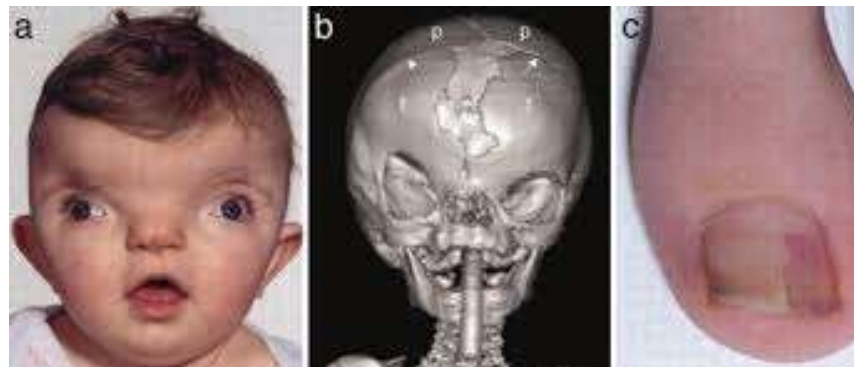
اگر اسی پھیلے اور اس کی یہ اوب

حکایت نامہ

Mucopolysaccharidosis

لا اي شيء ينتج لانه لا يكون منسج القدره ياني اخلطه
الا شيا يلي بجنبها ويوجد على Golgi ويعتقد على ال Surface لما بدي الحسها بعولها
Phagocytosis
بالداخل بربطها مع ال lysosomes
lysosomal hydrolases
ويبتل الحس فسيم
Polysaccharide extracellularly (GAG)
الاشياء لتكبر ال
احا يكون قسم نقصى

- Glycosaminoglycans are degraded by lysosomal hydrolases. They are first broken down to oligosaccharides, which are degraded sequentially from the non-reducing end of each chain
- A deficiency of one of the hydrolases results in a mucopolysaccharidosis.
- These are hereditary disorders in which glycosaminoglycans accumulate in tissues, causing symptoms such as skeletal and extracellular matrix deformities, and mental retardation
- Examples of these genetic diseases include Hunter and Hurler syndromes



Glycoproteins

هم ال mador
وفي ثوية
سكر

- Glycoproteins are proteins to which oligosaccharides are covalently attached.
- They differ from the proteoglycans in that the length of the glycoprotein's carbohydrate chain is relatively short (usually two to ten sugar residues long, although they can be longer)
- The carbohydrates of glycoproteins do not have serial repeats as do glycosaminoglycans.

ماي ا طول المador هو سكر / والبروتين قليل

يعني ما في sequence
واشع / ممكن مختلف
السكر

الجليكو بروتين

Function of glycoproteins

➤ Membrane-bound glycoproteins participate in a broad range of cellular phenomena, including:

➤ Cell surface recognition (by other cells, hormones, viruses)

like glycoprotein يعتمد على حجم البروتين

➤ Cell surface antigenicity (such as the blood group antigens)

↑ عالية للبروتين الكبير
↓ قليلة للبروتين الصغير

↳ AB+ ... etc

➤ As components of the extracellular matrix and of the mucins of the gastrointestinal and urogenital tracts, where they act as protective biologic lubricants.

➤ Almost all of the globular proteins present in human plasma are glycoproteins.

+ lysosomes that degradate GAG many of them are glycoprotein

Structure modification \rightarrow يعني جناه عيانات و بالتالي بدي

(RER) Rough endoplasmic reticulum

Protein + sugar

Synthesis of Glycoproteins

يكونوا إما تحت ال lysosomal vesicles او برا الخلية

التي تؤدي عن عملية تصنيع ال glyco-Protein

secreted outside the cell \rightarrow يعني بدي اولا

- Glycoproteins are synthesized in the endoplasmic reticulum and the Golgi.
- The precursors of the carbohydrate components of glycoproteins are sugar nucleotides.

السكر لازم لما اتميزه يكون على شكل UDP وفي قسم نوويج

- O-linked glycoproteins are synthesized by the sequential transfer of sugars from their nucleotide carriers to the protein

يتم البروتين بعدها بضيف ال sequant تبع السكر

- N-linked glycoproteins contain varying amounts of mannose. They are synthesized by the transfer of a pre-formed oligosaccharide from its membrane lipid carrier, **dolichol**, to the protein

N-linked \rightarrow مسؤول عن ال lipid \rightarrow membrane of ER

- They also require **dolichol**, an intermediate carrier of the growing oligosaccharide chain.

بعدها يرتبط ال السكر من جهة ال protein \rightarrow N-linked glycoprotein و بتغير كندري

كارة عن Pirophosphate (2 Phosphate + oxygen) يرتبط ال sequence تبع السكر لي بربنا نشيفه

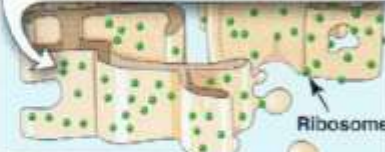
يحي هو بالعادة

ASN (Asparagine)

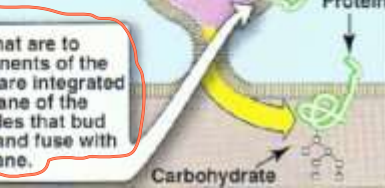
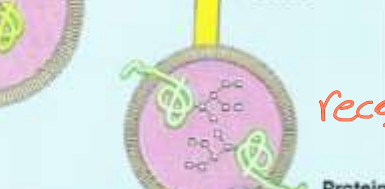
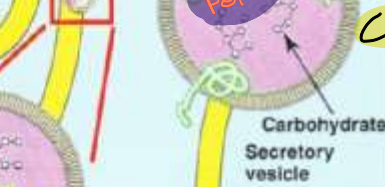
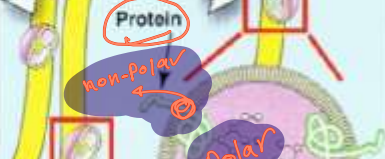
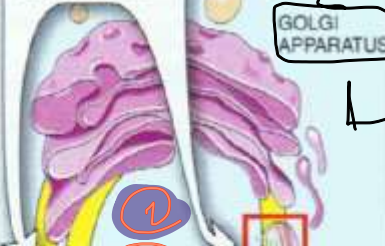
من صون ببتلته عالية
النخيلج

ROUGH ENDOPLASMIC RETICULUM (RER)

- RER is series of interconnected membrane-bound sacs.
- Ribosomes are bound to the cytosolic side of the membrane.



Vesicles bud off from the Golgi and their contents are targeted to the cell membrane, the extracellular environment, or the lysosomes.



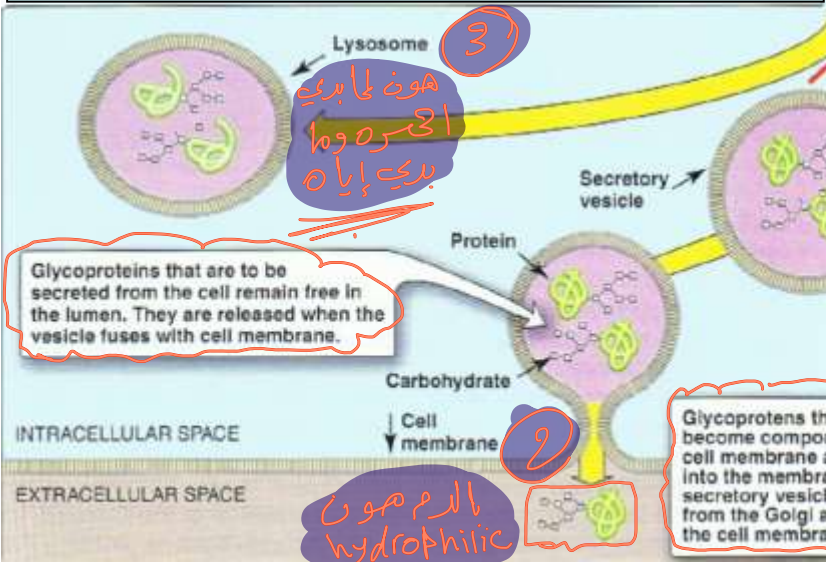
عن طريقها يتم
عليه افراز
glycoprotein

بفعل جوائه
عليه مبيد
بعدهما تكون
فيسار

Glycoprotein
السائي، بدنا
نعمله افراز على

حسب مكانه او وين
بدنا يشتغل، من
طريقه افراز
secretory vesicle

حسبنا فوق انا على
سطح الخلية بعمل
recognitin
او انه الى antigenity



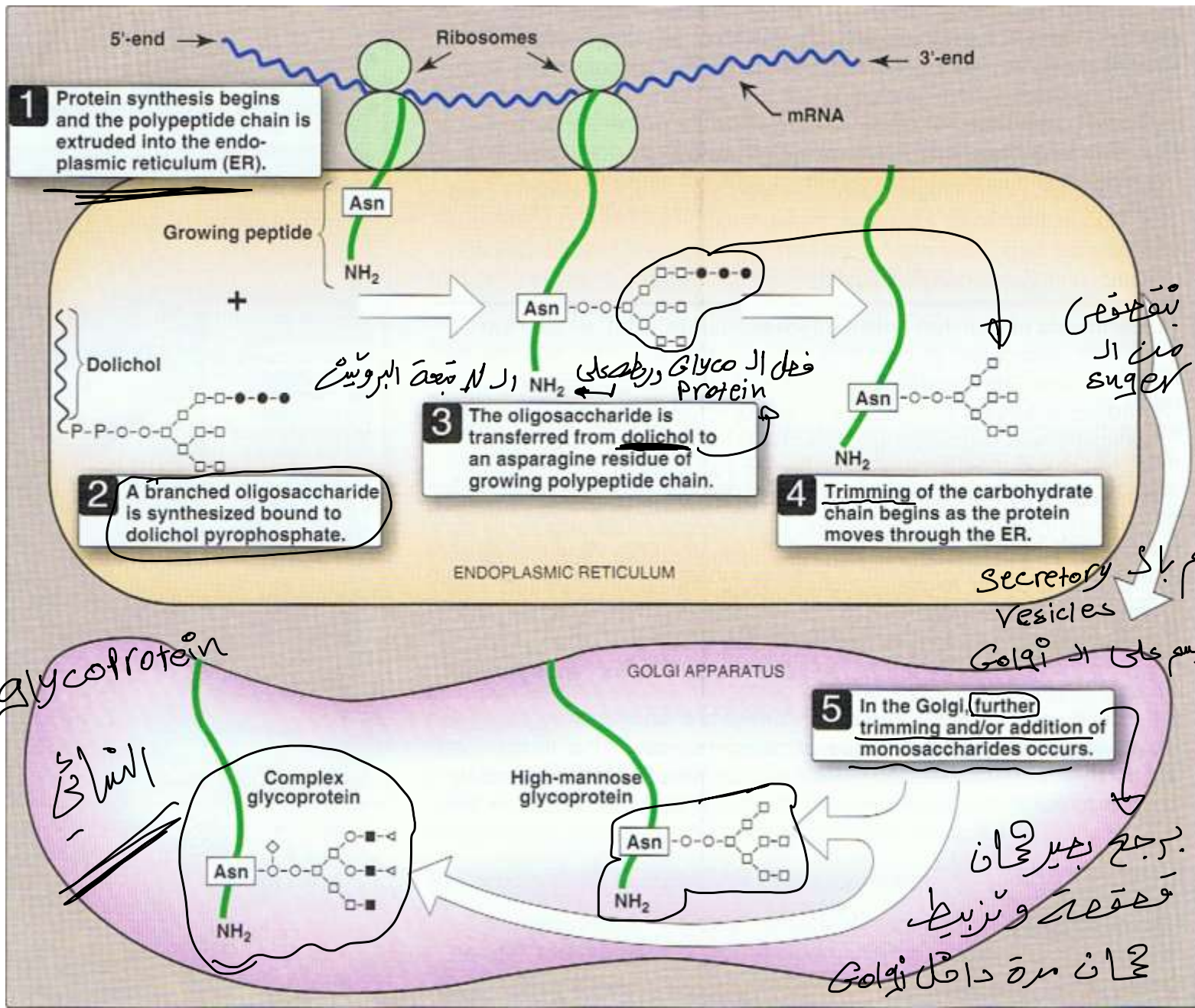
Glycoproteins that are to be secreted from the cell remain free in the lumen. They are released when the vesicle fuses with cell membrane.

Glycoproteins that are to become components of the cell membrane are integrated into the membrane of the secretory vesicles that bud from the Golgi and fuse with the cell membrane.

3
هون لما بدي
الحره وما
بدي اياه

2
بالرم صون
hydrophilic

Synthesis of N-linked glycoproteins.



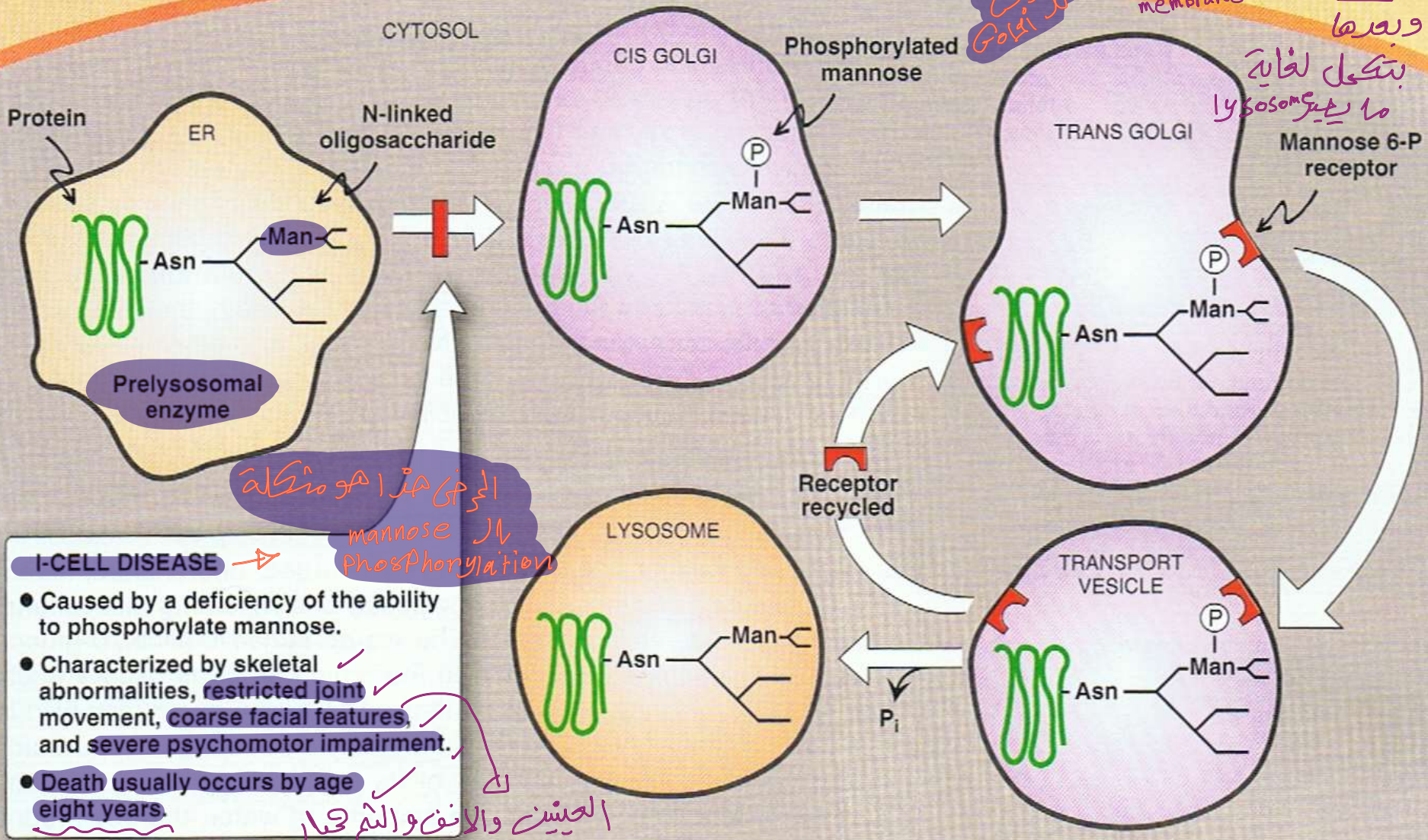
Lysosomal degradation of glycoproteins

لو جارت هون مسئلة

- A deficiency in the phosphorylation of mannose residues in N-linked glycoprotein pre-enzymes destined for the lysosomes results in **I-cell disease**
- Glycoproteins are degraded in lysosomes by acid hydrolases
- A deficiency of one of these enzymes results in a glycoprotein storage disease (**oligosaccharidosis**), resulting in accumulation of partially degraded structures in the lysosome

✱ الخلل بعملية الفسفرة بسبب الخرفي ✱

①
 لا يتم إحصاره فسفرة قبل ما يخرج من Golgi
 ②
 عملية الفسفرة بالسما receptor على إز vesicil بنفسا يبنى على إز membrane
 ③
 يتحول عالية الفسفرة سطح Golgi إلى cis + trans وبعدھا



الخرفي هذا هو مشكلة mannose ال phosphorylation

I-CELL DISEASE →

- Caused by a deficiency of the ability to phosphorylate mannose.
- Characterized by skeletal abnormalities, **restricted joint movement**, **coarse facial features**, and **severe psychomotor impairment**.
- **Death usually occurs by age eight years.**

العينين والانف والتم جبار