16

BIOCHEMISTRY

faculty of medicine - JU2017

◉ Sheet ○ Slides

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Doctor

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Fibrous Proteins

There are two types of proteins: Fibrous and Globular. Fibrous proteins are one of the most abundant types of proteins in the body. Some examples of these proteins are: collagen, elastin and keratin.

Collagen

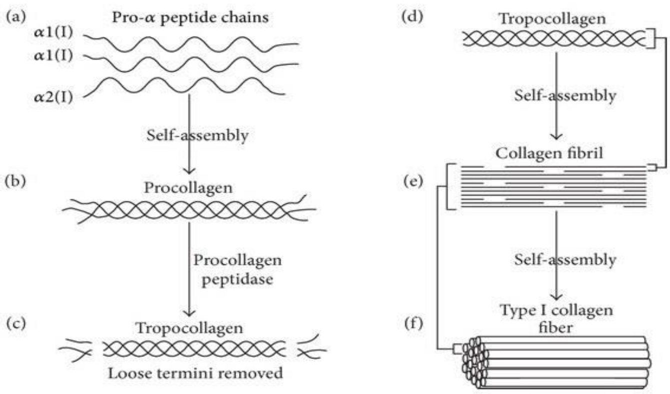
- Collagens are a family of fibrous proteins with 25 different types found in all multicellular animals. They share some characteristics, such as structure and amino acid sequence.
- To be able to identify these different types of collagens, we refer to them in numbers (Collagen type I, Collagen type II…etc.)
- They are the most abundant proteins in mammals, constituting 25% of their total protein mass.
- The main function of collagen molecules is to provide structural support to tissues. Thus, the structure of collagen needs to be rigid to be compatible with its function.
- The primary feature of a typical collagen molecule is its stiffness.

Characteristics of Collagen

The mature structure of collagen is:

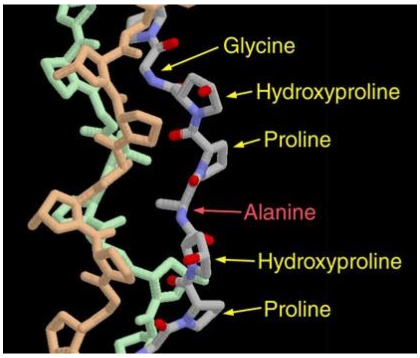
- **Left Handed**: Collagen moves towards to the left. (check the photo on the right)
- **Triple stranded**: three collagen polypeptide chains are wound around each other. One collagen polypeptide chain is not functional on its own.
- **Helical**: Collagen is not straight; instead, it has a helical structure. Collagen is also made of chains referred to as α-chains (look like the α-helices).
- Each polypeptide strand of collagen has an α type (α1, α2…). The triple stranded structure does not have to have 3 identical collagen polypeptide strands.
- Compared to the α -helix (which is found in the secondary structure of protein), the collagen helix is much more extended with 3.3 residues per turn (a residue is a sequence of 3 AAs).

- The basic unit of collagen is called tropocollagen. Tropocollagen consists of 3 polypeptide chains coiled around each other.



The Structure-Function Relationship of Collagen

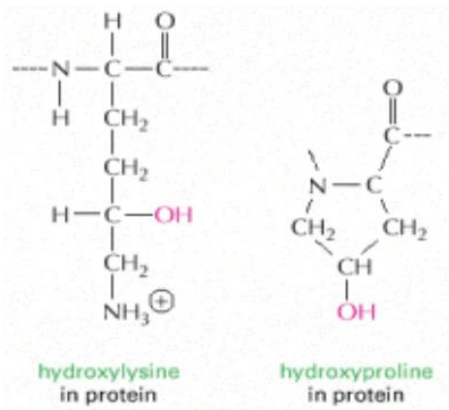
- 33% of all AAs in collagen are Glycine (Every third residue is glycine, which with the preceding residue being proline or hydroxyproline in a repetitive fashion as follows: **Gly-pro-Y** or **Gly-X-hydroxyproline**). Glycine is a very small AA because its R-sidechain is a Hydrogen atom. This allows the 3 strands to be packed, preventing the steric hindrance that is made from the R-groups (steric hindrance is when two molecules in proximity interact, disrupting a reaction or structure).



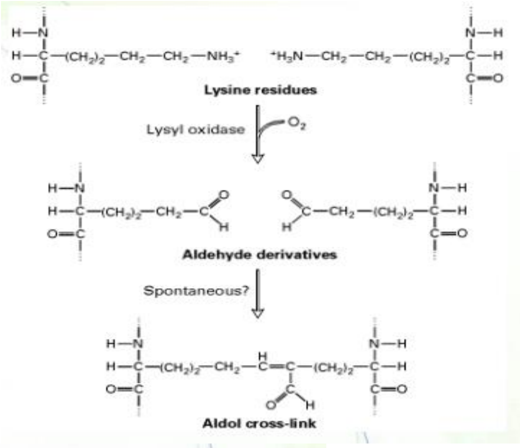
- 13% of all AAs are proline. Proline is a very stiff/rigid AA, making collagen a rigid protein. Proline is also the AA which is responsible for giving Collagen its helical structure, because proline bends the chain of AAs (makes kinks and curves).

- 9% of all AAs are Hydroxyproline. Hydroxyproline serves as another layer of strength for the structure, since two molecules of Hydroxyproline interact together through hydrogen bonds. (all in all, every fifth residue is Proline or Hydroxyproline).

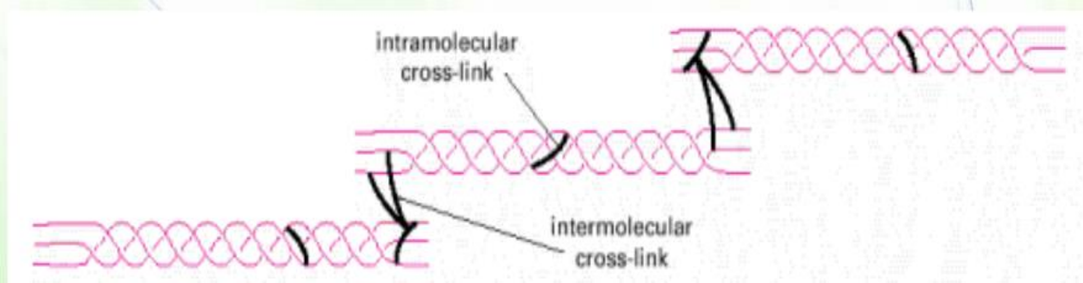
- Collagen also contains some lysine and hydroxylysine. Hydroxylysine is a modified lysine (-OH group added). This Hydroxyl group allows the attachment of sugars, making collagen a glycoprotein.



Cross Linkage in Collagen



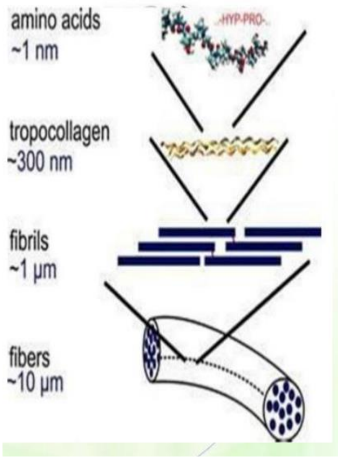
- Some of the lysine side chains are oxidized to aldehyde derivative known as allysine by the enzyme ***Lysyl Oxidase***. This enzyme combines the two aldehyde groups to form a covalent bond, called a cross link. Cross linkage may happen between lysine, allysine and hydroxylysine.



- These cross-links stabilize the side-by-side packing of collagen molecules and generate a strong fibril. Cross-linking can happen within a tropocollagen molecule (intra), and between tropocollagen molecules (inter), as shown above.
- If cross-linking is inhibited, the tensile strength of the fibrils is drastically reduced; collagenous tissues become fragile, and structures such as skin, tendons, and blood vessels tend to tear.
- The amount of cross-linking in a tissue increases with age. That is why meat from older animals is tougher than meat from younger animals. Thus, when cross-linkage is inhibited, tissues will be weak.

Formation of Collagen Fibers

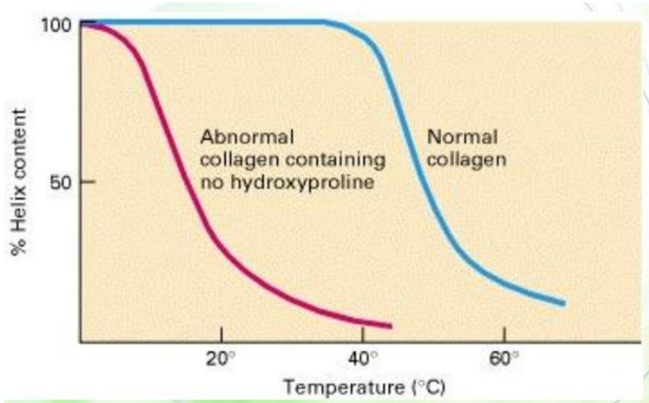
- Following cellular release of tropocollagen, 5 of them polymerize into a microfibril, which are connected with each other via aldehyde links.
- Microfibrils align with each other forming larger collagen fibrils, which are strengthened by the formation of covalent cross-links between lysine residues.
- Microfibrils assemble into collagen fibers.



Note: for more details, go to the first photo in page 2, which explains exactly how collagen is formed.

The Importance of Hydroxyproline

- The importance of hydroxyproline is prominent when there is a problem in the enzyme converting proline to hydroxyproline. This enzyme is Vitamin C. Collagen is stable at 40 ^{o}C, and normally denatures at around 50 ^{o}C, whereas collagen without hydroxyproline denatures at a lower temperature (above 20 ^{o}C). Hence, vitamin C deficiency directly results in weak collagen fibers, causing weak teeth, bones, easily ruptured blood vessels…etc.



- Scurvy is a disease is caused by a dietary deficiency of ascorbic acid (vitamin C). Vitamin C assists in proline hydroxylation, and defective pro-α chains fail to form a stable triple helix and are immediately degraded within the cell. Due to this, blood vessels become extremely fragile, and teeth become loose in their sockets.

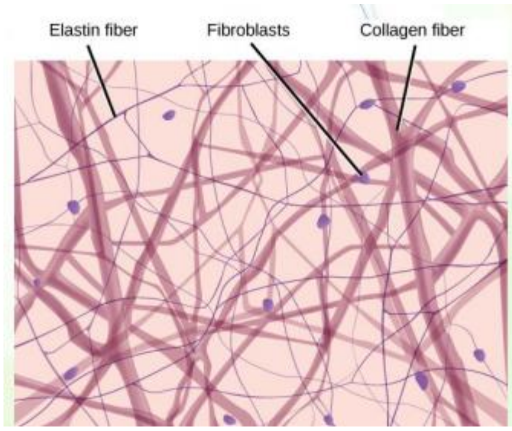
Elastin

- Elastin is another type of fibrous proteins.

- Many tissues, such as skin, blood vessels, and lungs need both strong, and elastic features in order to function.

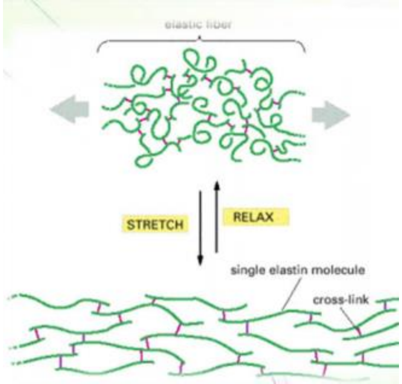
- A network of elastic fibers in the extracellular matrix of these tissues gives them the required resilience (elasticity) so that they can recoil after transient stretch.

- Long, inelastic collagen fibrils are interwoven with the elastic fibers to limit the extent of stretching and prevent the tissue from tearing.



The Structure-Function Relationship in Elastin

- The main component of elastic fibers is elastin, which is a highly hydrophobic protein and is rich in proline and glycine. The noncovalent interactions present in elastin are hydrophobic interactions. This allows elastin to be stretched and relaxed.

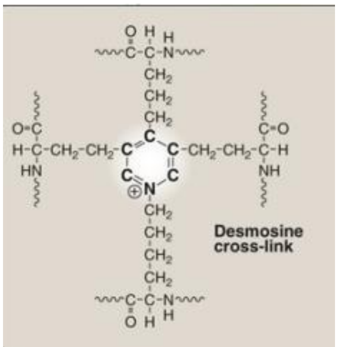


- It contains some hydroxyproline, but no hydroxylysine. Thus, it is not glycosylated (not a glycoprotein).

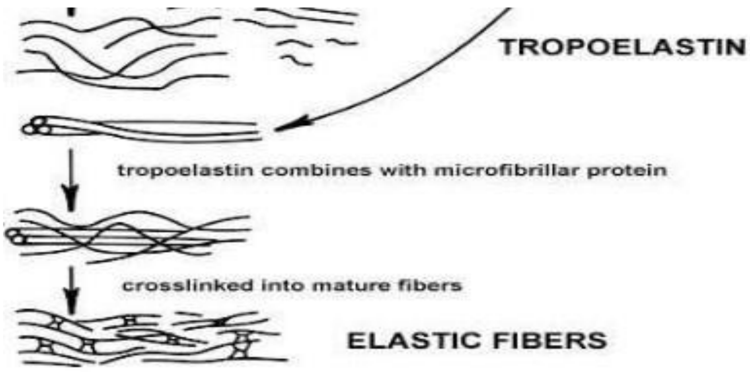
- The primary components, tropoelastin molecules, are cross-linked between lysines to one another.

- The elastin protein is composed largely of two types of short segments that alternate along the polypeptide chain:
    - Hydrophobic segments, which are responsible for the elastic properties of the molecule;
    - Alanine and lysine-rich α-helical segments, which form cross-links between adjacent molecules.

- A desmosine cross-link is formed from three allysyl side chains plus one unaltered lysyl side chain from the same or neighboring polypeptides. It is the region where the cell interacts with the cellular matrix.



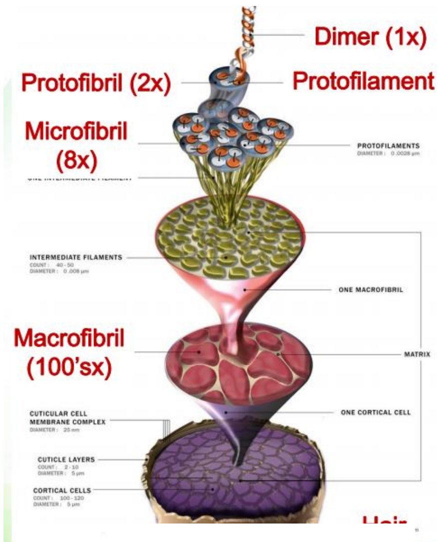
- it also contains some alanine and lysine which are important in the cross-linkage.



Keratins

- Keratins are also structural fibrous proteins.
- They form intermediate filaments; Thus, they are intermediate filament proteins.
- We have 3 types of filaments in the cell cytoskeleton: Actin, Tubulin and Intermediate filaments.
- We also have 2 types of keratin: α-and β-keratins, which are members of a broad group of intermediate filament proteins (our main focus is α-Keratin).
- α-keratin is the major protein of hair and fingernails as well as animal skin.
- α-keratin has an unusually high content of cysteine.
- Keratin is thin and soft in hair, whereas it is thick and rigid in nails. This is because of the disulfide bonds between Cystine molecules, which are highly abundant in nails.

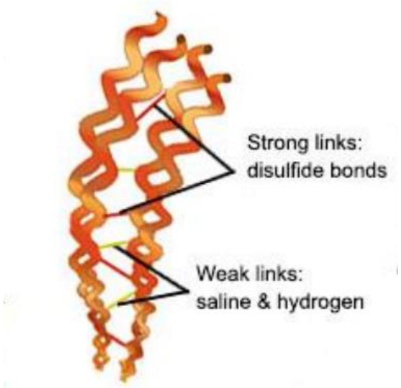
Formation of Keratin in Hair

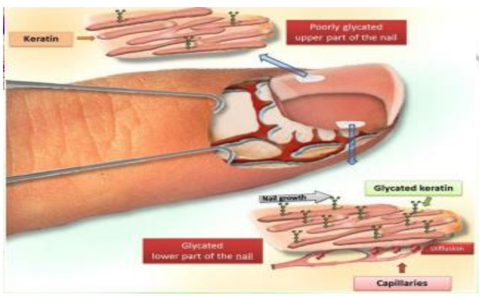


- Two helical α-keratin molecules (protofilaments) intertwine forming a dimer.
- Two dimers twist together to form a 4-molecule protofibril.
- Eight protofibrils combine to make one microfibril.
- Hundreds of microfibrils are joined into a macrofibril.

Formation of Keratin in Nails

- α-keratin can be hardened by the introduction of disulfide cross-links (fingernails).
- The rest of the process goes exactly as in hair. *





*note: disulfide bridges are found in both hair and nails, but nails have many more cysteines, causing more disulfide bridges to be formed.

Temporary Vs. Permanent Hair Waves

- Temporary Waves:
  When hair gets wet, water molecules disrupt some of the hydrogen bonds, which assist the alignment of alpha helices. When hair dries up, the hair strands are able to maintain the new curl in the hair for a short time.

- Permanent Waves:
  A reducing substance (usually ammonium thioglycolate) is added to reduce some of the disulfide cross-links. The hair is put on rollers or curlers to shift positions of alpha-helices. An oxidizing agent, usually hydrogen peroxide, is added to reform the disulfide bonds in the new positions until the hair grows out.

The End

Thank you for bearing!