Fibrous proteins

البروتينات الليفية

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Fibrous proteins

Collagen and elastin are fibrous proteins of the extracellular matrix that serve structural functions in the body. For example, collagen and elastin are found as components of skin, connective tissue, blood vessel walls, and cornea of the eye.
Fibrous proteins

I. collagen

Collagen is the most abundant protein in the human body. A typical collagen molecule is a long, rigid structure in which three α polypeptides are wound around one another in a rope-like triple helix and held together by hydrogen bonds between the chains (Figure 4.1).
Fibrous proteins

I. Collagen

A. Types

The collagen includes more than 25 collagen types. **Variations in the amino acid sequence** of the α chains result in structural components that are about the same size (approximately 1,000 amino acids long), but with slightly different properties. For example, the most common collagen, type I, contains two chains called α1 and one chain called α2 (α1₂α2), whereas type II collagen contains three α1 chains (α1₃).
Fibrous proteins

I. Collagen
A. Types
The collagens can be organized into three groups, based on their location and functions in the body (Figure 4.2).

<table>
<thead>
<tr>
<th>TYPE</th>
<th>TISSUE DISTRIBUTION</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Fibril-forming</td>
</tr>
<tr>
<td>I</td>
<td>Skin, bone, tendon,</td>
</tr>
<tr>
<td></td>
<td>blood vessels, cornea</td>
</tr>
<tr>
<td>II</td>
<td>Cartilage, intervertebral disk, vitreous body</td>
</tr>
<tr>
<td>III</td>
<td>Blood vessels, skin, muscle</td>
</tr>
<tr>
<td></td>
<td>Network-forming</td>
</tr>
<tr>
<td>IV</td>
<td>Basement membrane</td>
</tr>
<tr>
<td>VIII</td>
<td>Corneal and vascular endothelium</td>
</tr>
<tr>
<td></td>
<td>Fibril-associated*</td>
</tr>
<tr>
<td>IX</td>
<td>Cartilage</td>
</tr>
<tr>
<td>XII</td>
<td>Tendon, ligaments, some other tissues</td>
</tr>
</tbody>
</table>

Figure 4.2
The most abundant types of collagen. *Known as FACITs: fibril-associated collagens with interrupted triple helices.
Fibrous proteins

I. Collagen

A. Types

1. Fibril-forming collagens: 
   Types I, II, and III are the fibrillar collagens, and have the rope-like structure. (Figure 4.2 & Figure 4.3).
Fibrous proteins

I. Collagen

A. Types

2. Network-forming collagens: Types IV and VIII form a three-dimensional mesh (Figure 4.2 & Figure 4.4).

3. Fibril-associated collagens: Types IX and XII bind to the surface of collagen fibrils, linking these fibrils to one another and to other components in the extracellular matrix (Figure 4.2).
Fibrous proteins
I. Collagen
B. Structure
1. Amino acid sequence:
   - Collagen is rich in proline and glycine, for formation of the triple-stranded helix.
   - Proline facilitates the formation of the helical conformation because its ring structure causes “kinks” in the peptide chain. [Note: α chain cannot be an α helix because the presence of proline.]

The repeating sequence, –Gly–X–Y–, where

X = proline; Y = hydroxyproline (but can be hydroxylysine), (Figure 4.5). α chain can be regarded as a polytripeptide.

Figure 4.5
Amino acid sequence of a portion of the α1 chain of collagen. [Note: Hyp is hydroxyproline and Hyl is hydroxylysine.]
Fibrous proteins
I. Collagen
B. Structure

2. Triple-helical structure:
collagen, a fibrous protein, has an elongated, triple-helical structure.

3. Hydroxyproline and hydroxylysine:
Collagen contains hydroxyproline (hyp) and hydroxylysine (hyl), (posttranslation amino acids). Hydroxyproline is important in stabilizing the triple-helical structure of collagen because it maximizes interchain hydrogen bond formation.

4. Glycosylation:
Enzymatically glycosylated of the hydroxyl group of the hydroxylysine residues of collagen. Glucose and galactose are sequentially attached to the polypeptide chain prior to triple-helix formation.
Fibrous proteins; C. Biosynthesis

1. Genes for pro-α₁ and pro-α₂ chains are transcribed into mRNAs.

2. mRNA is translated on the RER into prepro-α chains that are extruded into the lumen of the RER, where the signal sequence is removed, converting prepro to pro.

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, and procollagen is produced.
Figure 4.7
Synthesis of collagen. RER = rough endoplasmic reticulum; mRNA = messenger RNA. (continued on the next page)
Fibrous proteins; C. Biosynthesis

Figure 4.7
Synthesis of collagen. (continued from the previous page)

Self-assembly of tropocollagen molecules into fibrils, with subsequent cross-linking to form mature collagen fibers.
Fibrous proteins; C. Biosynthesis

7. Cross-link formation

Figure 4.9
Formation of cross-links in collagen.
[Note: Lysyl oxidase is irreversibly inhibited by a toxin from plants in the genus Lathyrus, leading to a condition known as lathyrisim.]
Fibrous proteins
I. Collagen
D. Degradation of collagen
Collagens are stable, having half-lives as long as several years. Breakdown of collagen fibers is dependent on the proteolytic action of collagenases (metalloproteinases).
E. Collagen diseases: Collagenopathies
Defects in collagen fiber synthesis can result in a genetic disease involving an inability of collagen to form fibers properly.
Fibrous proteins
E. Collagen diseases: Collagenopathies

1. Ehlers-Danlos syndrome (EDS):

- EDS can result from a deficiency of collagen-processing enzymes (example, lysyl hydroxylase or N-procollagen peptidase), or from mutations in the amino acid sequences of collagen types I, III, or V.

- Classic EDS caused by defects in type V collagen (Figure 4.10). Defect in type III collagen is the most serious form of EDS (lethal arterial rupture).
Fibrous proteins
E. Collagen diseases: Collagenopathies

2. Osteogenesis imperfecta (OI):
This syndrome, known as brittle bone syndrome (Figure 4.11).

Mutation cause **replacement of glycine** in (-Gly-X-Y-) with **amino acid with bulky side chains**. The resultant abnormal α-chains so prevent triple-helical conformation.

Figure 4.11
Lethal form (type II) of osteogenesis imperfecta in which the fractures appear in utero, as revealed by this radiograph of a stillborn fetus.
Fibrous proteins

II. ELASTIN

• *Elastin* is a connective tissue protein with rubber-like properties.

• Elastic fibers composed of *elastin and glycoprotein microfibrils* are found in the lungs, the walls of large arteries, and elastic ligaments.

• They can be stretched to several times their normal length, but recoil to their original shape when the stretching force is relaxed.
Fibrous proteins
II. ELASTIN

A. Structure of elastin

• Elastin is an **insoluble protein polymer synthesized from tropoelastin**, which is a linear polypeptide composed of about **700 amino acids** that are primarily **small and nonpolar** (example, glycine, alanine, and valine).

• **Some of the lysyl side chains of the tropoelastin poly peptides are oxidatively deaminated by lysyl oxidase**, forming allysine residues. Three of the allysyl side chains plus one unaltered lysyl side chain from the same or neighboring polypeptides form a **desmosine cross link** (Figure 4.12).
Fibrous proteins

III. ELASTIN

A. Structure of elastin

• Elastin are interconnected, rubbery network that can stretch and bend in any direction when stressed, giving connective tissue elasticity (Figure 4.13).

• Mutations in the fibrillin-1 protein are responsible for Marfan syndrome, a connective tissue disorder cause impaired in skeleton, eye, and cardiovascular system.
Fibrous proteins

III. ELASTIN

B. Role of α1-antitrypsin in elastin degradation

1. α1-Antitrypsin: Blood and other body fluids contain a protein, α1-antitrypsin (AAT, A1AT) which inhibits a number of proteolytic enzymes that hydrolyze and destroy proteins.

- Because lung tissue cannot regenerate, the AAT inhibit neutrophil elastase a powerful protease that is released into the extracellular space, and degrades elastin of alveolar walls (Figure 4.14).
Fibrous proteins

III. ELASTIN

B. Role of α1-antitrypsin in elastin degradation

2. Emphysema resulting from α1-AT deficiency:

- Emphysema caused by different mutations in the gene for α1-AT cause a deficiency of this protein, but one single purine base mutation (GAG to AAG, resulting in the substitution of lysine for glutamic acid at position 342 of the protein) is clinically the most widespread.

- the mutation causes the normally monomeric AAT to polymerize within the endoplasmic reticulum of hepatocytes, resulting decreased secretion of AAT by the liver. The accumulated polymer may result in cirrhosis (scarring of the liver).
Thinking of your kindness and sending you many thanks.