Structural proteins
Fibrous proteins

Fibrous proteins

البروتينات الليفية

- Serve structural function in the body

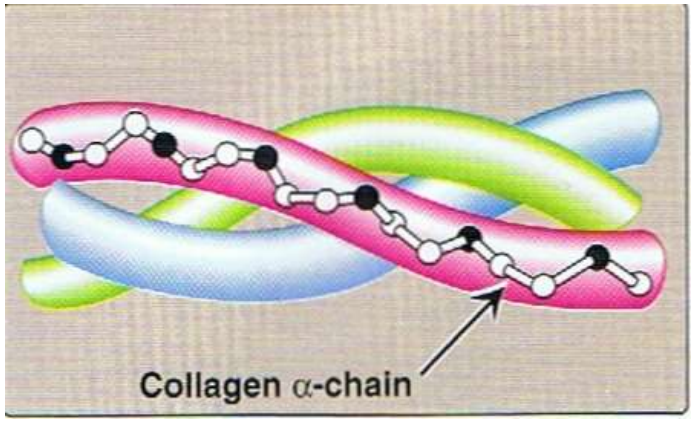
- Collagen is a component of skin, connective tissue, blood vessel wall, sclera and cornea of the eye.

- 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

- 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



Types of Collagen

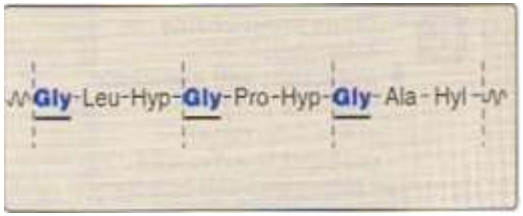
- Collagen can be organized into three types depending on their locations and functions.
  - Fibril-forming collagen: type I, II and III have rope-like structure
  - Network forming collagen: type IV and VII form a three dimensional mesh that constitute a major part of basement membrane
  - Fibril associated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

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

Structure of Collagen

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

يعني هيك : حمض أميني ، حمض أميني ، جلايسين ، حمض أميني ، حمض أميني ، جلايسين



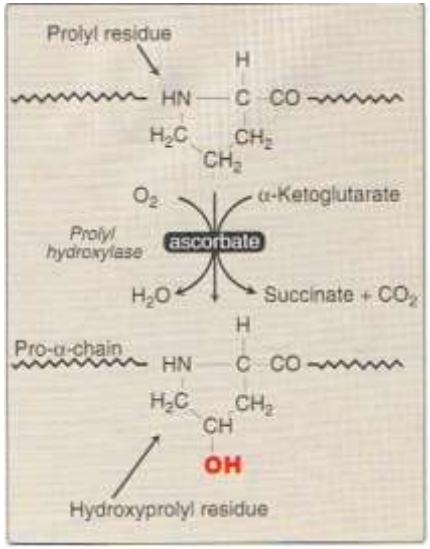
- **Triple helical structure**: elongated, triple helical structure

هيكل ثلاثي حلزوني

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

تعديل ما بعد الترجمة

add (OH-) to main compound

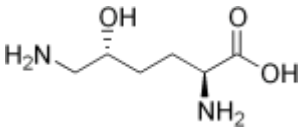


- **Glycosylation**: enzymatic glycosylation of the hydroxyl group of hydroxylysine. Mainly by glucose and galactose.

الارتباط السكري

بعد تصنيع الكولاجين يتم التعديل عليه بإضافة (OH) إلى الأليسين

ثم إضافة سكر (جلوكوز جالاكتوز) إلى (OH) في هيدروكسيلايسين بواسطة الزيمات



hydroxylysine

Biosynthesis of collagen

التمثيل الحيوي للكولاجين

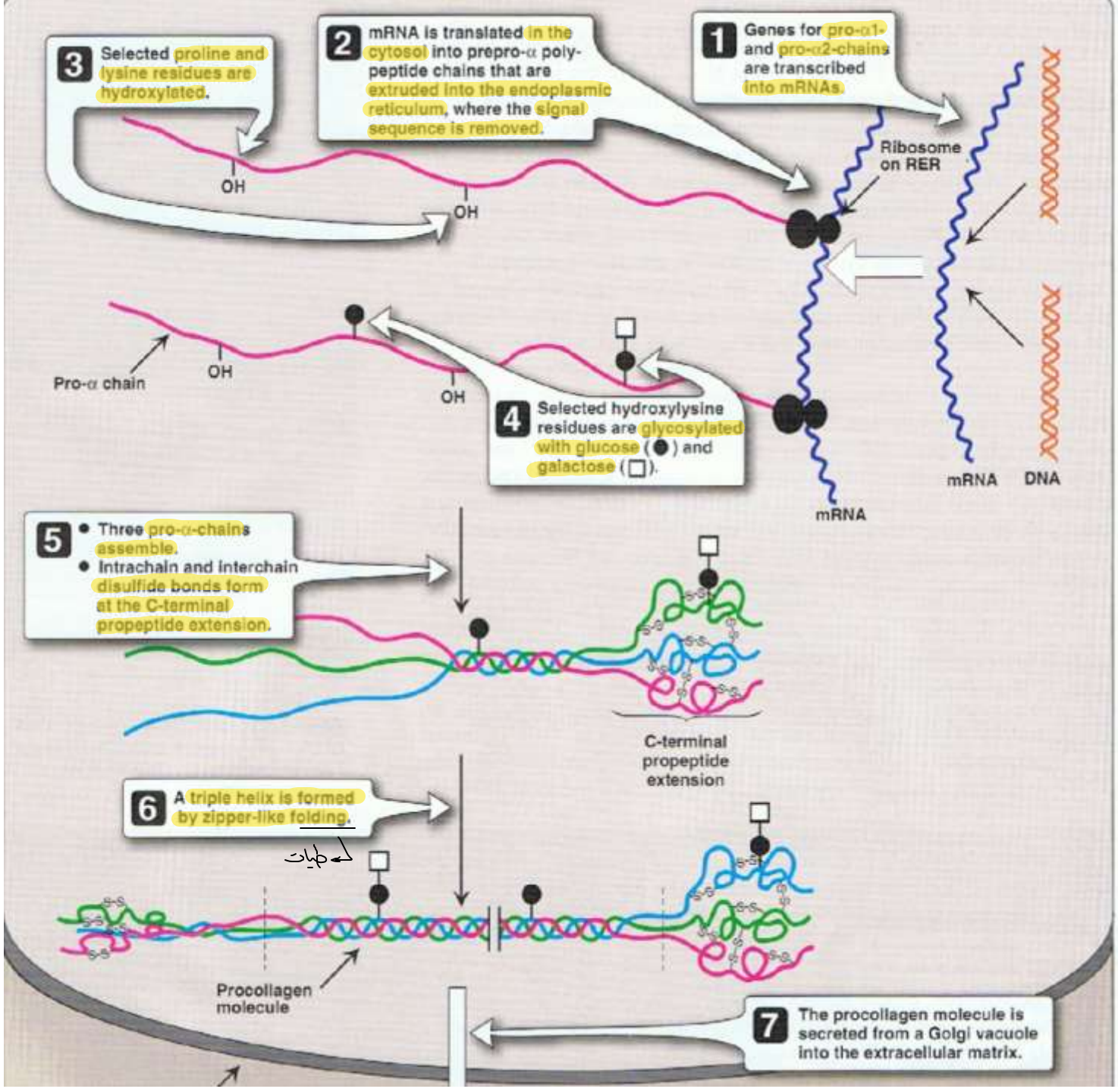
- Precursors of collagen are formed in fibroplast, secreted into the extracellular matrix after enzymatic modification, the mature collagen monomers aggregate and become crosslinked to form collagen fibrils

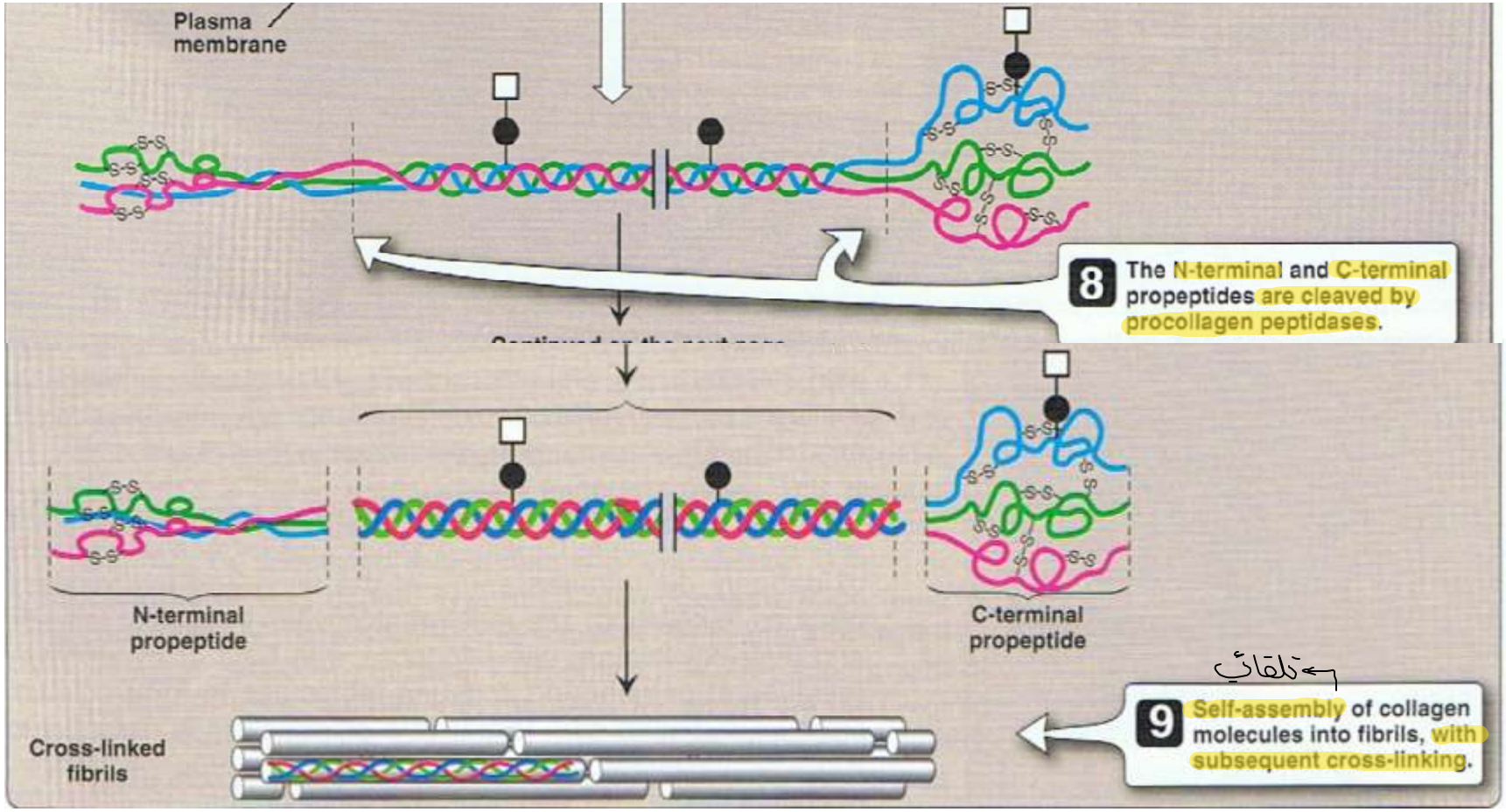
سلائف الكولاجين — ناضج — لتتجمع — ترابط

خطوات تكوين الكولاجين

1. Formation of pro-α-chain ⇒ سلسلة طويلة تحتوي على الأحماض الأمينية اللازمة لتكوين الكولاجين
2. Hydroxylation : performed by prolyl hydroxylase and lysyl hydroxylase, requires molecular oxygen and vitamin C.
   - add OH for some amino acid in chain by spicific enzyme → proline and lysine
3. Glycosylation
   - add sugar (glucose, glactose) to some amine acid this help to increase solubility
4. Assembly and secretion ⇒ ثم تجميعها في حويصلات ونقلها خارج الخلية لتفرز
5. Extracellular cleavage of procollagen molecule ⇒ قطع الأطراف غير الحلزونية لجزيء البروكولاجين ليصبح كولاجين (by pro-collagen peptidase)
6. Formation of collagen fibrils ⇒ بعد أن يصبح الكولاجين ناضج يتجمع بشكل تلقائي ليكون ألياف الكولاجين
7. Cross-link formation ⇒ تشكيل روابط متقاطعة بين جزيئات الكولاجين by lysyl oxidase enzyme

تجميع السلاسل البروتينية في هيكل تالاتي (بروكولاجين)


1 Genes for pro-α1- and pro-α2-chains are transcribed into mRNAs.
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.
3 Selected proline and lysine residues are hydroxylated.
4 Selected hydroxylysine residues are glycosylated with glucose (●) and galactose (□).
5 • Three pro-α-chains assemble.
• Intrachain and interchain disulfide bonds form at the C-terminal propeptide extension.
6 A triple helix is formed by zipper-like folding.
7 The procollagen molecule is secreted from a Golgi vacuole into the extracellular matrix.
Ribosome on RER
mRNA
DNA
mRNA
Pro-α chain
OH
OH
OH
C-terminal propeptide extension
Procollagen molecule


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

Degradation of Collagen

تحلل الكولاجين

- Normal collagen are highly stable molecules
- As response to growth or injury, the breakdown of collagen is mainly due to collagenase

هون بنحكي الاستجابة للنمو والجروح الكولاجين بينكسر بواسطة كولاجينيز

- For type I collagen the cleavage is specific, generating three-quarter and one quarter

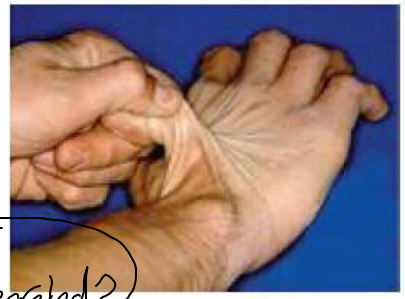
Land randomly

- Further degradation to amino acids occurs by other matrix proteinases

الإنزيمات البروتينية مسؤولة عن تكسير الثلاث أرباع والربع من جزيء الكولاجين المتبقي إلى أحماض أمينية

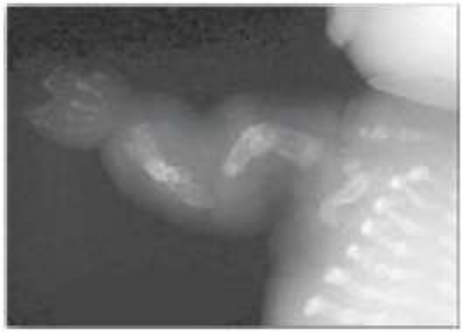
Collagen diseases

- Ehlers- Danlos syndrome → [متلازمة إهلرز دانلوس]
  - 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



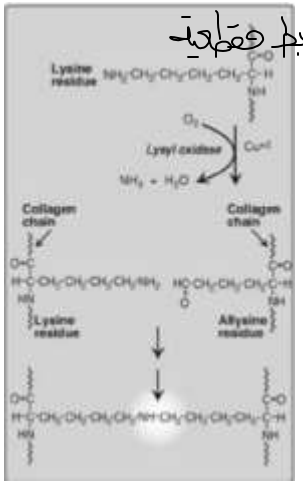
what happen if collagen 3 mutation is not secreted?

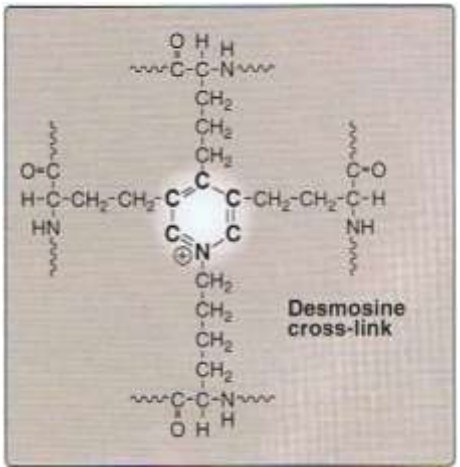
- Osteogenesis imperfecta → [تكون العظام الناقص]
  - Inherited disorder, characterized by bones that easily bend and fracture
  - Humped back is a common feature of the disease
  - There are two types:
    - Osteogenesis imperfecta tarda: early infancy with fractures secondary to minor trauma
    - Osteogenesis imperfecta congenita: more severe, pateints die before birth.

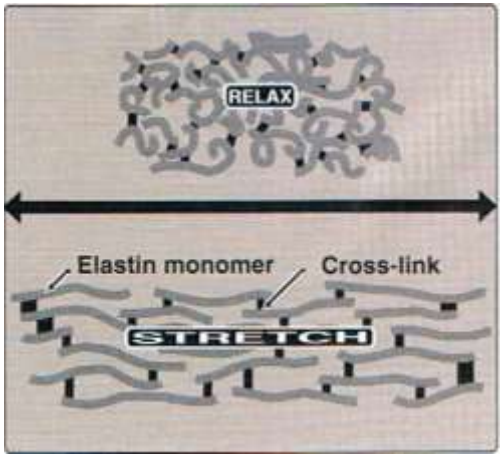


Elastin

- 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





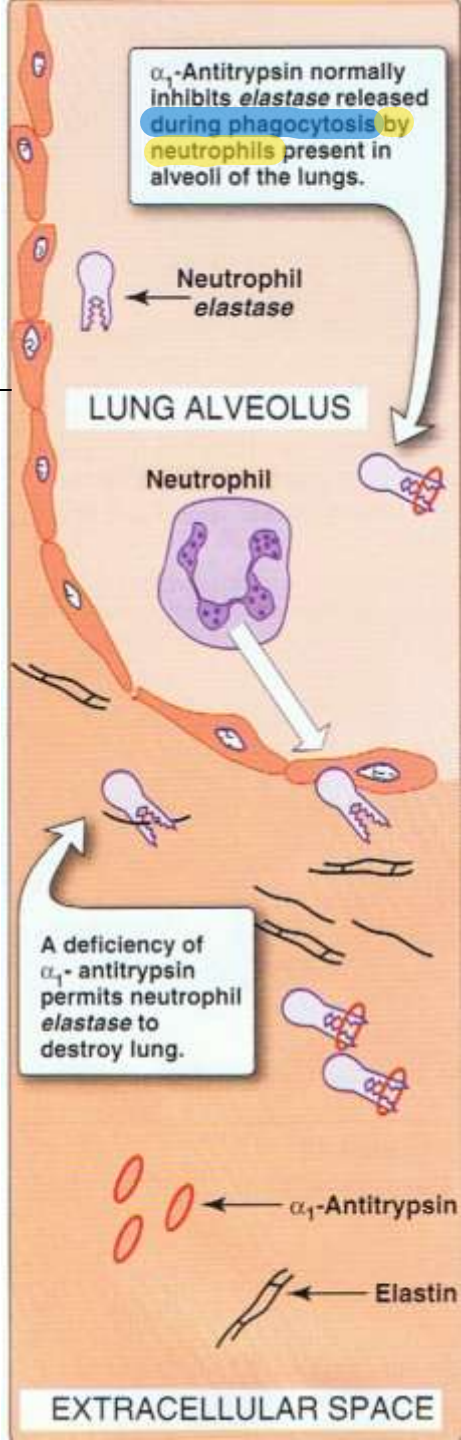


Elastin

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

لو بصير نقص بالإيلاستين وبصير أمراض رئوية مزمنة

↳ example : emphysema



α1 antitrypsine deficiency

- 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

في حالة الشخص غير الحامل للجينات

- 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.

عاجز

  - 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