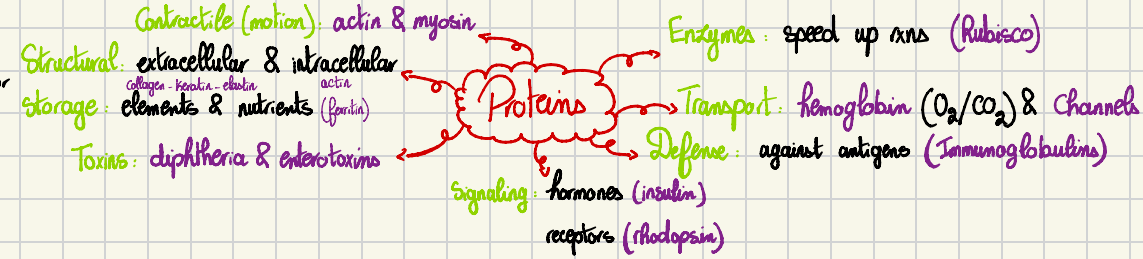
Fibrous Proteins

Summary by:
Fatma attia
Edited by:
Layan Al-amir
(lies🎀)

* we can classify proteins depending on their biological functions:

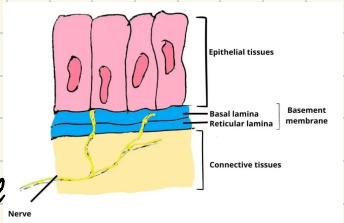


* we can also classify them depending on structure: (2 groups)

↳ fibrous: elongated (secondary structure ONLY)
→ main function: structural ←
Collagen, elastin, keratin ...

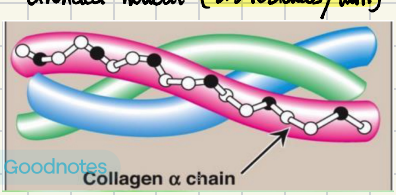
↳ Globular: spherical + 3D compact structures
→ has multiple functions ←
myoglobin - hemoglobin - immunoglobin ...

* The ECM: outside the cell → has a basement membrane that contains:
1- Basal lamina: seperates the cell from other cells in connective tissue.
2- Reticular lamina: contains:
fibrous compact thick proteins (collgen & elastin..)
& proteoglycans → help in cell signaling & sensing changes in cell



* Let's dig deeper :

* Collagens: structural support to tissues. => Most abundant proteins in mammals (25% of protein mass) ←
family of 40 types (type I collagen, type II ...) thick fibers that interact with proteoglycans & receptors.
features: stiffness, rigidity & tensile strength (= max amount of pressure without breaking)
→ Types: fibril forming / associated, Network forming, transmembrane ...
→ Structure:
- triple-stranded, helical (α chains) that turn around each other => Basic unit: Tropocollagen ←
1 strand = 1 seperate gene => diverse: (3 α_1) or (2 α_1 & 1 α_2) ...
extended helical (3.3 residues/turn) ≠ α-helix (3.6 residues/turn)



→ formation of collagen fibers:

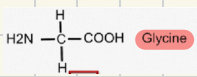
Note: interactions within tropocollagens & microfibrils make the collagen stiff & rigid.

3 strands of α-chains
↳ Tropocollagen → 5 tropocollagens together (via covalent cross linkage between lysine residues)
↳ Microfibrils → several microfibrils (strengthened covalently)
↳ fibrils → several fibers
↳ Collagen fiber ✱

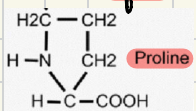
→ The amino acid sequence of collagen molecules: (specifically fibril forming)

mostly they contain glycine (33%) per 3 residues & Proline (13%) & sometimes hydroxyproline (9%) & hydroxylysine.

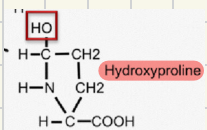
Glycine – X – Y



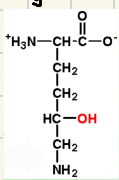
Can be often:



OR



Y → Any a.a ✱



✱ Note:

Proline or Lysine —Prolyl/Lysyl hydroxylase, Ascorbate (vit C)→ hydroxyproline or hydroxylysine + Succinate

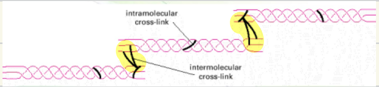
Name of a.a	Main function in collagen
Glycine (No R-group)	present internally flexible (no repulsion) & rotates freely Tightly packed
Proline	creates kinks ⇒ rotation stabilizes helical shape (in α chains) Provides RIGIDITY.
hydroxyproline	Hydrogen bond between residues (via OH molecules) without it, collagen is fragile & unstable measured by hydroxylation factors (prolyl hydroxylase, vit C...) at high temp (above 20°C), collagen loses most helical content.
hydroxylysine	makes collagen a glycoprotein serves attachment to sugar molecules sugar molecules → cell recognition ↳ cell interaction with surface receptors.

→ **Covalent cross linkage:** (within tropocollagen & microfibrils) ⇒ Stabilize side-by-side packing.

Caused by oxidation of lysine: from lysine → ALLYSINE

$(CH_2)_4NH_2 \rightarrow (CH_2)_4CHO$

amino group → aldehyde



⇒ allysine will react with either: lysine or hydroxylysine or allysine

→ within the same tropocollagen or between them ⇒ strong & rigid fibril

⇒ IF CROSS LINKING IS INHIBITED: deficiency of hydroxylation

Low tensile strength → fragile collagen → easy to tear (skin, blood vessels ..) ⇒ Ehlers-Danlos Syndrome

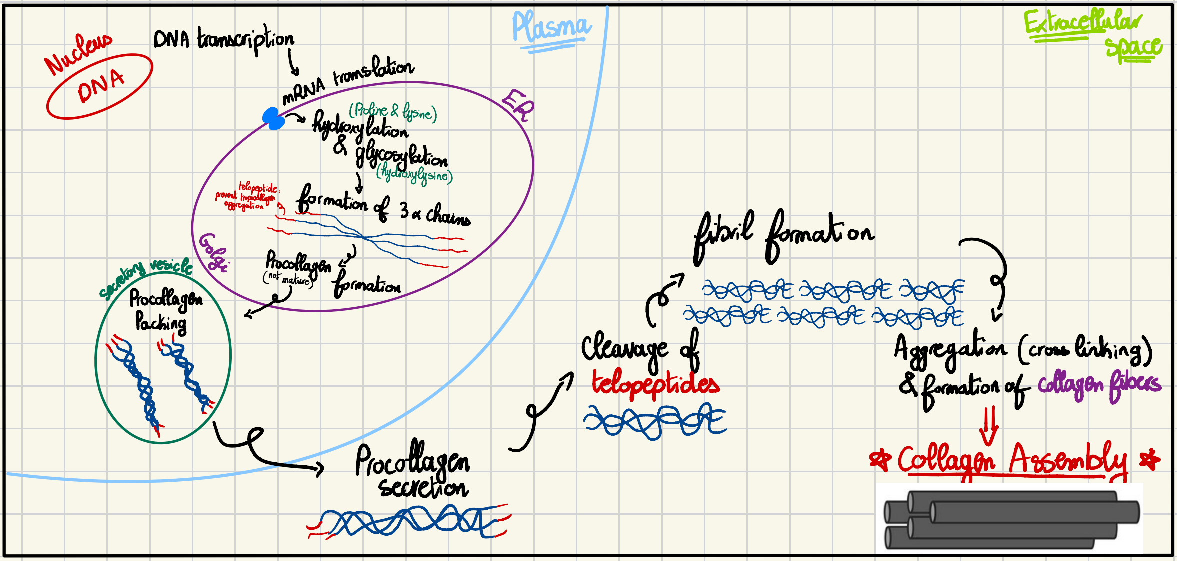
→ Cross linking increases with AGE (meat from older animals is TOUGHER)

→ **Advanced glycation end products (AGEs):** ⇒ Nephropathy - Atherosclerosis - Retinopathy - Cardiomyopathy

↓ uncontrolled diabetes

high glucose levels
- ↳ more protein glycation (nonenzymatic)
  - ↳ nonenzymatic oxidation
    - ↳ more cross links & inflammatory signals.
      - ↳ formation of AGEs ⇒ increase in oxidative stress ⇒ Cell & Tissue Damage

→ **Synthesis of collagen:**



→ **Scurvy disease (الإسقربوط):** caused by deficiency of Vit C (= ascorbic acid)

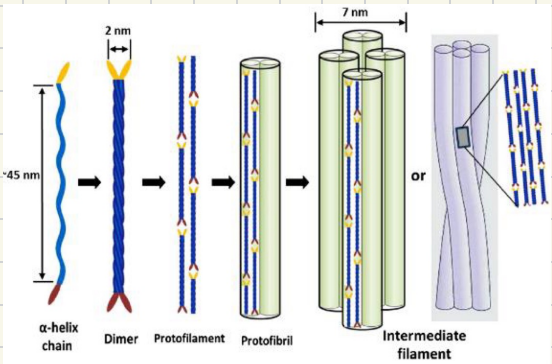
↳ unstable α chains → fragile blood vessels & loss of teeth

❖ Elastin: thin strands present in ECM → between collagen fibers → to limit the stretch & prevent tissue from tearing
↳ Provides: resilience (recoiling after stretch) & flexibility to tissues (skin, blood vessels ...) to function.

→ Elastin Structure: highly hydrophobic → Precursor: tropoelastin ←
↳ highly cross-linked, insoluble & undefined
tropoelastin contains repeated domains: hydrophilic (lysine & alanine) } alternating
hydrophobic (Valine, Proline & glycine) } consecutively
↳ elastin is NOT glycosylated (no hydroxylysine)
↳ lysines of tropoelastin are cross linked together via lysyl oxidase. (& all are aligned to microfibrils)
& During Stretching: hydrophobic regions are exposed to aqueous environment.
When Relaxed: ★ hydrophobic effect*: they cluster together ⇒ recoil / reform.

❖ α- Keratins: family of proteins → present in skin, nails, hair
→ formation: in hair:
2 α-keratin together → dimer with ends containing Cys (that form sulfur cross-links)
2 dimers together → Protofilament (tetramer)
2 protofilaments together → protofibril (8 α-keratin chains)
4 protofibrils → intermediate filament
8 intermediate filaments clustered → microfibril
Many microfibrils → Macrofibril
Many Macrofibrils → a single hair ★

❖ Note:
more Cys residues
↳ more cross linkage
⇒ more rigidity
⇒ nails have more cys



→ Temporary wave: non-covalent interactions in hair.
↳ H_2O disrupts hydrogen bonds → straight α-helices
⇒ when dried up → hydrogen bond reforms.

→ Permanent wave: lasts longer (fixed covalent bonds)
↳ reduction of disulfide cross-links (reducing subs)
→ ammonium thioglycolate ⇒ makes it straight.
↳ reformation of disulfide bonds → oxidation
→ hydrogen peroxide ⇒ makes it wavy.
+ → α-helices are shifted by fixating hair in a certain way.