# تفريغ كيمياء حيوية

اسم الموضوع: glycosaminoglycans part 2

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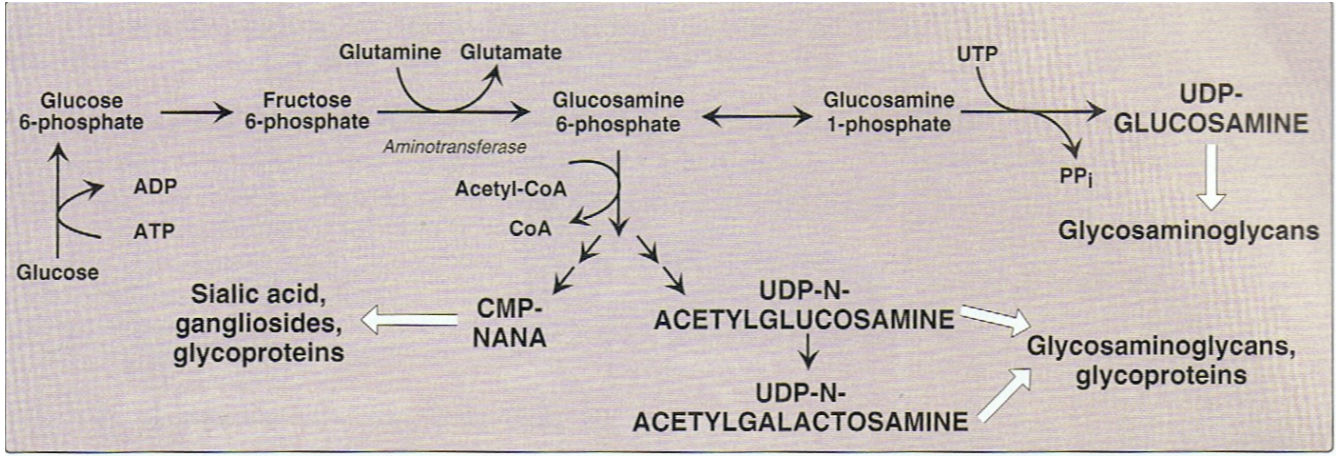
لجان الدُّفعات

# 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.



اول اشي الcore protein لازم يتصنع فلازمني rough endoplasmic reticulum و golgi apparatus

ال elongation لل polysaccharide chain بتم senquential

اول اشي لازم يعمل activation للsugar (ممكن اصنع glucosamine و galactosamine و بعدين اعمل acetylation بعدين بعمله activation عن طريق UTP فبكون عندي UDP sugar و بعدين منضيفه على ال senquential addition)

نبدأ بالغلوكوز بحوله ل glucose 6-phosphate عن طريق glucokinase بعدين بتحول ل fructose 6-phosphate

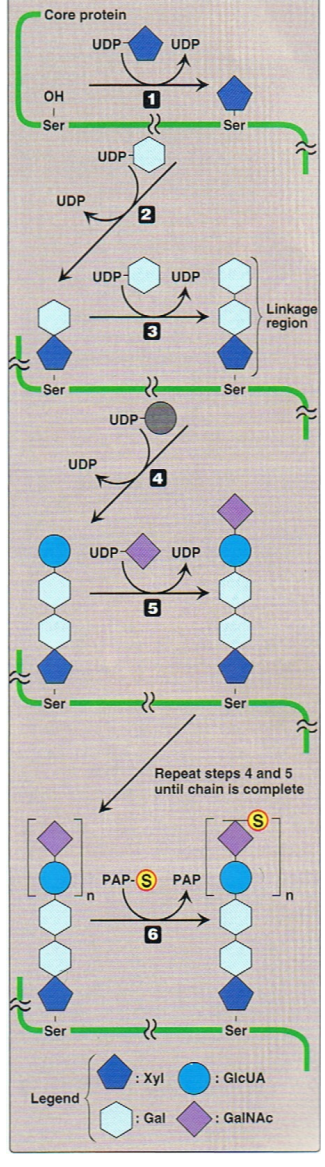
بعدين بصير عملية تبديل بين الOH اللي عالغلوكوز و ال amino group اللي موجودة عالغلوتامين فبحول ال glutamine ل glutamic acid و ال fructose 6-phosphate بحوله ل glucosamine 6-phosphate

ال glucosamine الموجود عشكل phosphate-6 بعمله acetylation من ال acetyl CoA فصار عندي N-acetyl glucosamine

شو ما كان ( glutamic acid , glucose galactose , glucosamine, galactosamine , n acetyl glucosamine...) لازم نعمله activation عن طريق ال UTP واللي هو uridine اللي هو عبارة عن uracil triphosphate و اله ٣ phosphate والglucosamine 1-phosphate عنده 1 صاروا ٤ بطلع ٢ phosphate فبضل عندي UDP-glucosmine

- sugar activation => UTP
- fatty acids => CoA
- amino acids => trna

عملية ال sulfation من ال phosphoadenosyl-phosphosulfate هاد بنقل ال sulfate group لل glucosamine او galactosamine او شو ما كان


Core protein
UDP
UDP
OH
1
Ser
Ser
UDP
UDP
2
UDP
UDP
3
Linkage region
Ser
Ser
UDP
UDP
4
UDP
UDP
5
Ser
Ser
Repeat steps 4 and 5 until chain is complete
S
PAP-S
PAP
n
n
6
Ser
Ser
Legend
: Xyl
: GlcUA
: Gal
: GalNAc

احنا جهزنا كل ال sugars وهسا منبلش نضيفهم واحد واحد

اول اشي منعمله .. منصنع ال core proteins وفي عندي ال serine عليها OH ومنبلش باضافة UDP xylulose وال UDP بطلع وال xylulose بركب على ال serine بعدين ال UDP galactose و UDP galactose تانية حيكونوا linkage region

بعدين منضيف glucorunic acid و n acetyl galactosamine

بعدين منضيف sulfate من ال phosphoadenosyl phosphosulfate

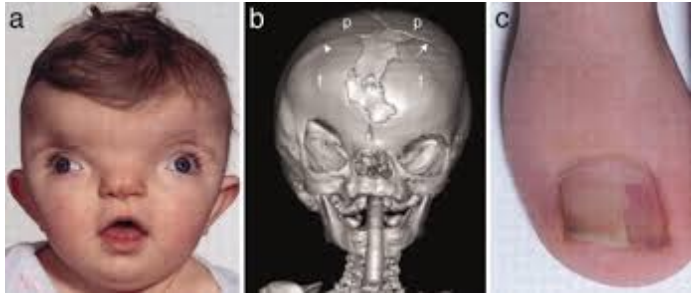
# Mucopolysaccharidosis

- 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



اي اشي ببنيه لازم يكون عندي القدرة اكسره .. وهدول موجودين على سطح الخلية فبالعادة عملية ال degradation بتكون من خلال ال lysosomes لانه بصيرلهم زي phagocytosis و بتبلعهم الخلية و بتدخلهم لجوا وبتحدوا مع ال lysosomal vesicle و ال lysosomal enzyme الموجودة جوا بتبلش تعمللهم degradation و تكسرهم و هاي العملية بتصير لما الخلية بدها تعمل turnover وتموت وتطلع وحدة جديدة بدالها و اللي بصيرلها تصنيع زي الشرح فوق

في حال انه واحد من هاي ال hydrolases الموجودة كان فيها defect وراثي و النتيجة بتكون عبارة عن mucopoly-saccharidosis اللي هو accumulation لل glycosaminoglycans جوا ال lysosomes يعني دخلت عال lysosomes بس ال hydrolases اللي جوا ما اشتغلت فبتبلش تتراكم

فال result features اذا بحكي عن طفل بكون شكله زي اللي بالصورة فرح يصير عنده skeletal and extracellular matrix deformities و deformities يعني تشوهات بالعظام وال extracellular matrix و بصير عنده mental retardation

# 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.

ال glycoproteins عكس ال proteoglycans ( الglycan هو الكبير وال proteo الصغير) بينما الglycoprotein البروتين هو الكبير وال sugar هو الصغير الموجود عالسطح

ما فيهم serial repeats زي ال glycosaminoglycans

** اي glycoprotein بتصنع بالجسم كل مرة بنضاف عليه sugar unit .. بنضافوا بنفس ال sequence

حجم الكربوهيدرات بكون صغير

# 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.

وظائفهم

وجدوا انهم عسطح ال membrane و بعرفوا عالخلية cell surface recognition للخلايا التانية من هرمونات
وفيروس يعني الفيروس اللي بعمل hepatatis بروح على ال liver ما بروح على اي organ تاني

# Synthesis of Glycoproteins

- 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.

التصنيع بال rough endoplasmic reticulum لانه بدي ribosomes بتصنيع البروتين وكمان بال golgi عشان يصيرلهم secretion لبرا

بتصير عمليات ال addition لل sugar units و اللي لازم ينعمللهم activation عشكل nuecleotides

في نوعين منهم
١- O linked يعني برتبط مع serine او threonine او tyrosine عال OH عبارة عن sequential addition
٢- N-linked يعني برتبط عال asparagine و في اشي اسمه lipid carrier زي fatty acid طويل اسمه dolichol مرتبط مع ال membrane تبع ال endoplasmic reticulum و بتصير عملية اضافة ال sugar بال oligosaccharide chain بعدين بشيلها وبركبها عالبروتين

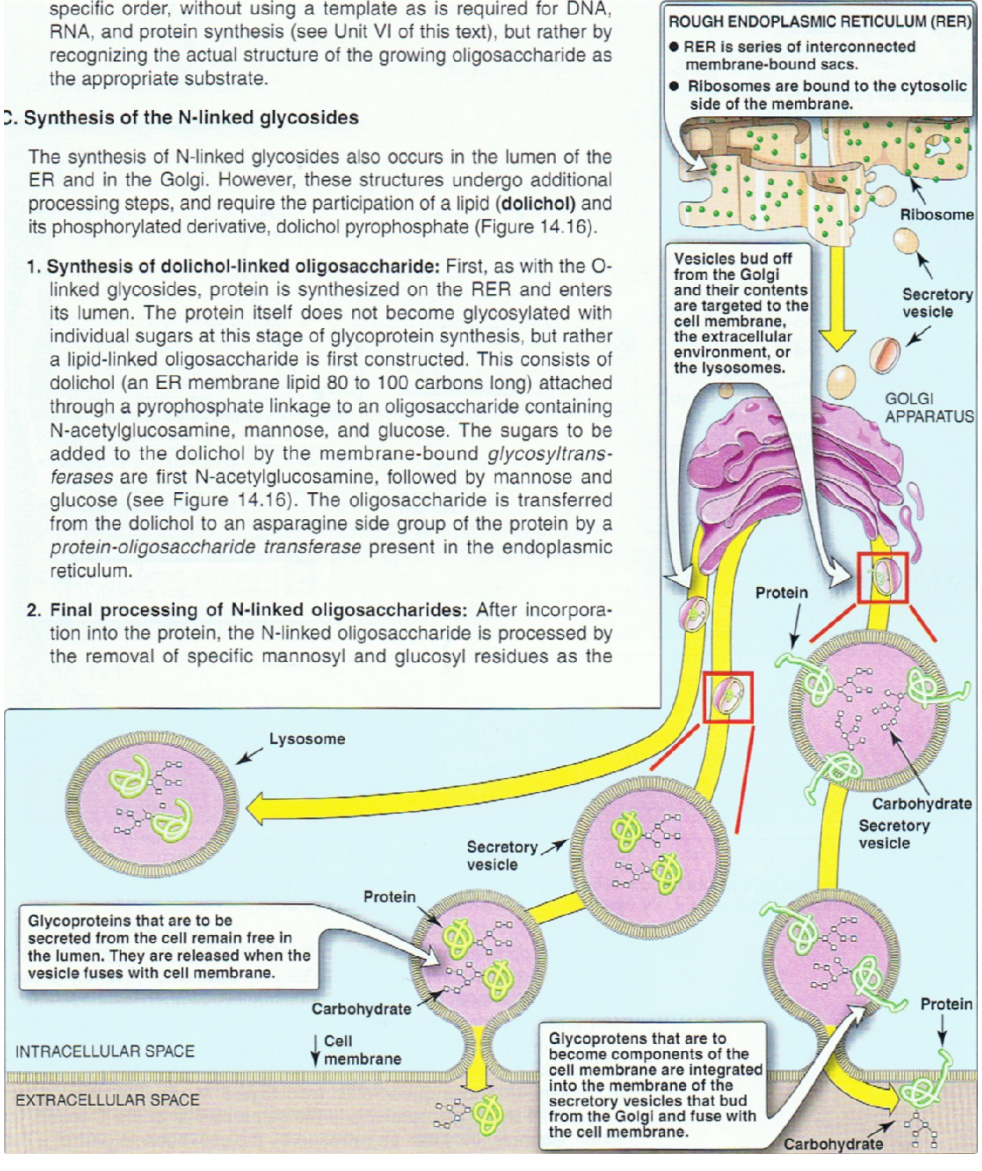
specific order, without using a template as is required for DNA, RNA, and protein synthesis (see Unit VI of this text), but rather by recognizing the actual structure of the growing oligosaccharide as the appropriate substrate.

### C. Synthesis of the N-linked glycosides

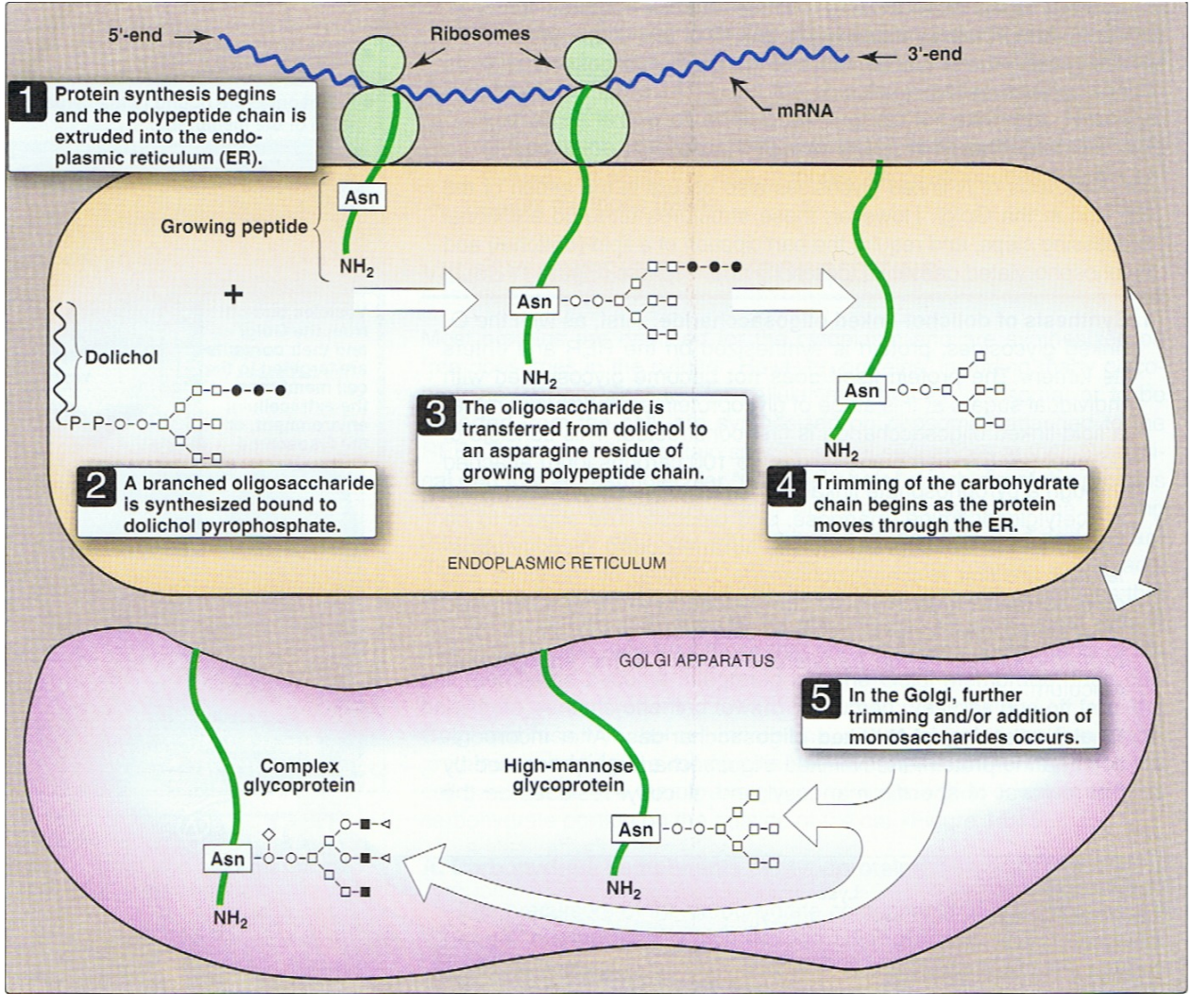
The synthesis of N-linked glycosides also occurs in the lumen of the ER and in the Golgi. However, these structures undergo additional processing steps, and require the participation of a lipid (**dolichol**) and its phosphorylated derivative, dolichol pyrophosphate (Figure 14.16).

1. **Synthesis of dolichol-linked oligosaccharide:** First, as with the O-linked glycosides, protein is synthesized on the RER and enters its lumen. The protein itself does not become glycosylated with individual sugars at this stage of glycoprotein synthesis, but rather a lipid-linked oligosaccharide is first constructed. This consists of dolichol (an ER membrane lipid 80 to 100 carbons long) attached through a pyrophosphate linkage to an oligosaccharide containing N-acetylglucosamine, mannose, and glucose. The sugars to be added to the dolichol by the membrane-bound *glycosyltransferases* are first N-acetylglucosamine, followed by mannose and glucose (see Figure 14.16). The oligosaccharide is transferred from the dolichol to an asparagine side group of the protein by a *protein-oligosaccharide transferase* present in the endoplasmic reticulum.

2. **Final processing of N-linked oligosaccharides:** After incorporation into the protein, the N-linked oligosaccharide is processed by the removal of specific mannosyl and glucosyl residues as the



# Synthesis of N-linked glycoproteins.



# Lysosomal degradation of glycoproteins

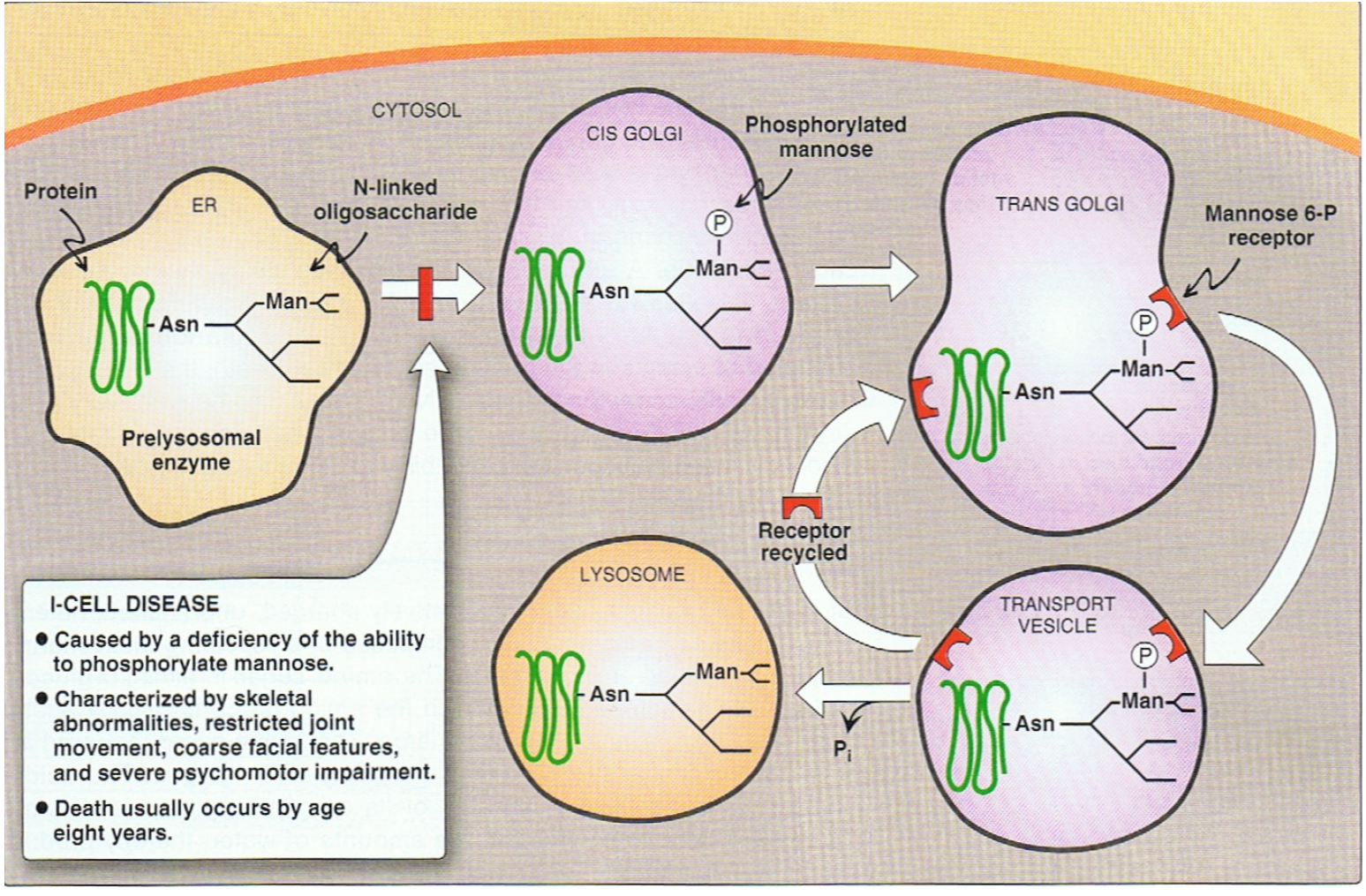
- A deficiency in the phosphorylation of mannose residues in N-linked glycoprotein pre-enzymes destined for the lysosomes results in **I-cell disease**

- 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

بصير في اتحاد بين الglycoproteins والlysosomes عن طريق phagocytosis وال hydrolases هي المسؤولة عن عملية ال degradation

ال defficiency فيها بنتج oligosaccharidosis ... الoligosaccharides ما بتتكسر فبتضل تتراكم جوا ال lysosomes




بصير secretion لل
oligosaccharide من ال
golgi و ال mannose بصيرله
عملية phosphorylation
عشان ال receptor الموجود
يرتبط مع الphosphate و يغير
شكل ال golgi من cis ل trans
و بعد هيك بتحول ل transport
vesicle و بتروح على شكل
lysosome

اللي بنتج من هاي العملية هو ال
i cell disease