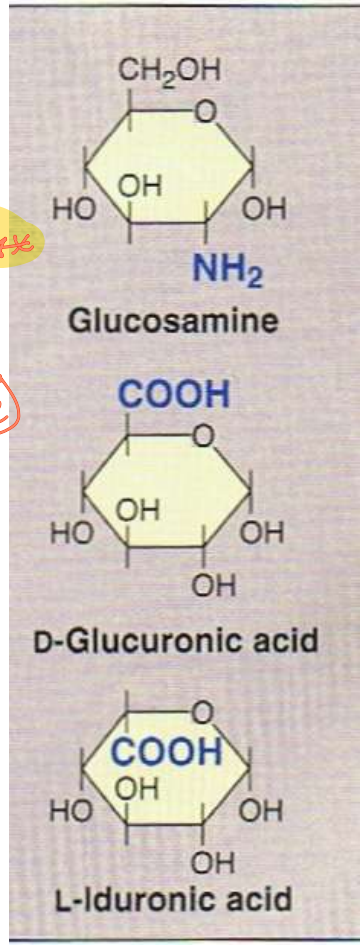
اختصارهم بـ GAG

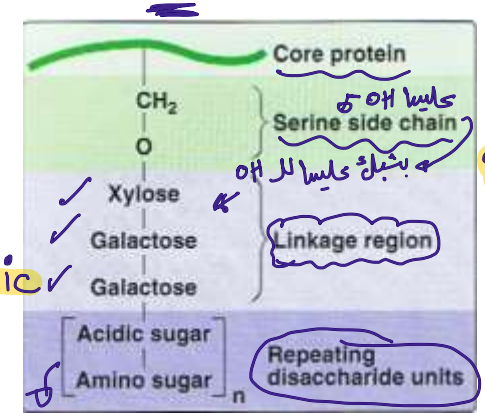
Glycosaminoglycans

- هم عبارة عن Structural sugar or carbohydrate
- بيدخل بتركيب الخلية
- يعني لما بتفتح الخلية، لازم اتفتح معها
- بيشتغلوا في mucas مكان يعمل ترطيب للمنطقة وبحمي الخبرة زال MO
  يلي بتحاول تفوت الجسم، ومكن يتجمعوا الحمات
- ولما تتكسر الخلية بتتكسر معها.

Glycosaminoglycans

- 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.





مكرر بالترتيب آلاف المرات

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**. ← GAG اسم ثاني لل
- 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.

كل واحد منهم إله disaccharide seq مختلف عن الثاني

- 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

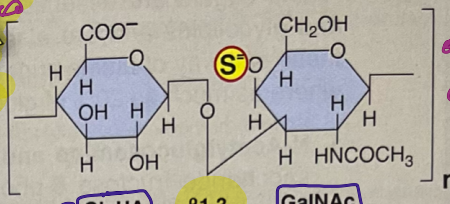
non-covalent (H-bond) يربط مع الـ GAG بشكل

مع الـ OH بتبع الـ serine

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

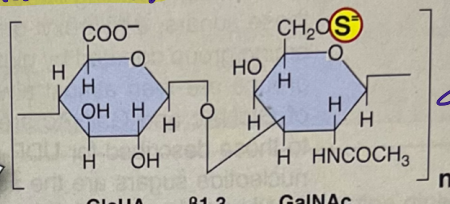
CHONDROITIN 4- AND 6-SULFATES

- 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



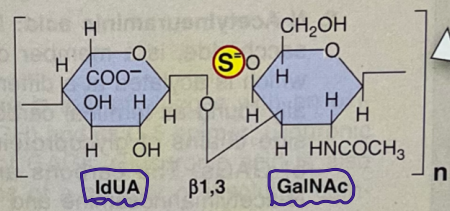
DERMATAN SULFATE

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



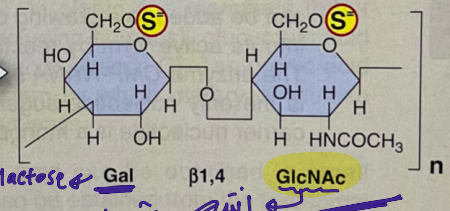
KERATAN SULFATES (KS) I and II

- 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-acetyl-neuraminic acid, and mannose
- KS I found in corneas; KS II found in loose connective tissue proteoglycan aggregates with chondroitin sulfate



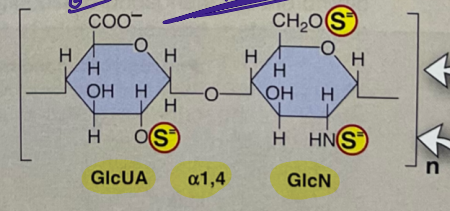
HEPARIN

- 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



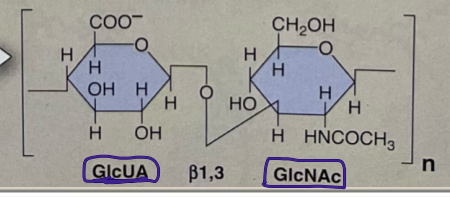
HYALURONIC ACID (HYALURONATE)

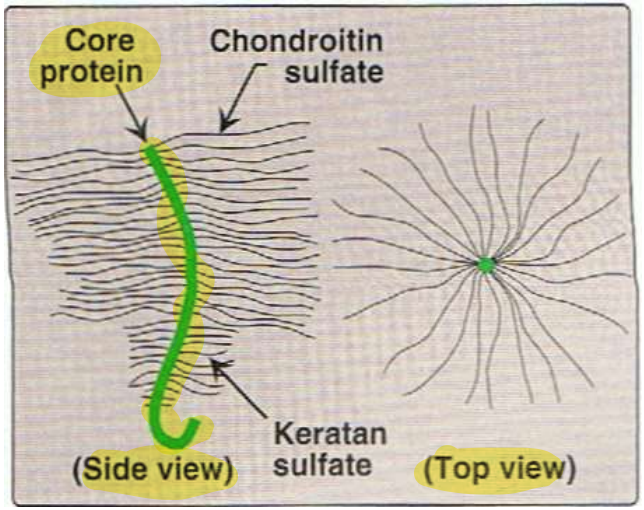
- Disaccharide unit: N-acetylglucosamine and glucuronic acid
- Different from other GAGs: unsulfated, not covalently attached to protein, and only GAG not limited to animal tissue, but also found in bacteria
- Serves as a lubricant and shock absorber
- Found in synovial fluid of joints, vitreous humor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

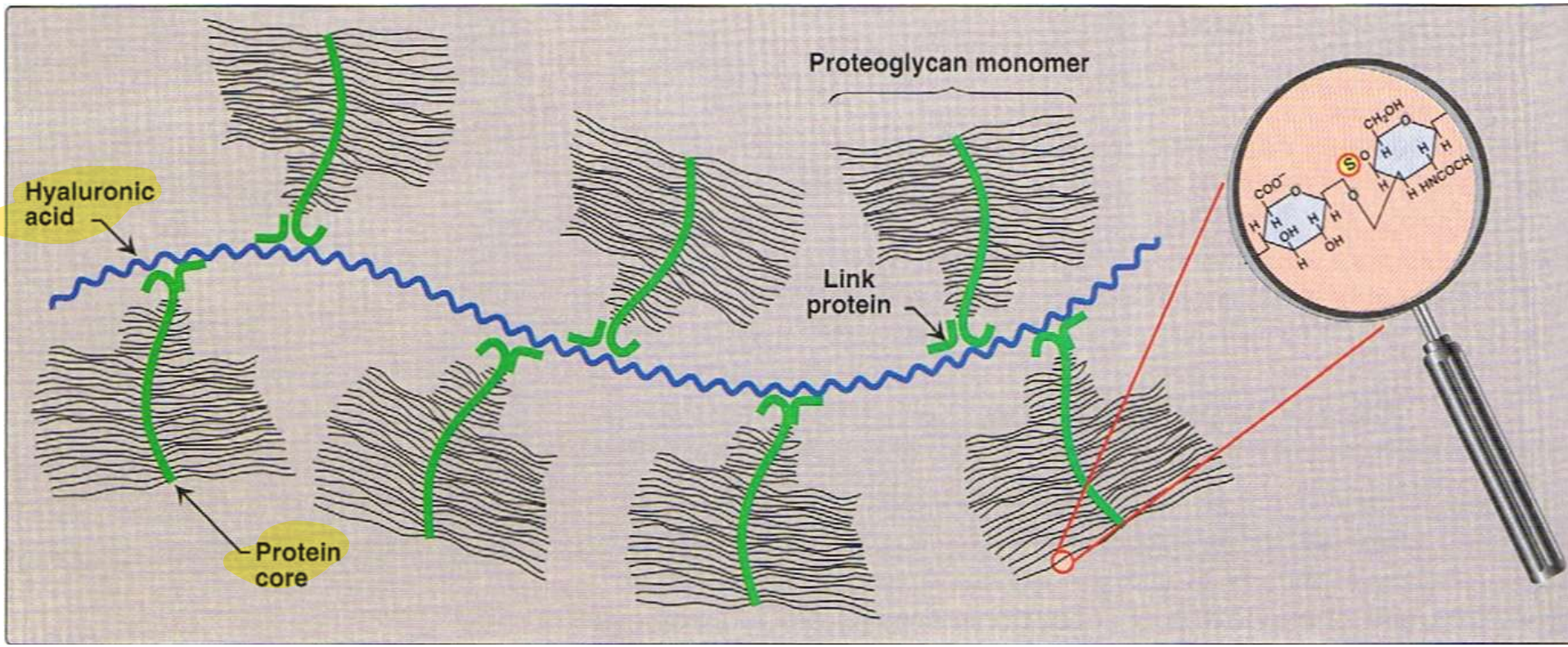


HEPARAN SULFATE

- 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

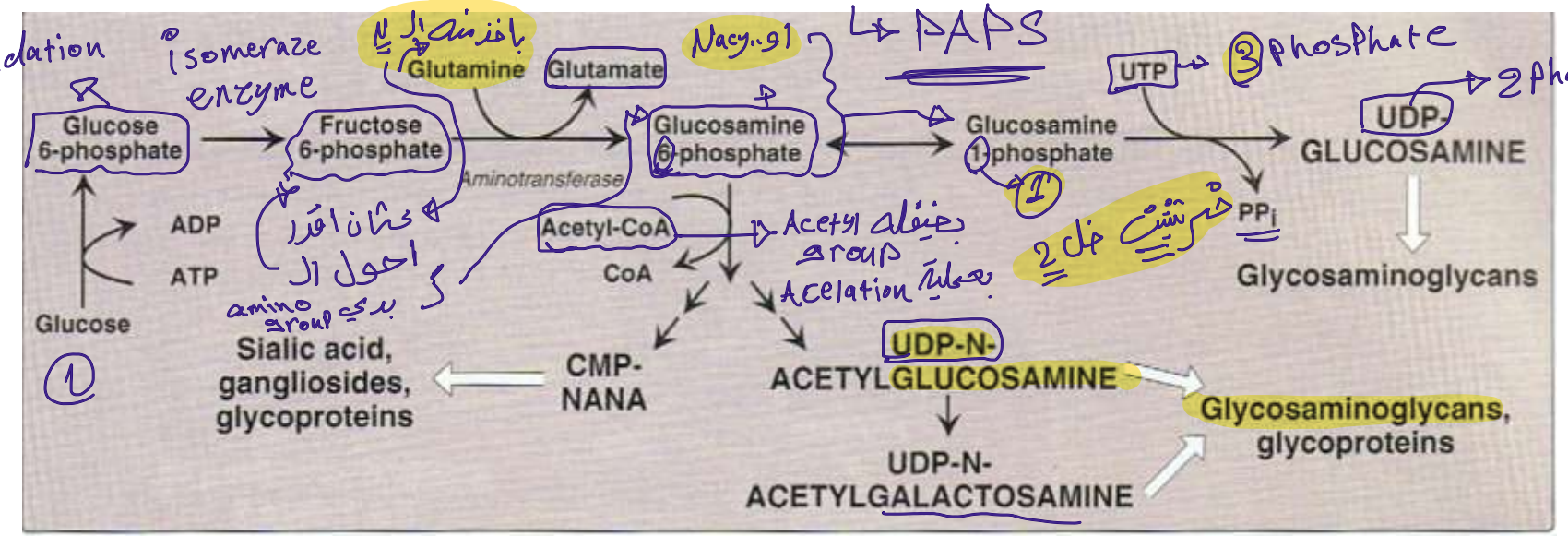


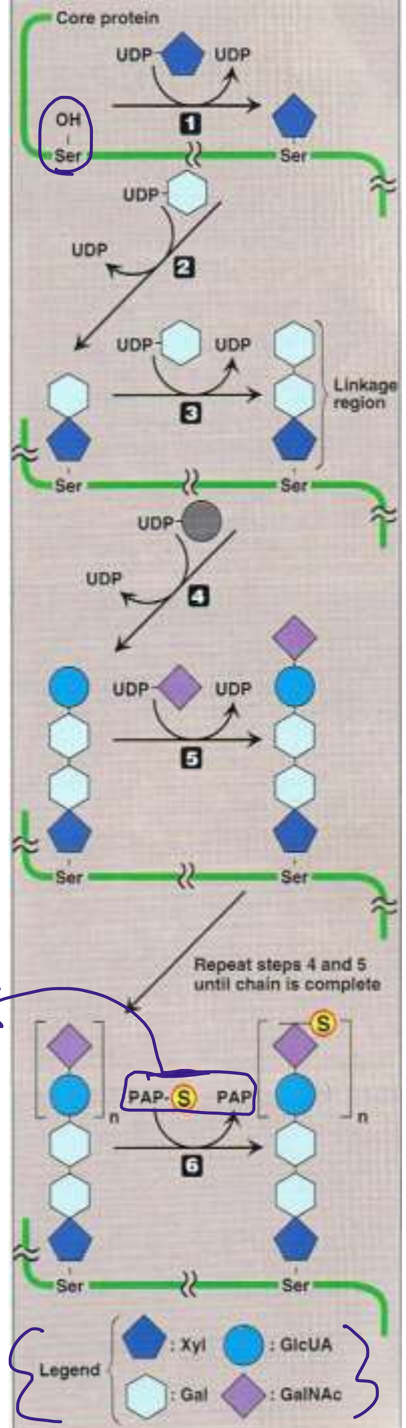

Core protein
Chondroitin sulfate
Keratan sulfate
(Side view)
(Top view)


Proteoglycan monomer
Hyaluronic acid
Link protein
Protein core

Synthesis of Glycosaminoglycans

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





اخر اشي بضيف الـ S على الراوية

حفظهم

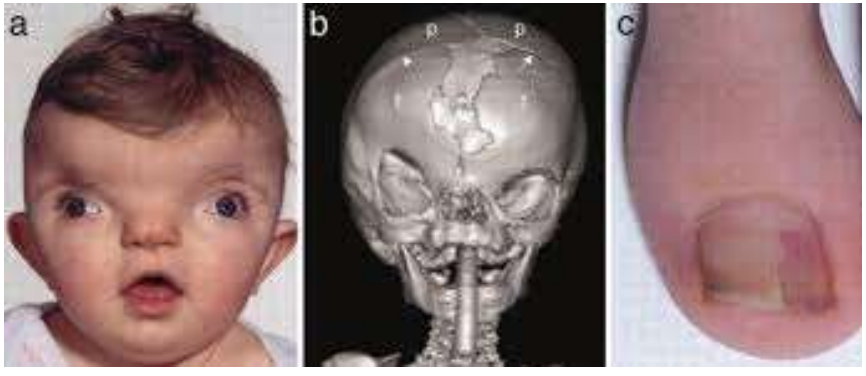
Mucopolysaccharidosis

- 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 mucopoly-saccharidosis.

- 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

- 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.

Function of glycoproteins

- Membrane-bound glycoproteins participate in a broad range of cellular phenomena, including:
  - Cell surface recognition (by other cells, hormones, viruses)
  - Cell surface antigenicity (such as the blood group antigens)
  - 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.

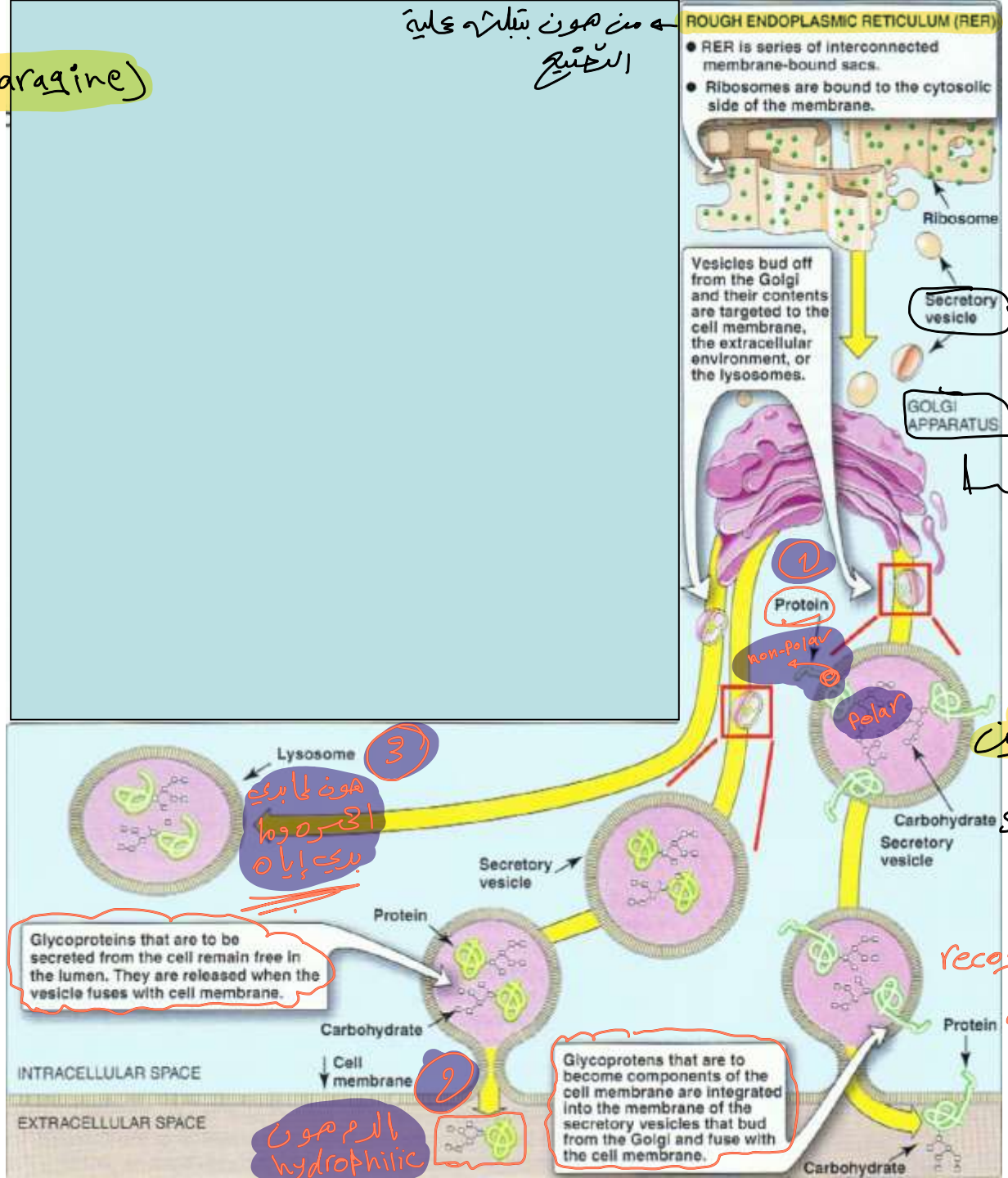
+ lysosomes that degradate GAG many of them are glycoprotein

Synthesis of Glycoprotein

- Glycoproteins are synthesized in the endoplasmic reticulum and the Golgi.
- The precursors of the carbohydrate components of glycoproteins are sugar nucleotides.
- O-linked glycoproteins are synthesized by the sequential transfer of sugars from their nucleotide carriers to the protein
- 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
- They also require **dolichol**, an intermediate carrier of the growing oligosaccharide chain.

يلي هو بالعادة
ASN (Asparagine)

من هون بتبلش عملية التصنيع



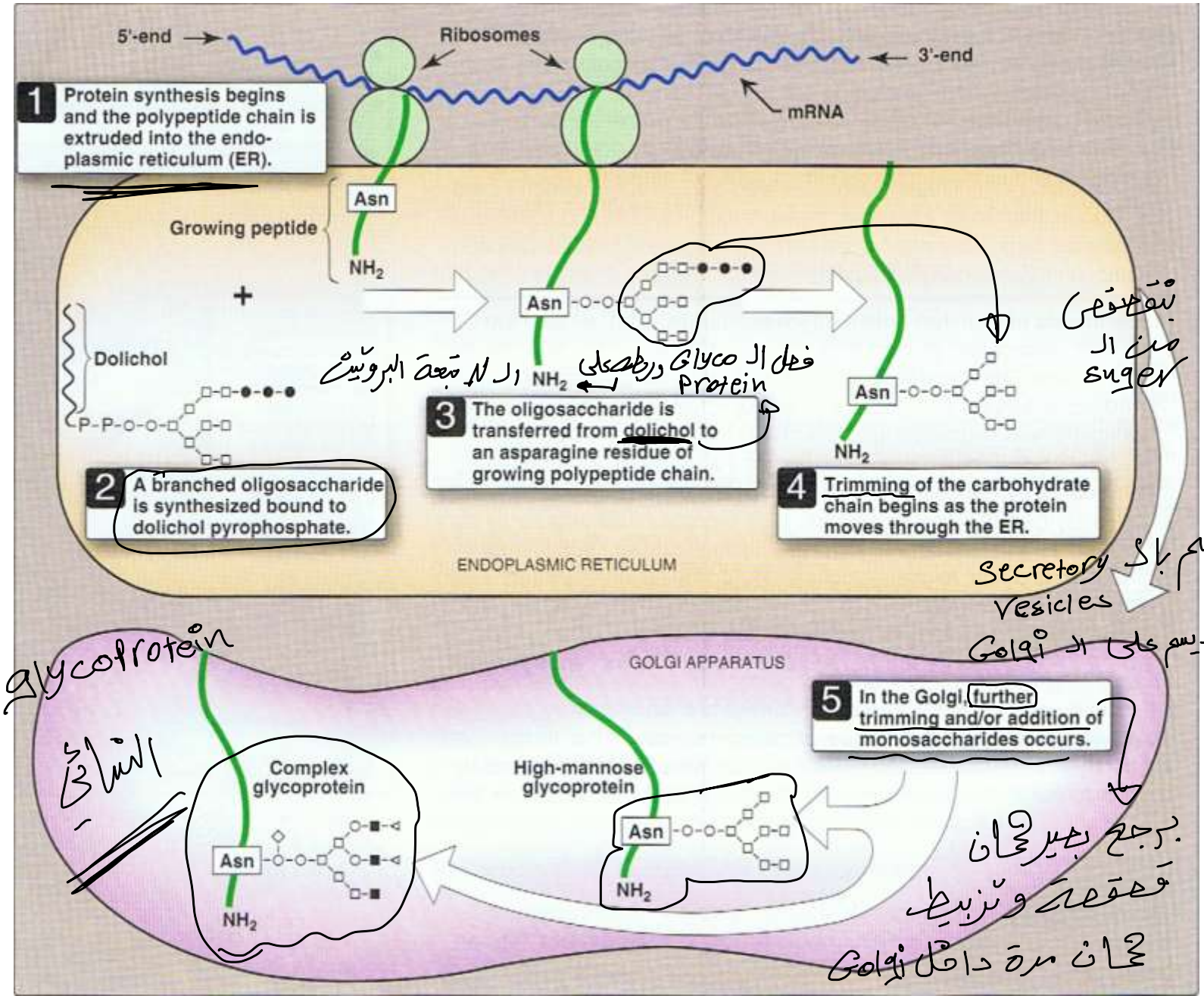
عن طريقها بتم عملية افراز الـ glycoprotein

بتفصل جواته عمليات معينة

بعد ما تكون قبل الـ Glycoprotein النهائي، بدنا نفصله افرازه على حسب مكانه اووين بدنا يشتغل، عن طريق الـ Secretory vesicle

حكينا فوق إنه على سطح الخلية بفصل recognition او انه إله antigenicity

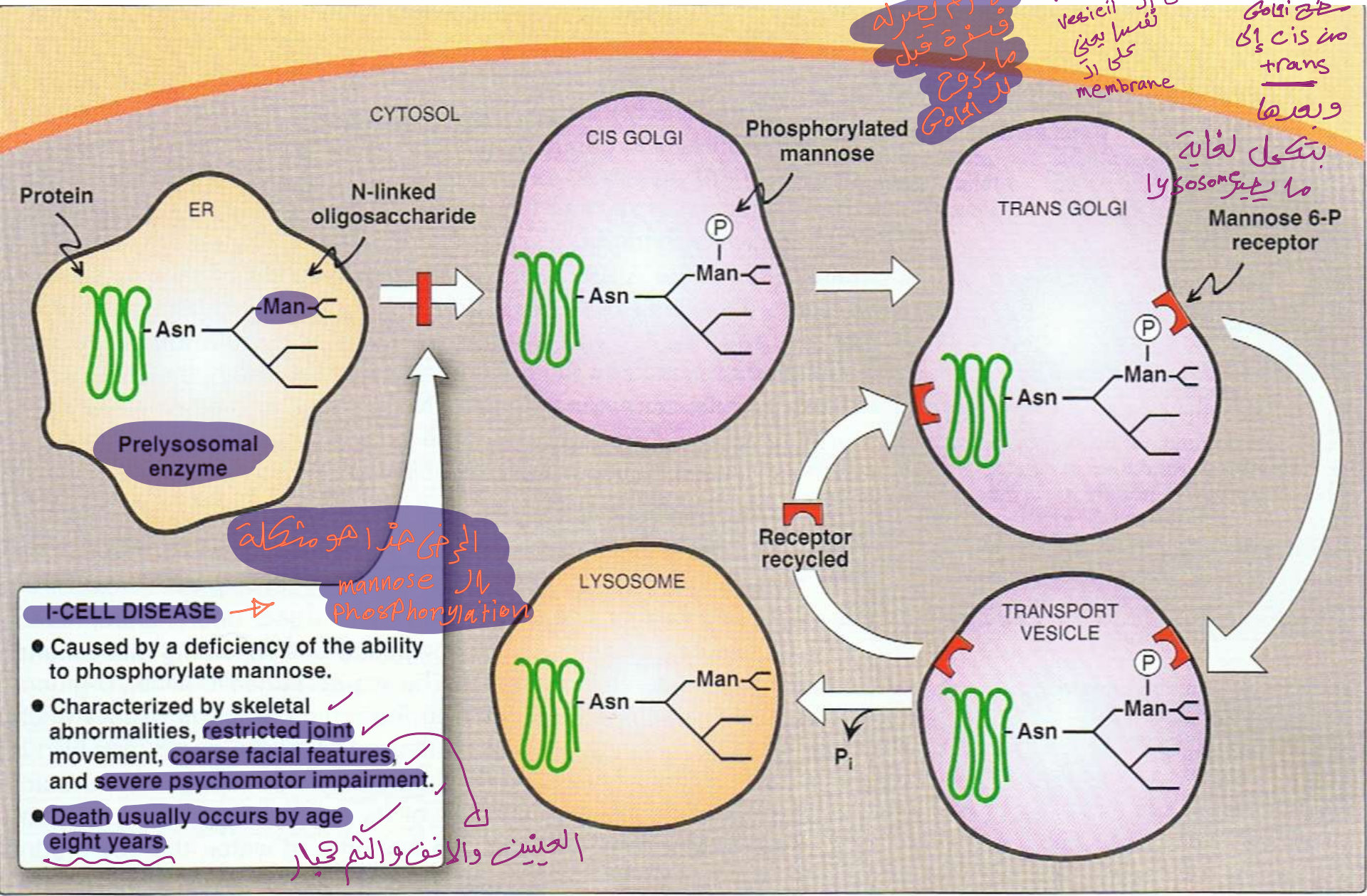
Synthesis of N-linked glycoproteins.



Lysosomal degradation of glycoproteins

لو جاءت هون مشكلة

- 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 المرض

1. لا يتم إضافة فسفرة قبل ما يروح لـ Golgi
2. عملية الفسفرة إلها receptor على الـ vesicle تقسيا يعني على الـ membrane
3. يتحول عملية الفسفرة Golgi على cis من trans وبعدها بتكمل لغاية ما يصير lysosome

المرض هذا هو مشكلة mannose الـ phosphorylation

الحبيبين والأنف والثم كبار