



\* denatured easier to break down than degradation.

↓ reversible.

↓ irreversible break to peptide bond.

\* Synthesis of Collagen: ① Transcription of mRNA. genes for synthesis  $\alpha$ -peptide.

② pre-pro-peptide formation. mRNA (nucleus → cytoplasm).  
↓ ribosome for translation  
↳ signal seq. (N terminal) recognition center → ER for post translation process

③  $\alpha$ -peptide to pro collagen. 3 modifications:

- A. N-terminal dissolved  $\Rightarrow$  propeptide (XX procollagen).
- B. **Hydroxylation (OH)** of lys + pro [prolyl hydroxylase / lysyl hydroxylase]  $\Rightarrow$  **Crosslinking of the  $\alpha$ -peptides [U.C collector]**  
\* lack of OH on pro, lys insecurity  $\Rightarrow$  loose triple helix.
- C. **Glycosylation** (glucose, galactose) onto OH in **lysines** not proteins. \* each (OH, G) peptide twists towards left very tightly  $\Rightarrow$  procollagen.

④ Golgi Apparatus modification.

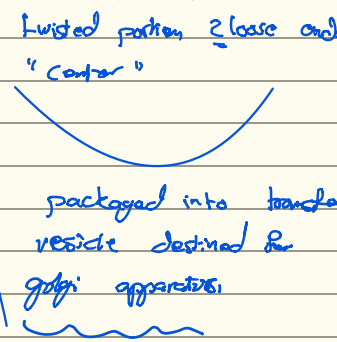
\* the last modification on post translation  $\Rightarrow$  + Oligosac. not mono  $\rightarrow$  put in secretory vesicle destined for extracellular spaces.

⑤ Formation of tropocollagen.

In extracellular space. \* outside the cell. "collagen peptidase" remove "loose end"  
↓  
Tropocollagen.

⑥ Formation of the collagen fibril.

\* lysyl oxidase, EC enzyme" final step. lys + hydroxylysines  $\Rightarrow$  aldehyde groups  $\Rightarrow$  covalent bond  $\cup$  the tropocollagen  $\Rightarrow$  collagen fibril.



Some of the lysine side chains are oxidized to aldehyde derivatives, which react with another lysine or another oxidized lysine via the action of lysyl oxidase

\* Aldehyde + Aldehyde  $\rightarrow$  Aldol cross-link.

Collagen	Genes
I	COL1A1, 2
II	COL2A1
III	COL3A1
IV	COL4A1, 2, 3, 4, 5, 6
V	COL5A1, 2, 3
VI	COL6A1, 2, 3

Most forms of the condition are inherited in an autosomal dominant pattern

Inheritance	Characteristics	Type
Autosomal <u>dominant</u>	Joint hypermobility, skin hyperextensibility, and fragility	<u>Classical type</u>
Autosomal <u>dominant</u>	Joint hypermobility, frequent dislocations	<u>Hypermobility type</u>
Primarily autosomal <u>dominant</u> , <u>recessive</u> described	Spontaneous rupture of arteries and bowel, can lead to death	<u>Vascular type</u>
Autosomal <u>recessive</u>	Fragile eyes, significant skin and joint laxity, severe scoliosis	<u>Kyphoscoliosis type</u>
Autosomal <u>dominant</u> and <u>recessive</u>	Short height, severe joint laxity and dislocations, variable skin involvement	<u>Arthrochalasia type</u>
Autosomal recessive	Severely fragile skin, soft and doughy with sagging and folding	<u>Dermatosparaxis type</u>
Autosomal <u>recessive</u>	Joint hypermobility, hyperelastic skin, and fragile tissue	<u>Tenascin-X deficient type</u>

## Ehlers Danlos syndrom (EDS)

⇒ group of inherited connective tissue disorders, caused by a defect in the synthesis of collagen (Type I or III). The collagen in connective tissue helps tissues resist deformation. abnormal collagen leads to increased elasticity

Abnormalities in tenascin protein also

play role in regulation the normal distribution of collagen.

Mutations can cause EDS:

Fibrous  $\alpha$

- COL1A1 / COL1A2
- COL3A1
- COL5A1 / COL5A2
- TNXB

Enzymes

- ADAMTS2
- PLD1
- B4GALT7

Description	Symptoms/Risk Factors	Causes	Condition
Affects connective tissue, caused by defects in type II or XI collagen.	Abnormal bone <u>development</u> , short stature, enlarged joints, etc.	Mutations in COL11A1, COL11A2, COL2A1	<b>Collagenopathy (Type II &amp; XI)</b>
Results from defects in the COL2A1 gene affecting connective tissues.	Abnormal bone development, short stature, premature arthritis, etc.	Defects in the COL2A1 gene	<b>Collagenopathy, Type 2 Alpha 1</b>
Genetic disorder characterized by end stage kidney disease, hearing loss.	End-stage kidney disease in <u>male</u> relatives, hearing loss before <u>age 30</u>	Mutations in COL4A3, COL4A4, COL4A5	<b>Alport Syndrome</b>
Affects skeletal muscles, severe muscle weakness from birth.	Severe muscle weakness, inability to walk unassisted.	Mutations in COL6A1, COL6A2, COL6A3	<b>Ullrich Congenital Muscular Dystrophy</b>

