Structural proteins

Fibrous proteins

- collagen
- elastin

welcome back ☆

Fibrous proteins

- Serve structural function in the body
- Collagen is a component of skin, connective tissue, blood vessel wall, sclera and cornea of the eye.
- Exhibit special mechanical properties, resulting from its unique structure, which are obtained by combining specific amino acids into regular, secondary structural elements
- Collagen and elastin are examples

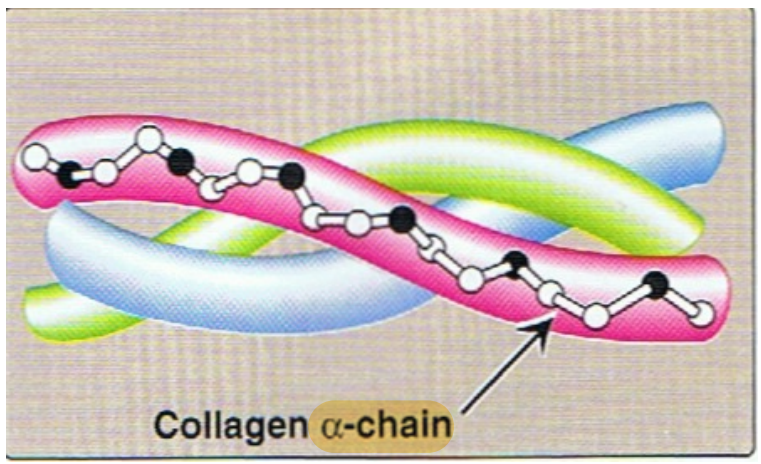
Collagen

3 α-chains

can't produce helices bc of prolines

- Has long rigid structure with three α-chains wound around each other in a triple helix (1000 aa each)

- Their types and organization depend on the tissue:
  - May be dispersed as a gel to give support to the structure as in vetreous humer of the eye
  - May be bundled in tight parallel fibers that provide strength as in tendons
  - Collagen of bone occurs as fibers arranged at an angle to each other so as to resist mechanical shear from any direction



من الدكتورة
الأرقام مش حفظ

3 Types of Collagen

1- fibril forming collagen
2- network forming collagen
3- fibril associated collagen

- Collagen can be organized into three types depending on their locations and functions.
- Fibril-forming collagen: type I, II and III have rope-like structure
- Network forming collagen: type IV and VII form a three dimensional mesh that constitute a major part of basement membrane (شبكة)
- Fibril associated collagen: type IX and XII bind to the surface of collagen fibril

TYPE	TISSUE DISTRIBUTION
	تشكيل
	Fibril-forming
I	Skin, bone, tendon, blood vessels, cornea
II	Cartilage, intervertebral disk, vitreous body
III	Blood vessels, fetal skin
	شبكة **Network-forming**
IV	Basement membrane
VII	Beneath stratified squamous epithelia
	Fibril-associated
IX	Cartilage
XII	Tendon, ligaments, some other tissues

الأمثلة حفظ

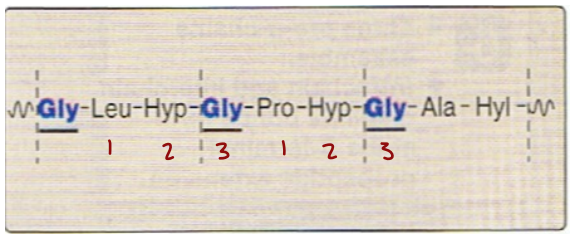
مثال ع network forming

Structure of Collagen

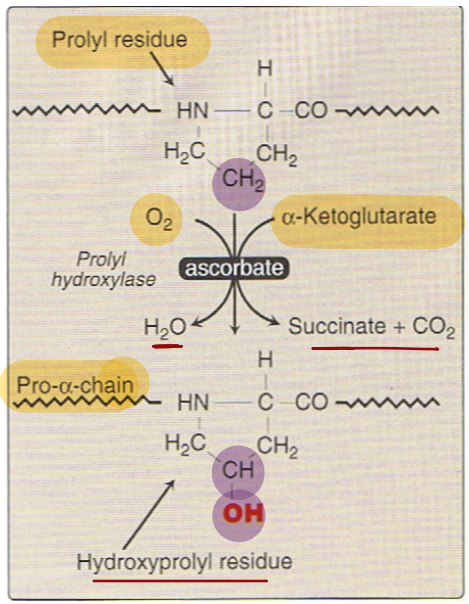
- Amino acid sequence: it is rich in proline and glycine. Glycine is present in every third position

Gly aa aa Gly aa aa Gly

1 2 3 1 2 3



- Triple helical structure: elongated, triple helical structure



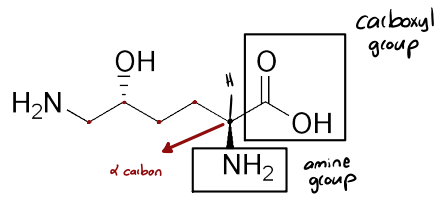
- Hydroxyproline and hydroxylysine: come from the hydroxylation of proline and lysine residues (posttranslational modification) necessary for the stabilization of the triple-helical structure

OH

بعد الترجمة

- Add suger

Glycosylation: enzymatic glycosylation of the hydroxyl group of hydroxylysine. Mainly by glucose and galactose.



hydroxylysine

OH

Enzymatic glycosylation for :

-Proline

-lysine

- hydroxylysine

- hydroxyproline... عرض المزيد

Biosynthesis of collagen

مواد أولية

Precursors of collagen are formed in fibroplast, secreted into the extracellular matrix after enzymatic modification, the mature collagen monomers aggregate and become crosslinked to form collagen fibrils

يتراكم

1. Formation of pro-α-chain — -enzymes-
2. Hydroxylation : performed by prolyl hydroxylase and lysyl hydroxylase, requires molecular oxygen, Iron and vitamin C. (O_2)
3. Glycosylation
4. Assembly and secretion
5. Extracellular cleavage of procollagen molecule
6. Formation of collagen fibrils
7. Cross-link formation

ايش المادة الي ما بتدخل بتصنيع الكولاجين

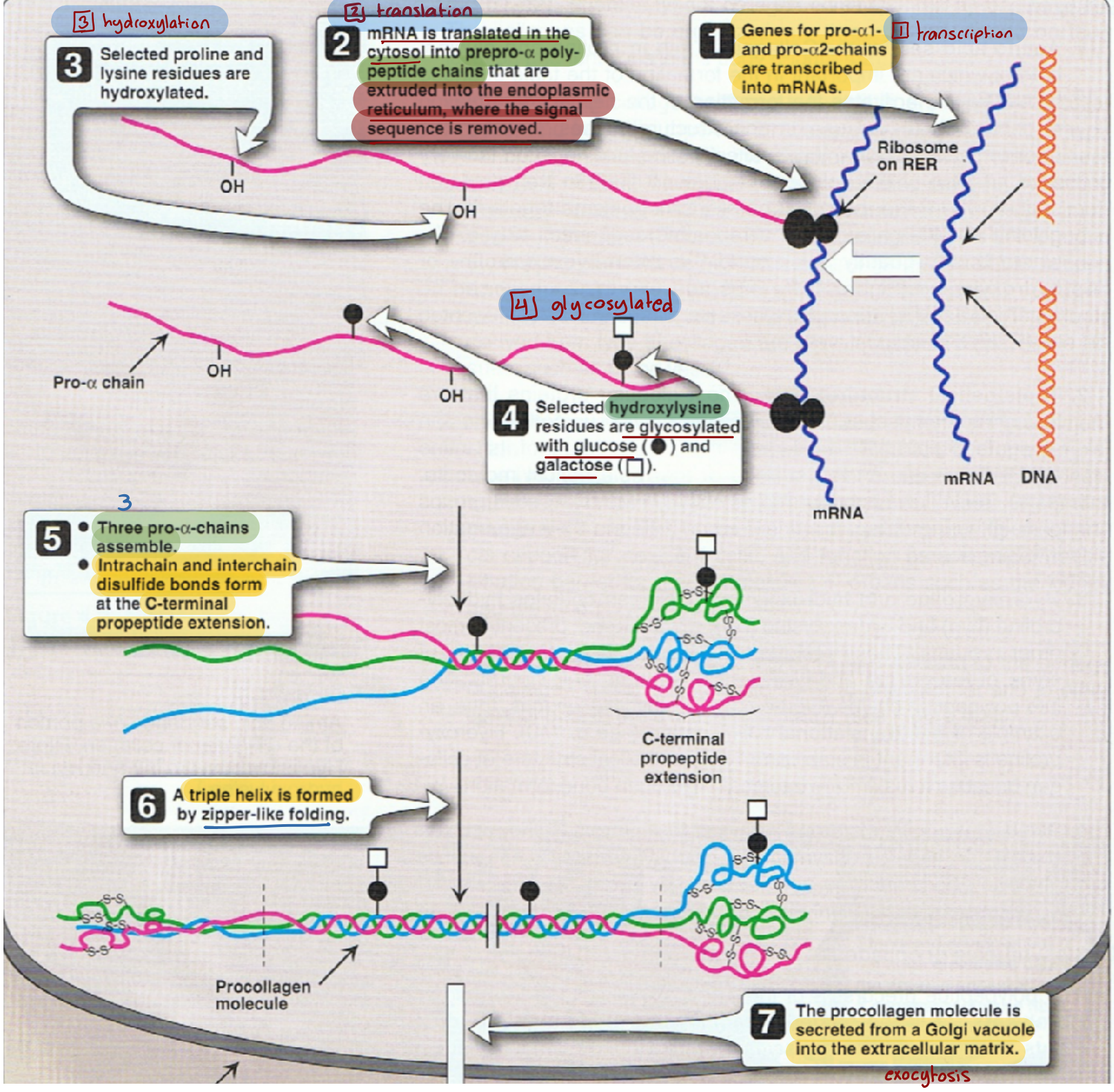
- zinc

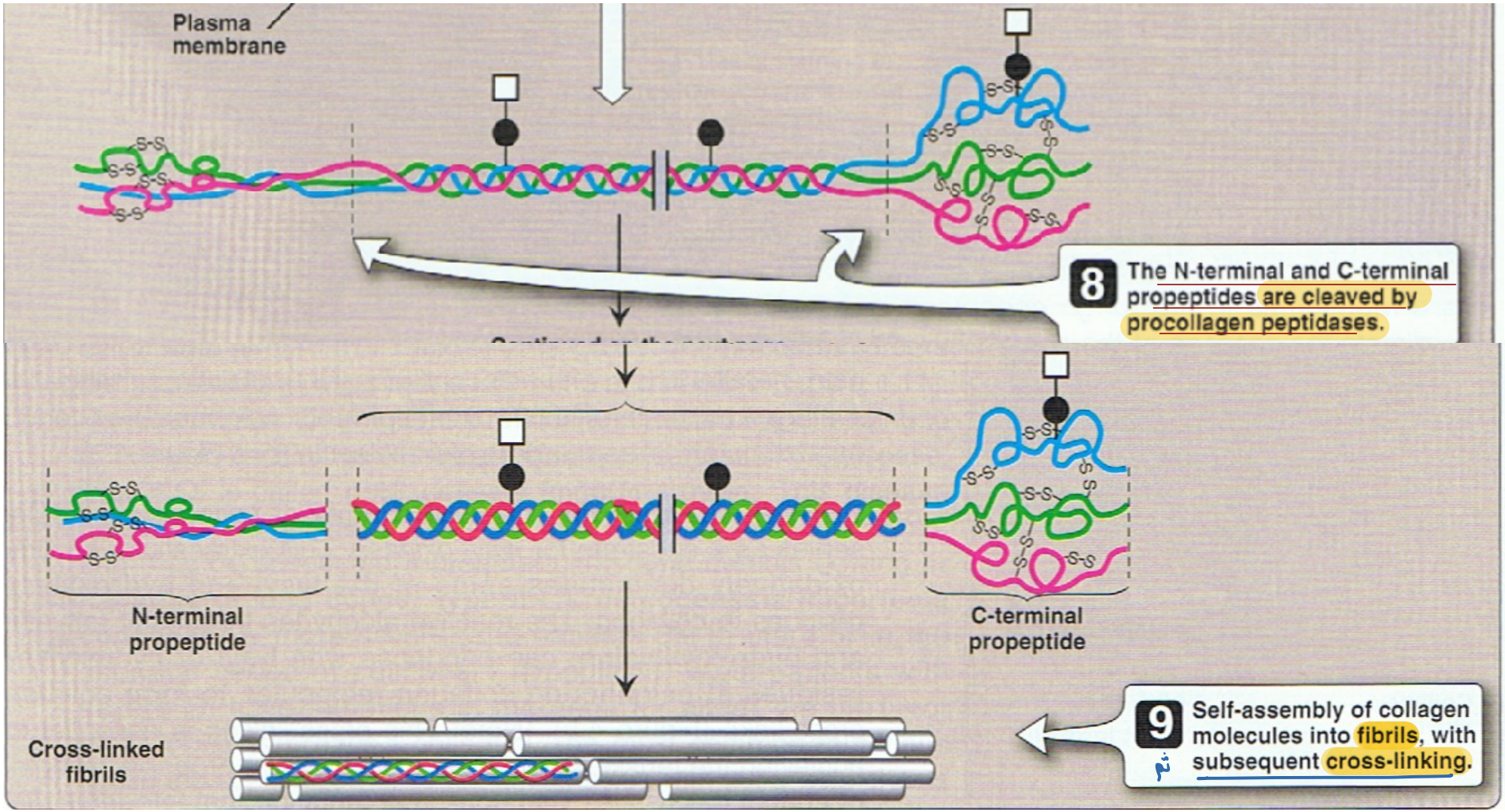
طيب شو بدخل؟

O_2

vitamin C

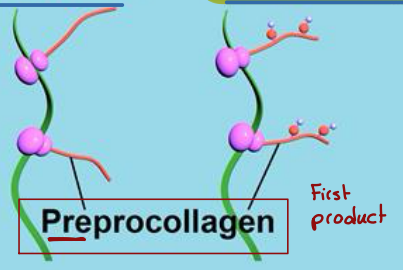
iron


[3] hydroxylation
3 Selected proline and lysine residues are hydroxylated.
OH
OH
[2] translation
2 mRNA is translated in the cytosol into prepro-α polypeptide chains that are extruded into the endoplasmic reticulum, where the signal sequence is removed.
1 Genes for pro-α1- and pro-α2-chains are transcribed into mRNAs.
[1] transcription
Ribosome on RER
mRNA
DNA
[4] glycosylated
Pro-α chain
OH
OH
4 Selected hydroxylysine residues are glycosylated with glucose (●) and galactose (□).
mRNA
3
5 Three pro-α-chains assemble.
Intrachain and interchain disulfide bonds form at the C-terminal propeptide extension.
S-S
C-terminal propeptide extension
6 A triple helix is formed by zipper-like folding.
Procollagen molecule
7 The procollagen molecule is secreted from a Golgi vacuole into the extracellular matrix.
exocytosis


Plasma membrane
8 The N-terminal and C-terminal propeptides are cleaved by procollagen peptidases.
N-terminal propeptide
C-terminal propeptide
Cross-linked fibrils
9 Self-assembly of collagen molecules into fibrils, with subsequent cross-linking.

Collagen Synthesis

1. Translation on ribosome
2. Hydroxylation of Pro and Lys

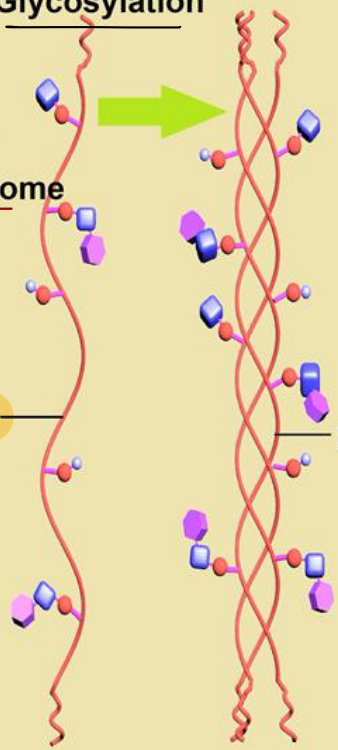


Endoplasmic reticulum

3. Release from ribosome

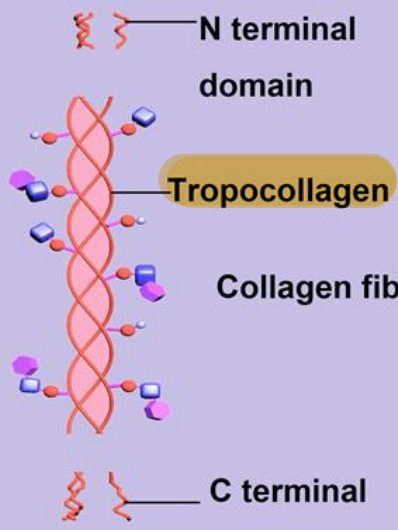
4. Glycosylation

5. Triple helix formation

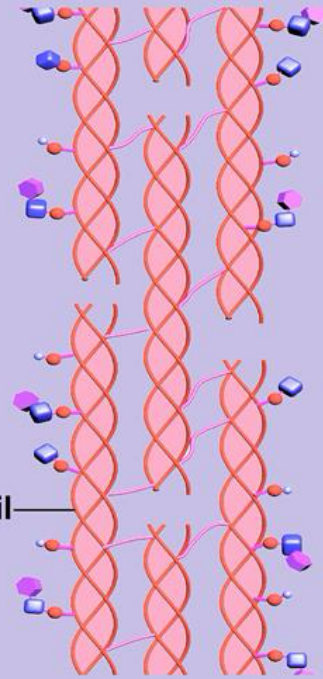


6. Secretion from cell

7. Removal of N and C terminal domains



8. Crosslink formation



H
O
Galactose
Glucose
Procollagen peptidases

Cytosol

Extracellular space

by XW Hou

Degradation of Collagen

- Normal collagen are highly stable molecules
- As response to growth or injury, the breakdown of collagen is mainly due to collagenase
- For type I collagen the cleavage is specific, generating three-quarter and one quarter
- Further degradation to amino acids occurs by other matrix proteinases

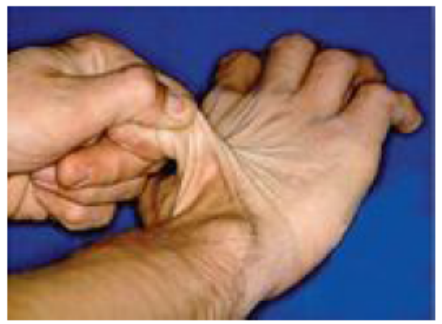
مكون ما بدخل بعملية تكون الcollagen

الجواب collagenase ⟹ Function in breakdown of collagen

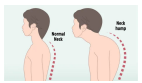
Collagen diseases

1. Ehlers Danlos syndrome
   - enzymes defficiency
   - a.a mutation type 1 + 3 + 5
2. Osteogenesis imperfecta

- **Ehlers- Danlos syndrome**
  - Results from a defficiency in lysyl hydroxylase or procollagen peptidase enzymes or amino acid mutation of collagen I, III or V
  - In collagen III mutation (present in arteries), collagen is not secreted so **lethal vascular problems** occur, in addition to **stretchy skin and loose joints**

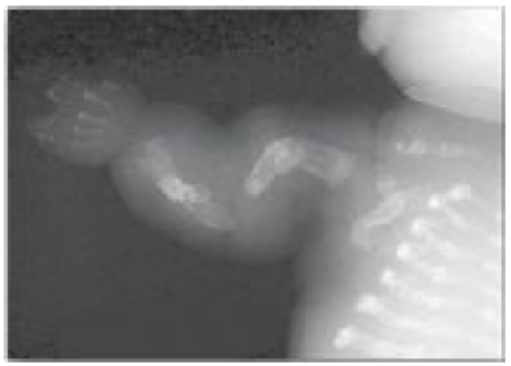


- **Osteogenesis imperfecta** هشاشة عظام
  - Inherited disorder, characterized by bones that easily bend and fracture



ظهر منحني

  - Humped back is a common feature of the disease
  - There are two types:
    - Osteogenesis imperfecta tarda: early infancy with fractures secondary to minor trauma
    - Osteogenesis imperfecta congenita: more severe, pateints die before birth.



procollagen peptidase

سؤال

نقصان بال college peptidase يسبب ما عدا

-stretchy skin

-humped back ✓ osteogenesis imperfecta

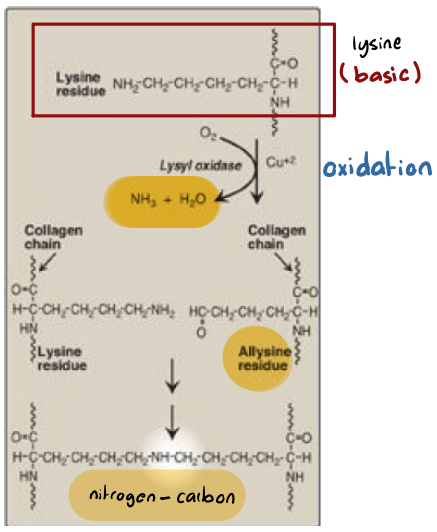
-loose joint

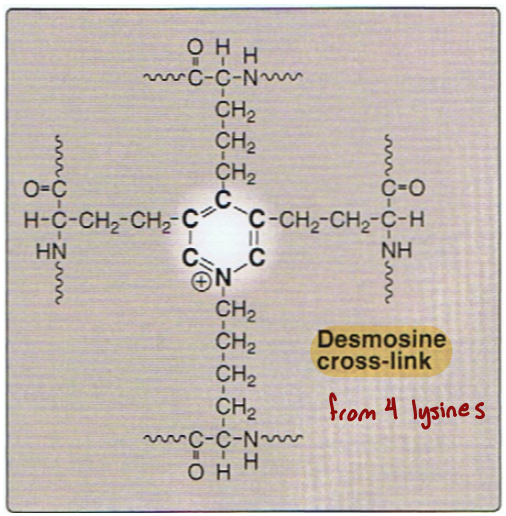
-vascular problem

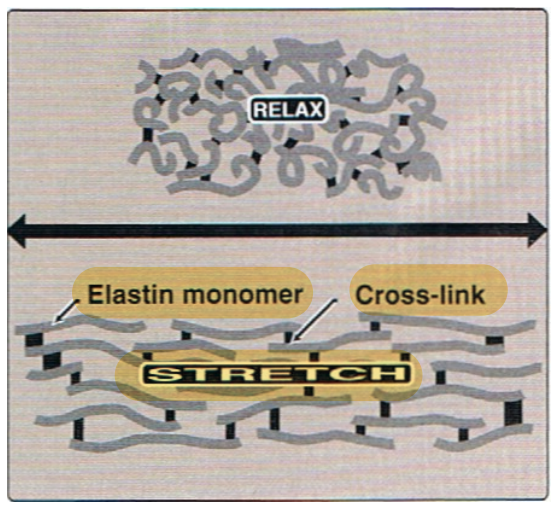
اجا سؤال عن collage III mutation وانه ايش
بسببّ

Elastin

- Is a connective tissue protein with rubber like properties which can stretch and bend in any direction when stressed.
- Found in lung, walls of large arteries and elastic legaments
- Structure of elastin
  - Protein polymer synthesized from a precursor (tropoelastin)
  - 700 aa of small, nonpolar aa, rich in proline and lysine
  - Secreted and deposited onto fibrillin
  - Oxidative deamination of lysine by lysine oxidase produces allysine which forms the desmosine cross-link







neutrophil elastate
↳ it breaks down elastin

protector ؟

α-1 antitrypsin
↳ inhibit - trypsin
- neutrophil elastate

Elastin

good for lungs elasticity

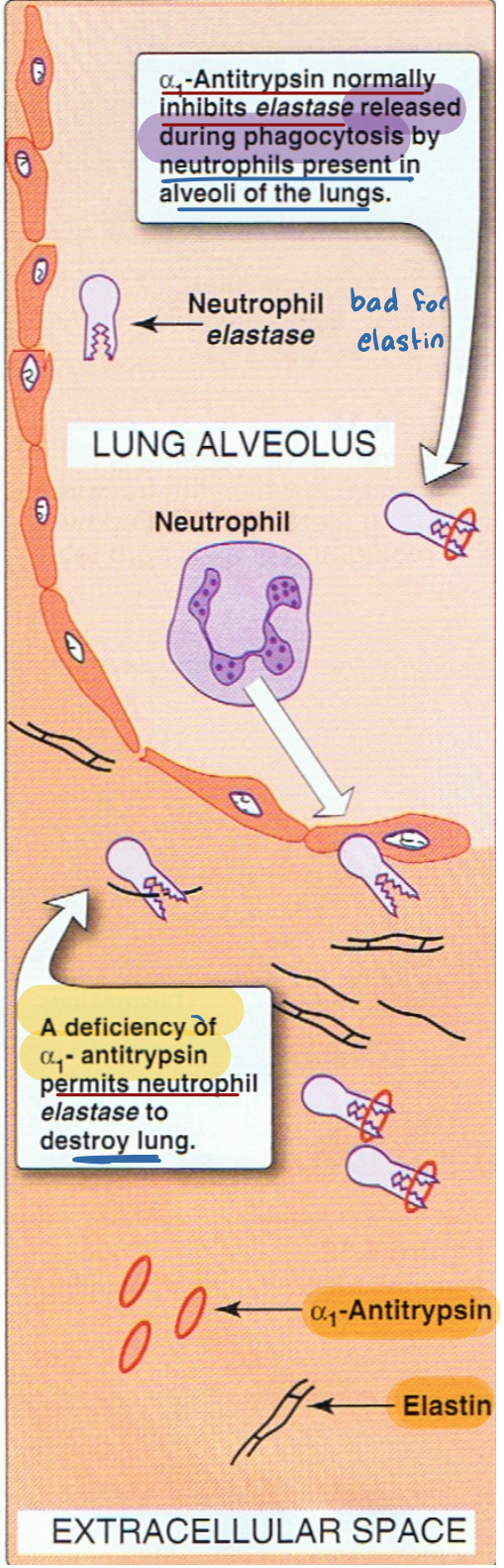
- Role of α1 antitrypsine in elastin degradation
- Produced by liver and other tissues as monocytes and alveolar macrophages

محلل البروتينات

- Inhibit no. of the proteolytic enzymes including trypsin and neutrophil elastase so prevents elasin degradation in the alveoli.

- α1 antitrypsine defficiency

- In the alveoli: elastase released by activated and degenerating neutrophils is normally inhibited by α1 antitrypsin



The main function of α1-antitrypsin is to:

A. Activate collagen synthesis
B. Inhibit elastase
C. Increase oxygen binding
D. Break down fibrin

α1 - AT

α1 antitrypsine deficiency

GAG → AAG

glutamic acid → lysine

AT 342

- different mutations are known, but one single purine base mutation (GAG –AAG) resulting in the substitution of lysine for glutamic acid at position 342 of the protein is clinically the most widespread
- An individual must inherit two abnormal α1-AT alleles to be at risk for the development of emphysema. In a heterozygote, lung produces α1-AT sufficient to protect the alveoli from damage

انتقاء الوراثة

- A specific α1-AT methionine is required for the binding of the inhibitor to its target proteases.
- Smoking causes the oxidation and inactivation of that methionine residue, rendering the inhibitor powerless to neutralize elastase.

lungs damage !!

- Smokers with α1-AT deficiency, therefore, have a considerably elevated rate of lung destruction and a poorer survival rate than nonsmokers with the deficiency
- The deficiency of elastase inhibitor can be reversed by weekly intravenous administration of α1-AT

IV administration

A mutation in α1-antitrypsin most commonly involves which of the following amino acid substitutions?

A. Lysine → Glutamic acid at position 342
B. Glutamic acid → Lysine at position 342
C. Valine → Glutamic acid at position 6
D. Histidine → Lysine at position 146

B

Why are smokers with α1-antitrypsin deficiency at higher risk of lung damage?

A. Smoking increases elastase production
B. Smoking decreases collagen synthesis
C. Smoking oxidizes a critical methionine residue
D. Smoking increases α1-AT synthesis