Biochemistry of connective tissue

- extracellular matrix

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Connective tissue

The connective tissue is formed by:

CELLS

and

EXTRACELLULAR MATRIX
(intercellular matrix)

Extracellular matrix

Function

- stabilisation of tissue structure
- regulation cell behavior
  - survival, development, migration, proliferation
- membrane filtration barrier (glomerules)
- exchange of different metabolites, ions and water
- reparation function
- immune processes
- participation in inflammation

Cells of connective tissue

- Fibroblasts
- Chondroblasts (cartilage)
- Osteoblasts (bone)
- Odontoblasts (tooth)

These cells synthetise extracellular matrix.

Extracellular matrix

Parts of the extracellular matrix

- **FIBRILLAR PROTEINS (collagen, elastin)**
  - insoluble in water, no hydratation
- **GLYCOPROTEINS (e.g. fibronectin,laminin)**
- **GLYCOSAMINOGLYCANS AND PROTEOGLYCANS**
  - soluble in water, easily hydratated

Saccharide content increases

Extracellular matrix

FIBRILLARY PROTEINS

- Structural proteins
  - collagen *firmness*
  - elastin *elasticity*

COLLAGENS

The most abundant proteins in mammals. They form approximately 25 % of all body proteins.

Collagens

Collagenum

gr. *kolla* glue;
gr. *gennao* constitute

By boiling collagen is denatured to a colloid solution (gelatine).
From the nonpurified collagen the glue arises.

Incidence

- main protein of the extracellular matrix
- component of tendons, cartilages, bones, and teeth (dentin and cement), skin and vessels.

Properties

- fibrillary proteins
- nonsoluble (glyco-) proteins
- HIGH STRENGHT, BUT ALSO SUPPLENESS

Structure of collagen

Collagens

Collagen has an characteristic amino acid composition and their specific sequence.

Primary structure

- Characteristic AA composition
- Characteristic AA sequence

Mature collagen contains no tryptophan and almost no cysteine – from the nutritional point of view not fully valuable protein.

Primary structure of collagen

Characteristic AA composition

- Fundamental amino acids
  - Glycine 33 % (x Hb 4 %)
  - Proline 13 % (x Hb 5 %)

High content

- Derived amino acids
  - 4-Hydroxyproline 9 % (x Hb 0 %)
  - 5-Hydroxylysine 0,6 % (x Hb 0 %)

Origin by posttranslational modification

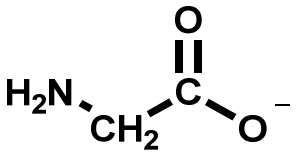
Chaacteristic for collagen

Hb = hemoglobin

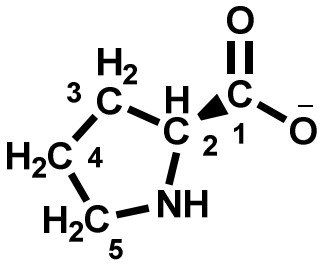
Primary structure of collagen

Fundamental AA

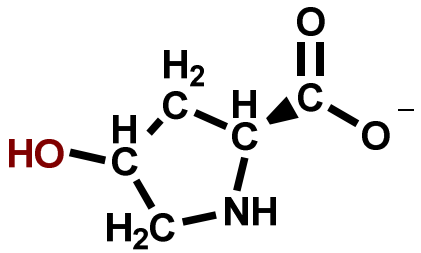
- Glycine



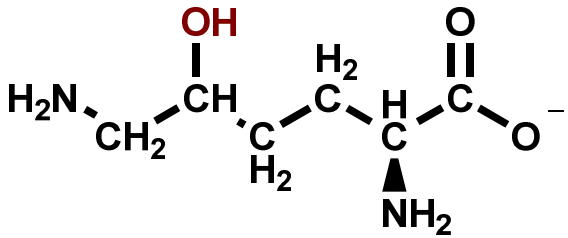
- Proline



- Derived AA
  - 4-Hydroxyproline



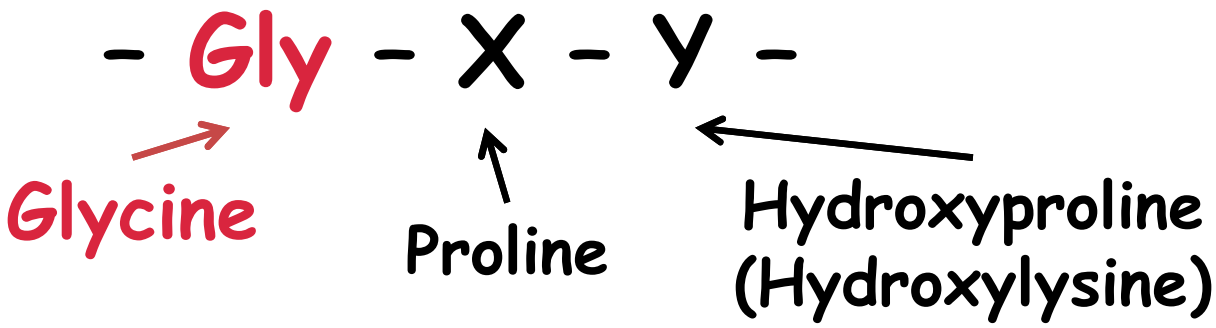
  - 5-Hydroxylysine



Primary structure of collagen

Characteristic AA sequence

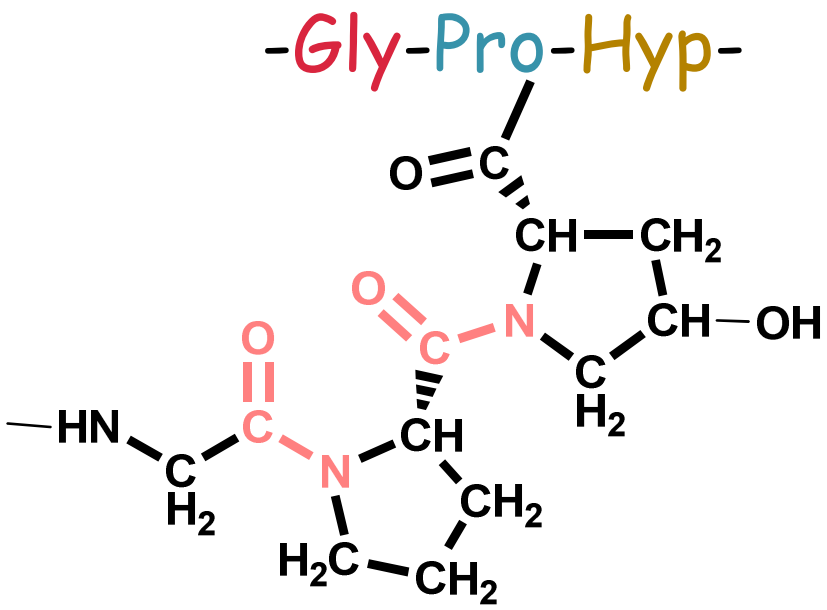
Triplet



- Every third AA is **GLYCINE**
- On the next position frequently **PROLINE**
- On the third position frequently hydroxyproline, ev. hydroxylysine

Primary structure of collagen

Example of AA sequence of a part of the polypeptide chain



Globular proteins rarely show periodicity in AA sequence.

Secondary structure of collagen

Comparison of collagen helix to the α-helix, which represents the most common secondary structure in proteins.

Collagen helix

- **levorotatory** helix
- steeper rising
- 3,3 AA/turn
- intrachain hydrogen bonds not present
- proline prevents formation of α-helix or β-pleated sheet

α-helix

(the most common secondary structure in proteins)

- **dextrorotatory** helix
- gradual rising
- 3,6 AA/turn
- stabilization by intrachain hydrogen bonds

Triple helix

Three α-chains of collagen

Triple helix

Relatively rigid

This structure is responsible for the tensile strenght.

Triple helix

The origin is dependent on the oddness of the primary structure

- High presence of glycine
  - *smallest amino acid, no side chain (only –H)*
  - *placed in the centre of triple helix, where no space is available*
  - *close contact between the chains*

Triple helix is stabilized by hydrogen bonds between each peptide bond -NH group of glycine and C=O group of the peptide bond of the adjacent polypeptide chain.

Collagen chains

The collagen chain is extraordinarly long and contains approximately 1000 AA.

The collagen chains are called $\alpha 1 - \alpha 3$.

- They differ in AA representation
- Products of different genes – e.g. $\alpha_{1(I)}$ or $\alpha_{2(V)}$
- Roman digit labels the collagen type

More than 30 different types of collagen exists.

Collagen chains

The representation of chains differs in individual types of collagens.

The collagens may form homotrimers or heterotrimers.

Homotrimers

- molecule of collagen is formed by three identical chains;
- e.g. collagen type III is formed by three $\alpha_{1(III)}$ chains

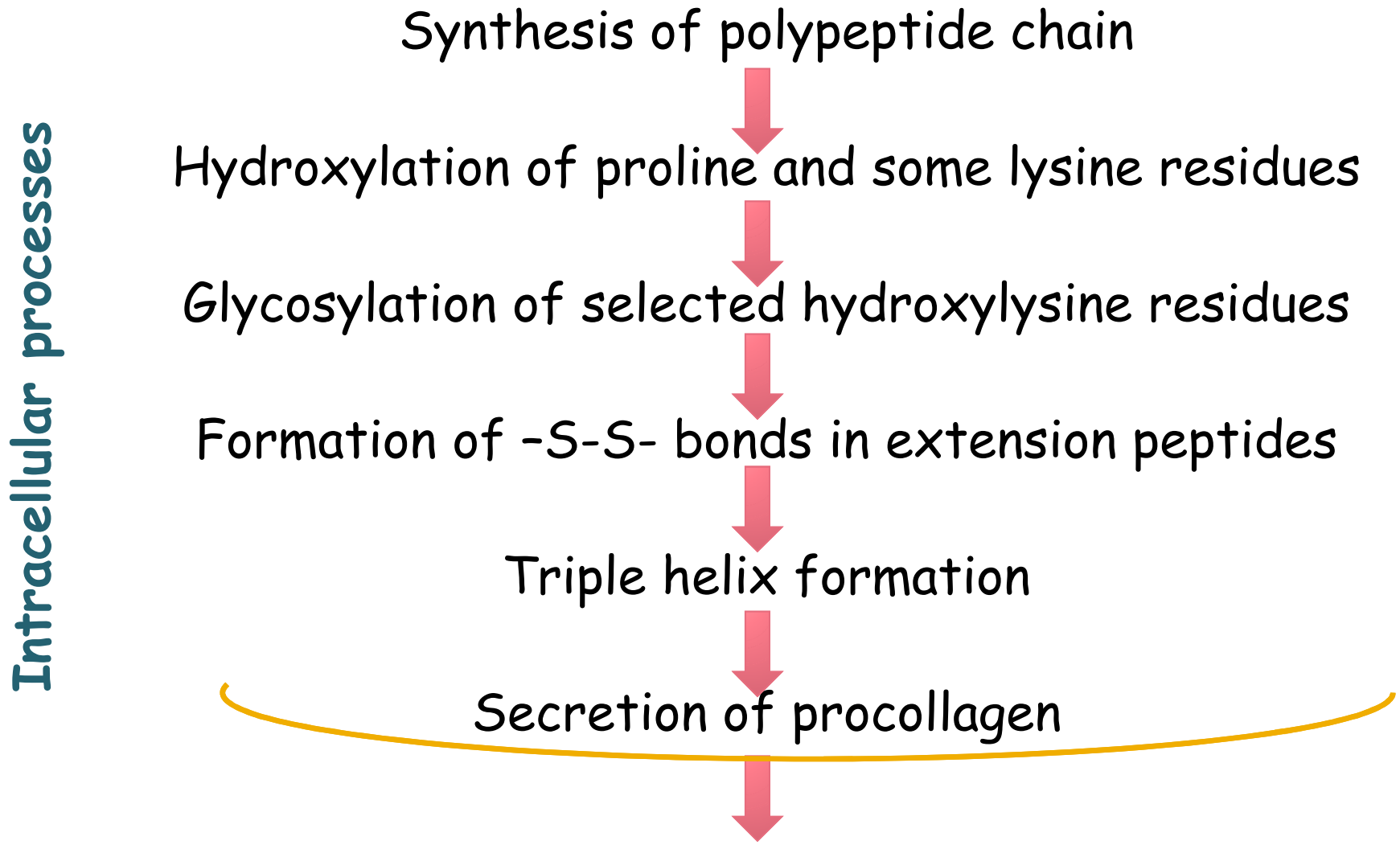
Heterotrimers

- molecule of collagen is formed by different chains;
- e.g. collagen type I is assembled of two $\alpha_1(I)$ $_{chains}$ and one $\alpha_2(I)$ $_{chain}$

Collagen synthesis

Collagen is an example of a protein, whose synthesis is connected with many posttranslational modifications (treatment of the polypeptide chain), which take part intra- and extracellularly.

Synthesis and posttranslational modifications of collagen



Posttranslational modifications of collagen

Extracellular processes

Proteolytic removal of propeptides

Assembling of collagen fibrils

Formation of cross-links

Posttranslational modifications in the course of collagen synthesis

INTRACELLULAR PROCESSES

Hydroxylation of proline and lysine residues

Enzymatically catalyzed reaction

- Prolylhydroxylase
- Lysylhydroxylase

Dioxygenases contain Fe

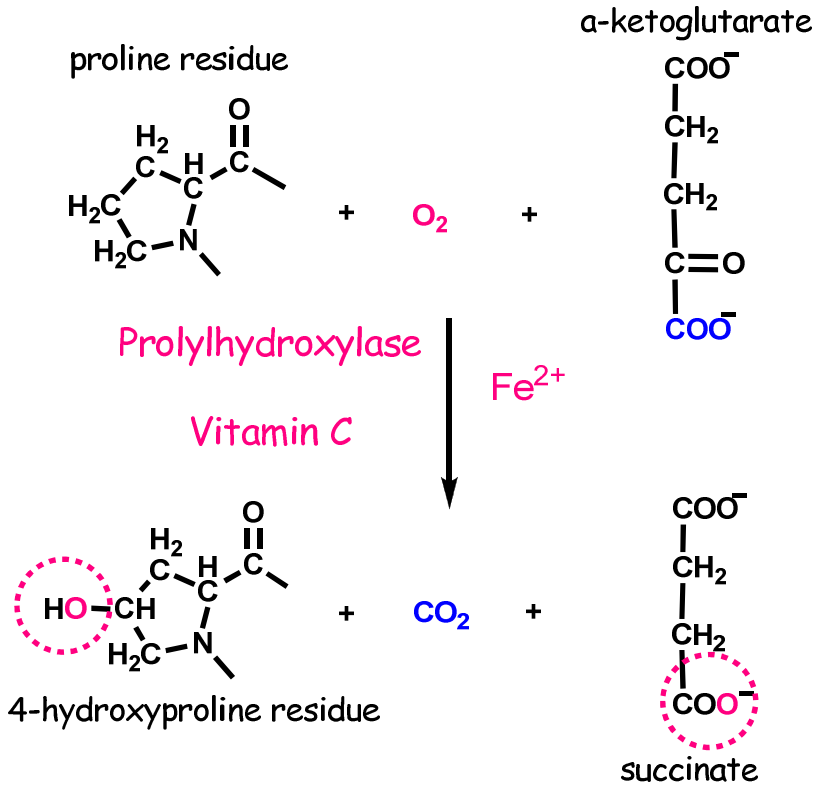
cofactors

- **Vitamin C !!!**
- **α-ketoglutarate**

Reaction needs oxygen. One O atom forms -OH group of hydroxyproline, the other becomes part of the originating succinate.

Hydroxylation of the proline and lysine residues

Reactions catalyzed by prolylhydroxylase



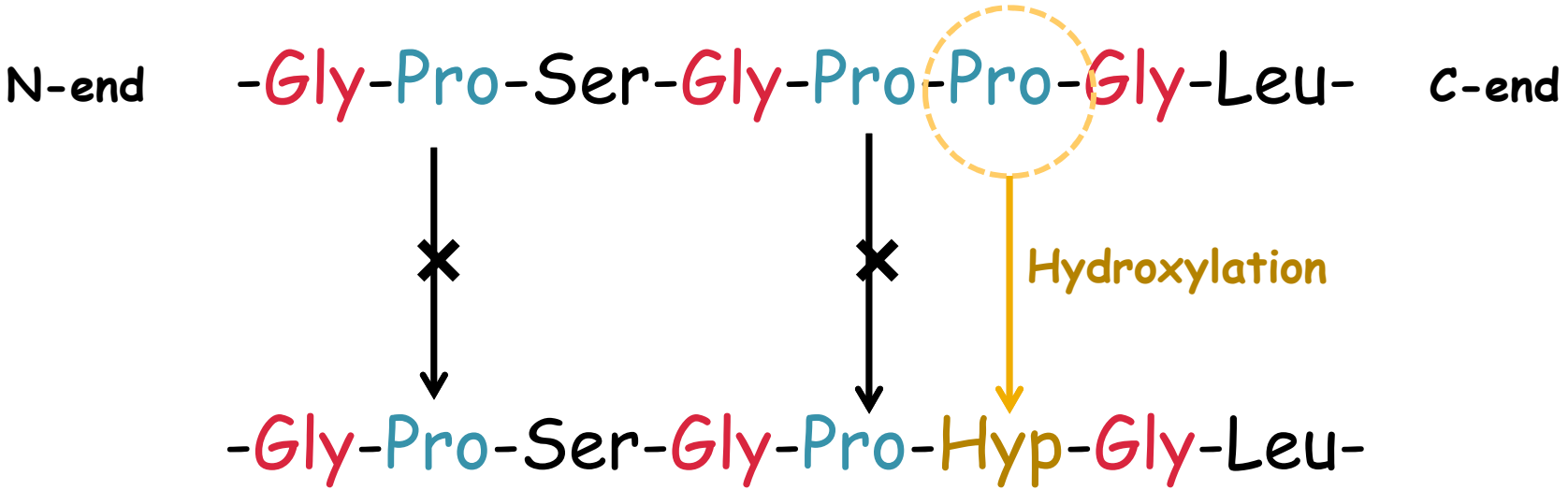
Dioxygenase contains Fe

Vitamin C
Maintains Fe^{2+} in a reduced state

Hydroxylation of proline and lysine

Reaction catalyzed by prolylhydroxylase

- reaction highly specific only for proline attached in the polypeptide chain to the amino group of the glycine



Hydroxylation of proline and lysine

Importance of proline and lysine residues hydroxylation

Hydroxyproline

- necessary for origin of triple helix by formation of hydrogen bonds between individual chains

Hydroxylysine

- glycosylation on the formed -OH group

Deficiency of vitamin C

Nonhydroxylated chain is not able to mature

↓

The stable triple helix cannot be formed

↓

Immediate degradation inside the cell

↓

Loss of collagen in the matrix

↓

Falling out of teeth
Vascular fragility
Poor wound healing

Vitamin C deficiency

Avitaminosis - scurvy

Manifestation of avitaminosis in oral cavity

- swollen reddish gums
- falling out of the teeth

Glycosylation

- Attachment of galactose or galactosylglucose to -OH group of the hydroxylysine

Enzymatically catalyzed reaction

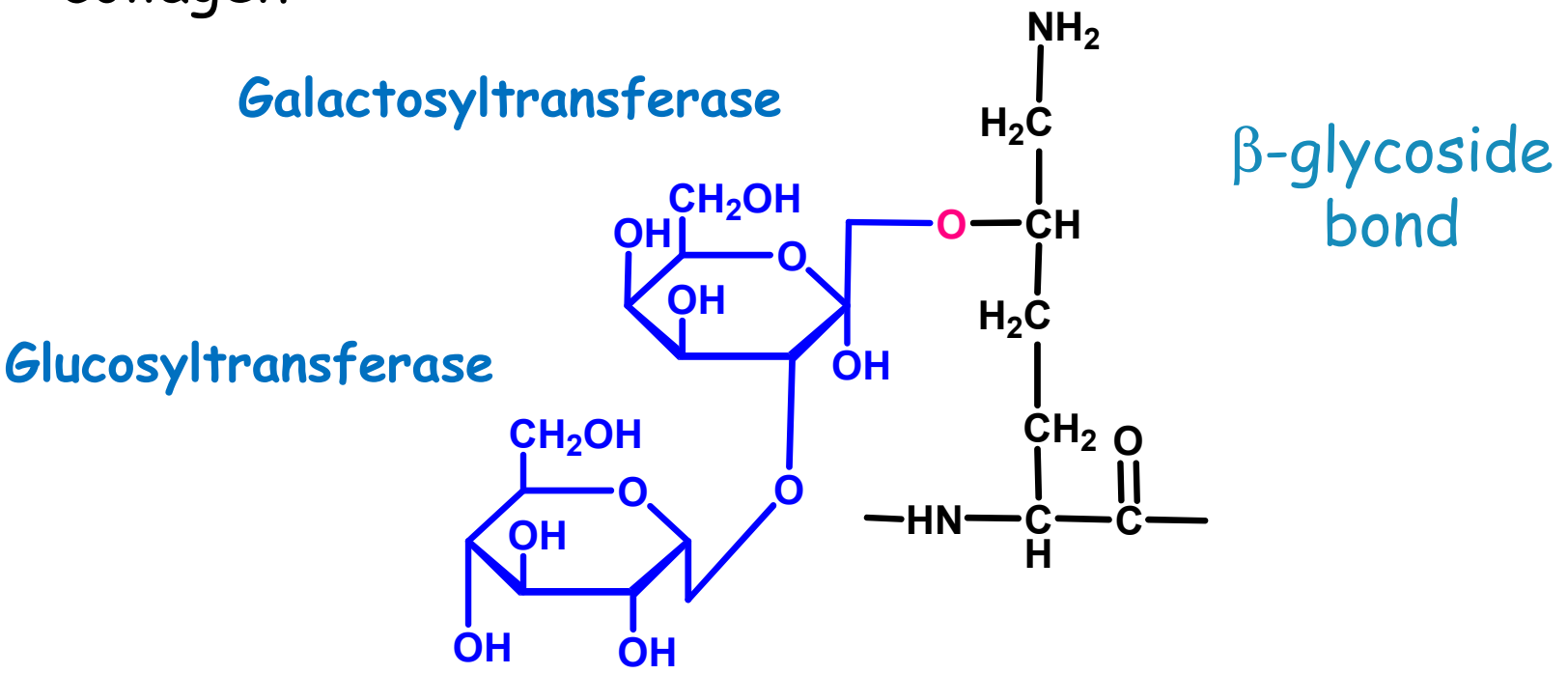
- Galactosyltransferase
- Glucosyltransferase

Number of saccharide units depends on the type of collagen - e.g.:

- Type I (tendons) – 6 units
- Type II (lens envelope) – 110 units

Glycosylation

Glycosylated residue of hydroxylysine in the molecule of collagen



Mechanism of glycosylation is different than that in the glycosylation of serine or asparagine.

Formation of -S-S- bonds

Disulphide bonds

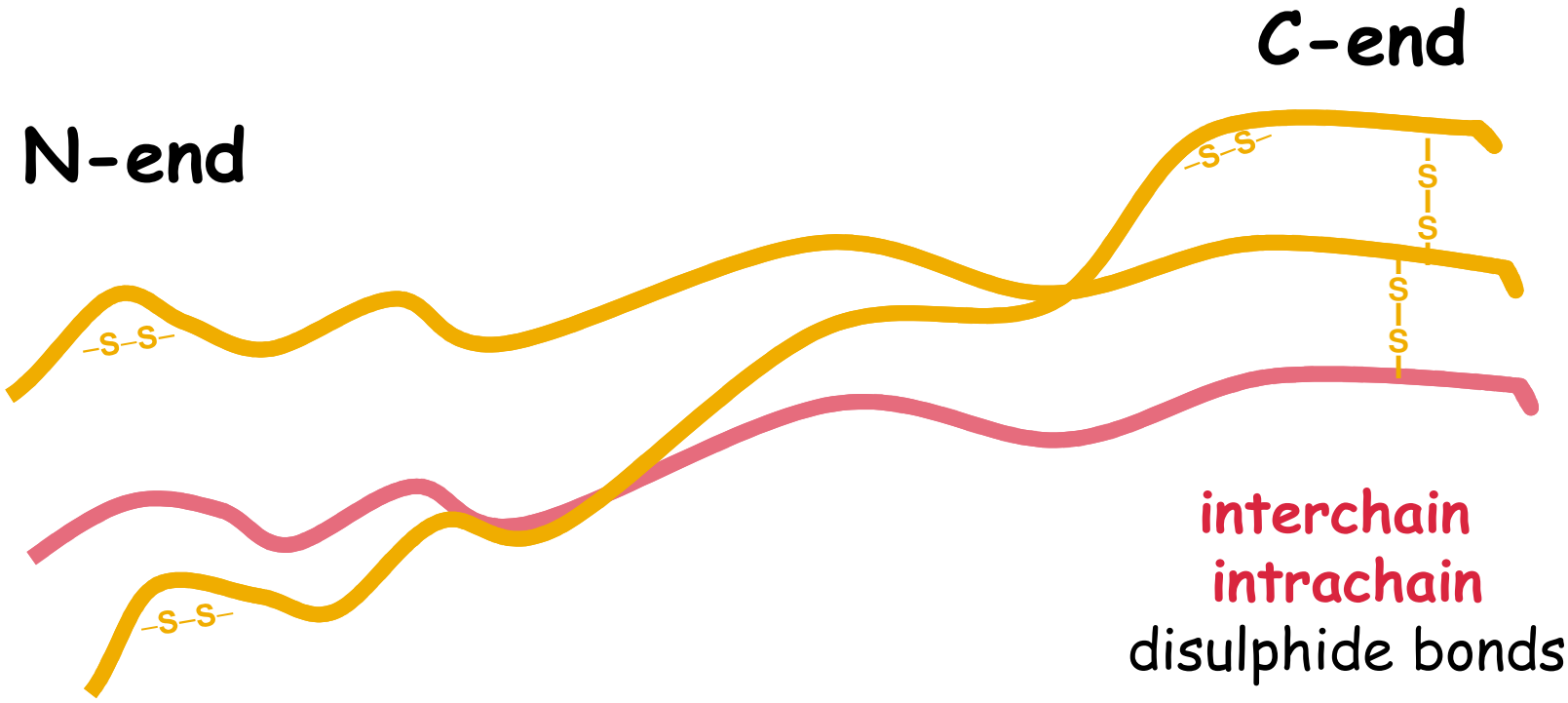
- in the region of C-terminal propeptides
  - **interchain and intrachain** disulphide bonds

- in the region of N-terminal propeptides
  - **intrachain** disulphide bonds

Importance

- necessary for initiation of triple helix formation
  starts from the C-end
- secretion out of the cell

Formation of -S-S- bonds



interchain
intrachain
disulphide bonds

intrachain
disulphide bonds

Procollagen

N-terminal propeptide of the procollagen

globular domain

TROPOCOLLAGEN
mature molecule of the collagen

C-terminal propeptide of the procollagen

globular domain

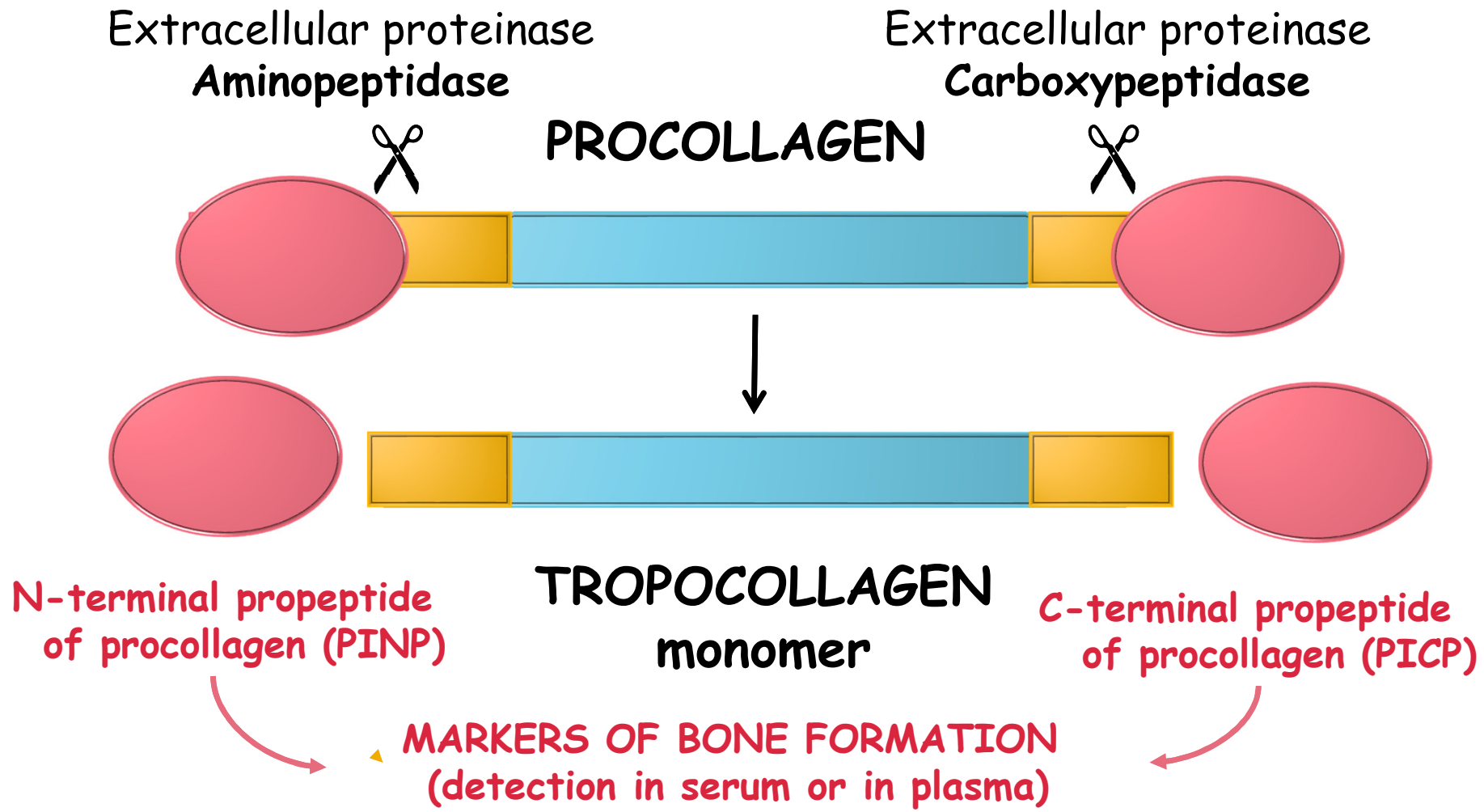
Function of propeptides

- Start the formation of triple helix in ER intracellularly.
- Prevent a premature fibril formation – extracellularly.

Posttranslational modifications in the process of collagen synthesis

EXTRACELLULAR PROCESSES

Cleaving of the propeptides



Tropocollagen

- Greek *tropé* - turn, induce a turn
- monomer of the collagen – mature molecule of collagen
- Mr = 300 000

TROPOCOLLAGEN
monomer

N-terminal
telopeptide of collagen (INTP)
nonhelical area of chains

C-terminal
telopeptide of collagen (ICTP)
nonhelical area of chains

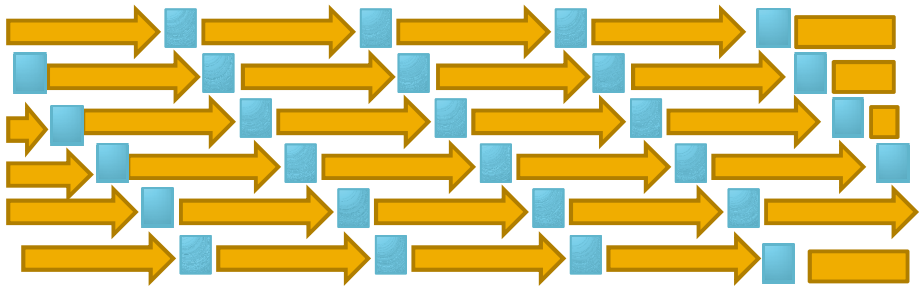
MARKERS OF BONE DEGRADATION
(detection in serum or in the urine)

Formation of fibrils

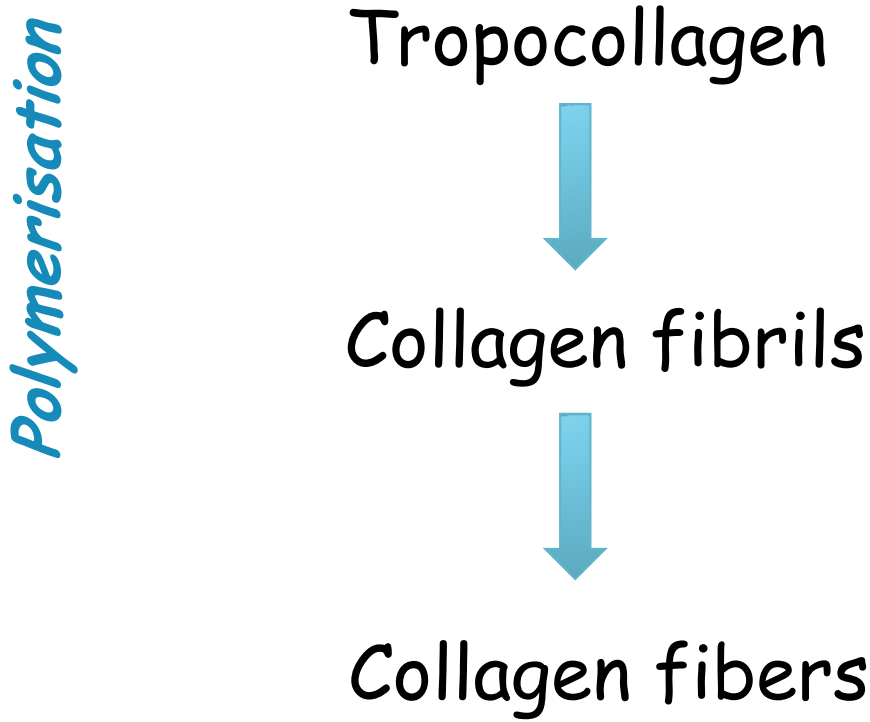
Tropocollagen —*Polymeration* (*spontaneous*)→ Collagen fibril

The way of aggregation of fibrillary collagen

- Regular arrangement along the row and in the adjacent row
- Monomers in one row are not linked end to end (gap 40 nm)
- The adjacent row is displaced by $\frac{1}{4}$ of the length
- In the arrangement of monomers act the weak noncovalent bonds

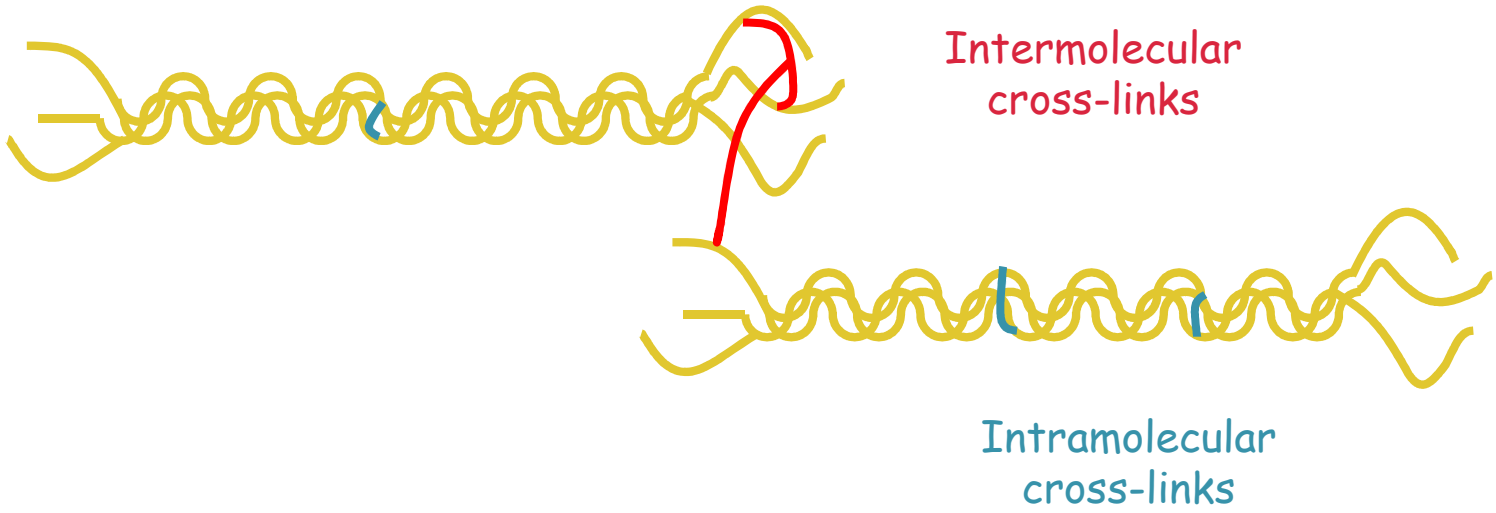


Assembling of collagen fibrils



Formation of cross-links

Collagen fibers are stabilized by formation of the covalent cross-links, which can be formed either within the tropocollagen molecule between the three chains – intramolecular cross-links and between the tropocollagen molecules – intermolecular cross-links.



Formation of cross-links

Function of cross-links

stabilization and strengthening of collagen fibril

Cross-linking

high breaking strength
lower extensibility

Formation of cross-links

Character of cross-links

- covalent bonds

Examples

- **aldol cross-link**
  - intramolecular
- **pyridinoline a deoxypyridinoline cross-links**
  histidine-aldol cross-link
  - intermolecular

Aldol cross-link

- Cross-link on the N-end of tropocollagen is formed between the lysine residues of two chains

Mechanism of formation

1. oxidative deamination of lysine, aldehyde formation
   - by the enzyme lysyloxidase
   - aminooxidase, containing Cu^{2+}
   - prosthetic group – pyridoxalphosphate

2. Aldol condensation of aldehyde groups

   spontaneous reaction, two aldehydes form a cross-link

Pyridinoline and deoxypyridinoline cross-link

- Cross-link between N-end of one tropocollagen molecule and C-end of the adjacent tropocollagen molecule

Pyridinoline

- of 3 hydroxylysine residues

Deoxypyridinoline

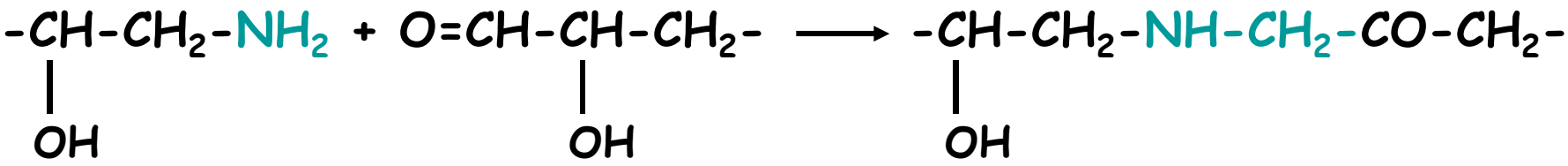
- of 2 hydroxylysine and 1 lysine residues
- more specific for bone and dentine

Pyridinoline and deoxypyridinoline cross-links

Mechanism of origin

1. step – oxidative deamination of lysine to aldehyde
   - catalyzed by lysyloxidase enzyme

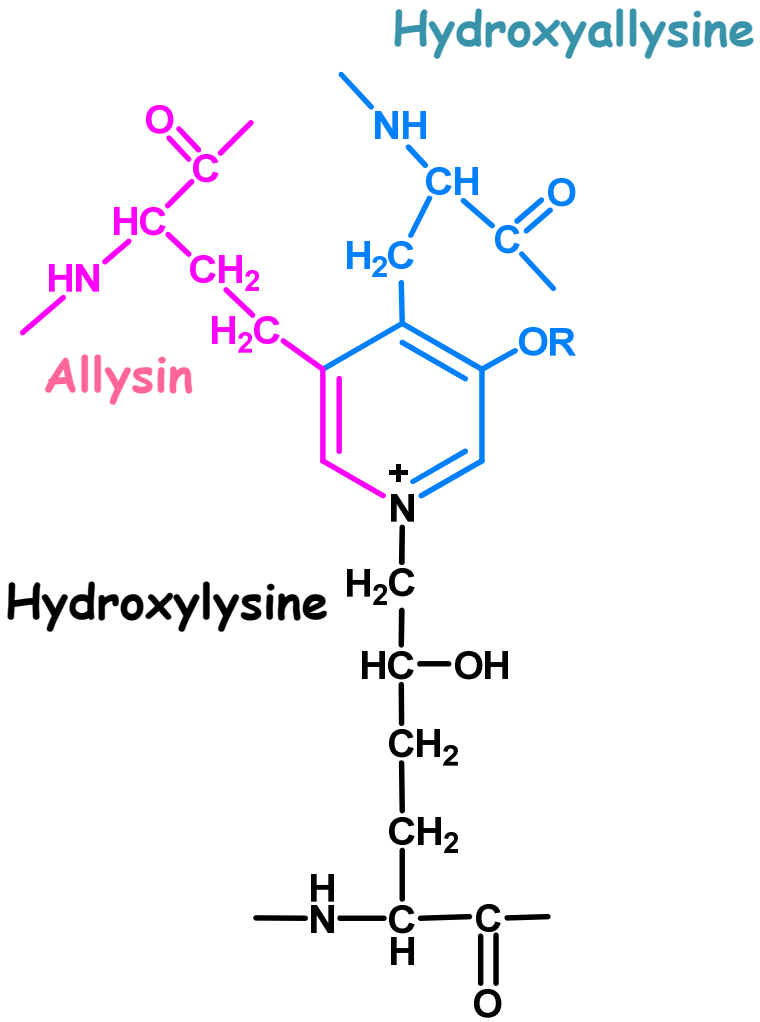
2. step – formation of ketoamine
   - nonenzymatic reaction of oxidized hydroxylysine with nonoxidized lysine (hydroxylysine)



Pyridinoline a deoxypyridinoline cross-links

3. step – formation of the pyridine ring
   - Interaction of ketoamine with the free aldehyde group of the hydroxylysine closes the heterocyclic pyridine ring, linking covalently three diferent collagen chains

Intermolecular cross-bridge



Pyridinoline a deoxypyridinoline cross-links

- In the course of bone degradation these cross bridges are separated from collagen fibers, released to blood and excreted to urine.
- The pyridinoline and particularly the deoxypyridinoline bridges may be determined in blood and urine.

MARKERS OF BONE DEGRADATION

Overview of collagens - classes

Fibrillar collagens – e.g. types I, II, III, V

- „typical" collagens forming fibrils

Collagens associated with collagen fibrils – for example types VI, IX, XII, XIV, XVI

- Triple helix is interrupted by sections making possible the bending of the molecule.
- These collagens attach to the surface of collagen fibrils and join them together and connect them to other constituents of extracellular matrix

Net forming collagens – types IV, VIII and X

- Do not form typical fibrils
- Net like arrangement
- Nonhelical globular domains on the ends of the molecule

Overview of collagens-classes

Anchoring collagens – type VII

- forms anchoring fibers
- strengthen the connection of dermis and epidermis

Transmembrane collagens – types XIII and XVII

- integral membrane proteins

Overview of collagens

Some fibrilar collagens

Type	Molecular structure	Occurrence
I	$[\alpha_1(I)]_2\ [\alpha_2(I)]$	widely present, skin, vessels, tendons, gingiva, bone, cement, dentin, periodontal ligaments
II	$[\alpha_1(II)]_3$	cartilage, vitreous body
III	$[\alpha_1(III)]_3$	skin, vessels, lungs, gingiva, cement, dentin, periodontal ligaments
V	$[\alpha_1(V)]_3$, $[\alpha_1(V)_2\ \alpha_2(V)]$	skin, smooth muscle, bone, cement, dentin

Types of collagen

Some collagens associated with fibrils

Type	Molecular structure	Occurrence
VI	$[\alpha_1(VI)\ \alpha_2(VI)\ \alpha_3(VI)]$	laterally associated with collagen type II, widely present, bone, gingiva, cement, periodontal ligaments
IX	$[\alpha_1(IX)\ \alpha_2(IX)\ \alpha_3(IX)]$	laterally associated with collagen type II, cartilage, vitreous body, periodontal ligaments
XII	$[\alpha_1(XII)]_3$	associated with collagen type I in soft tissues, periodontal ligaments

Oveview of collagens

Some net forming collagens

Type	Molecular structure	Occurrence
IV	$[\alpha_1(IV)]_2\ [\alpha_2(IV)]$	basal membranes, formation of two-dimensional net gingiva, periodontal ligaments

Disorders of collagen synthesis

Increased collagen synthesis

- fibroses

Decreased collagen synthesis

- genetic disorder
- acquired disorders

Disorders of collagen synthesis

Increased collagen synthesis - FIBROSIS

- hepatic cirrhosis
- pulmonary fibrosis
- atherosclerosis

Tissue damage stimulates collagen synthesis by fibroblasts

- e.g. damaged hepatocytes are replaced by fibrous connective tissue – hepatic cirrhosis

Disorders of collagen synthesis

Increased collagen synthesis

- bacterial infections also stimulate collagen synthesis

Prevention of infection spreading – **ABSCES**

X

Some bacteria (Clostridia) produce collagenases, which degrade tropocollagen.

Disorders of collagen synthesis

Decreased collagen synthesis

- Genetically conditioned
  - Ehlers-Danlos syndrome
  - osteogenesis imperfecta
- Acquired disturbances
  - lathyrism
  - copper deficiency
  - vitamin C deficiency

Disorders of collagen synthesis

Ehlers-Danlos syndrom

- heterogenous group of diseases caused by defects of enzymes necessary for synthesis of collagen or by abnormalities in the procollagen gene

Manifestations

- extreme extensibility of connective tissue and skin
- hypermobility of joints
- contortionists
- risk of rupture of vessels or of the intestine

Disorders of collagen synthesis

Osteogenesis imperfecta

- group of diseases caused by mutation in collagen type I
- exchange of Gly for an AA having larger side chain
- formation of triple helix is not possible
- degradation of polypeptide chains not forming triple helix

Manifestations

- abnormal bone fragility
- bone fractures even in small injuries
- in more serious cases prenatal fractures

Lat. *imperfectus* incomplete

Disorders of collagen synthesis

Dentinogenesis imperfecta

- group of diseases caused by mutation in α_1(I)
- associated with osteogenesis imperfecta

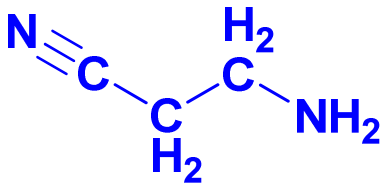
Manifestations

- thin enamel
- discolouring of teeth (yellow, brown, grey)
- opalescence of the teeth
- lower mechanical resistance of the teeth

Disorders of collagen synthesis

Disturbance of cross-link formation

- Causes
  - copper deficiency (part of lysyloxidase)
  - animal food containing β-aminopropionitrile (contained in seeds of sweet pea – *Lathyris odoratus)* – blocks lysyloxidase – lathyrism



Manifestations

extreme fragility of connective tissue (bones, vessels)

ELASTIN

Elastin is the main protein of elastic fibers, providing elasticity to the tissues.

Elastin

Occurrence

- in arteries, particularly in aorta
- in skin, tendons and loose connective tissue (relatively low content)
- in lungs

Synthesis takes place in early development or after tissue damage

Half-time is approximately 70 years (lower content in elderly people).

Elastin

Properties

EXTENSIBILITY AND CONTRACTILITY

- resembles the rubber
- after extension elastin is able to return to original size and original form
- tensile strength is lower than in collagen
- hydrophobic, practically insoluble in aqueous solutions

Primary structure of elastin

Occurrence of amino acids

- 1/3 glycine
- high content of nonpolar AA (Ala, Val, Leu, Ileu)
- low hydroxyproline
- no hydroxylysine – elastin is not glycosylated

Sequence of amino acids

- typical triplet as in collagen is not present

Alternation of short hydrophobic and hydrophilic sections.

Hydrophilic sections, which represent a minority part, are rich in lysine, which takes part in forming of cross - links.

Secondary and tertiary structure of elastin

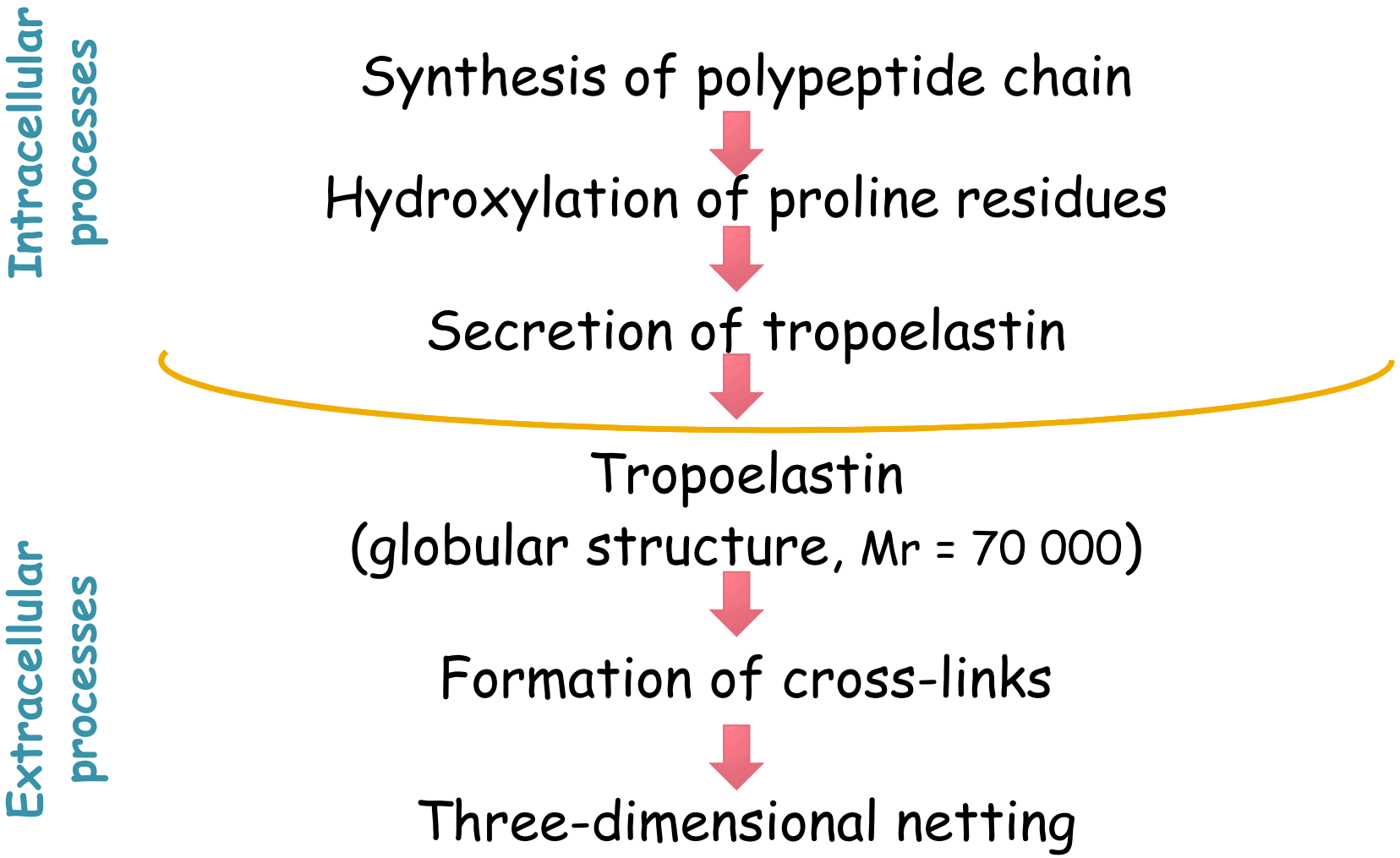
Secondary structure

- elastin does not form a regular secondary structure
- elastin has an character of random coil conformation enabling extension and contraction

Tertiary structure

- a stable secondary structure is not expressed

Elastin synthesis



Cross-links in elastin

Cross-links

- there is a large number of covalent cross-links in elastin
- some are similar as in collagen
- key step is an oxidative deamination of some lysine residues by copper-containing lysyloxidase (the same enzyme as in formation of cross-links in collagen)
- cross-links may be formed within one polypeptide chain or between 2 – 4 chains

Desmosine

- cross-link completely specific for elastin
- arises from 4 side chains of LYSINE (3 oxidized and 1 nonoxidized)
- determines the high elasticity of elastin

Linking of polypeptide chains of elastin by cross-links constitutes a three-dimensional netting explaining the „rubber-like" properties of elastin.

GLYCOSAMINOGLYCANS

Glycosaminoglycans (GAG) (Mucopolysaccharides)

Characteristic

- heteropolysaccharides (100% polysaccharides)
- not branched polysaccharide chains
- long chains (70 – 200 monosaccharides)
- repeating disaccharide units

Muco – these substances were first detected in mucus

Glycosaminoglycans

Polysaccharide chain of GAG is formed by repeating disaccharide units.

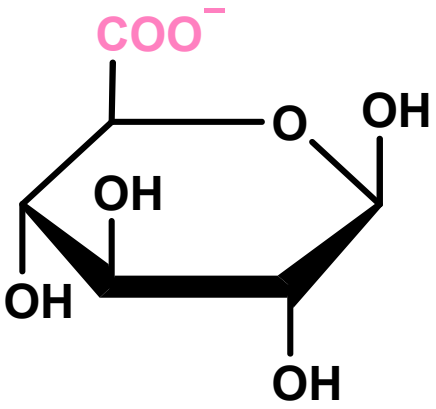
[URONIC ACID – AMINO SUGAR]$_n$

OR

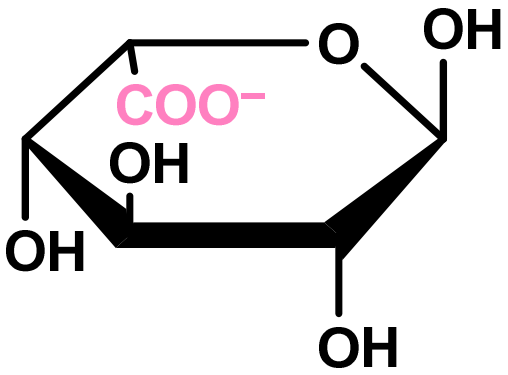
[MONOSACCHARIDE - SULFONATED AMINO SUGAR]n

Glycosaminoglycans

Uronic acids present in GAG



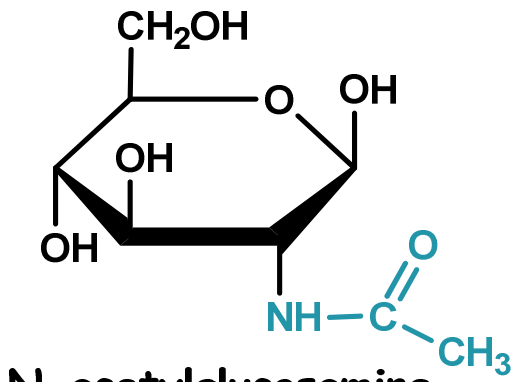
D-glucuronic acid



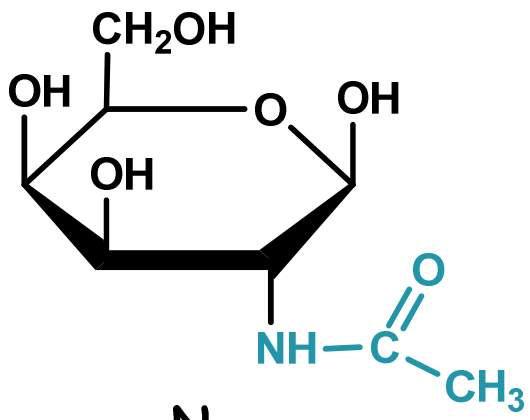
L-iduronic acid
(5-epimer)

Glycosaminoglycans

Amino sugars present in GAG



N-acetylglucosamine



N-acetylgalactosamine (4-epimer)

Glycosaminoglycans

Modifications of amino sugars in GAG

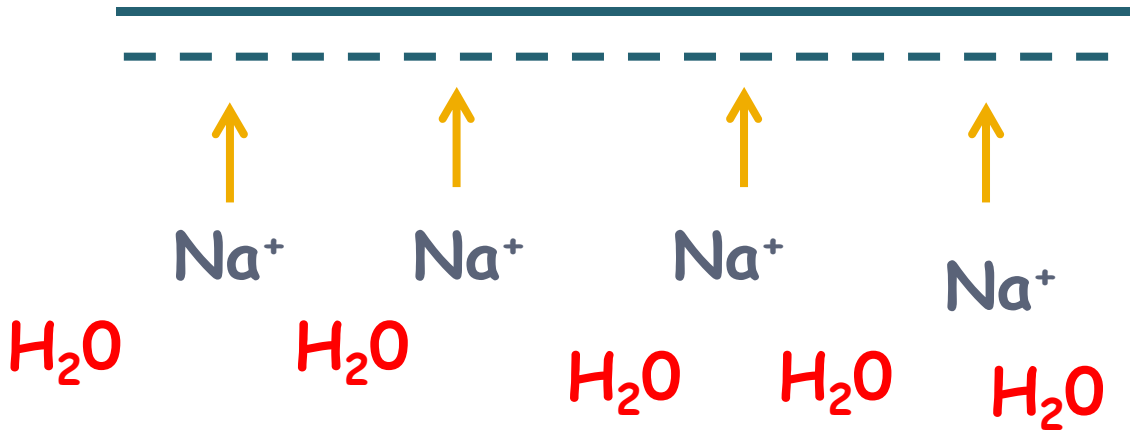
- Acetylation of aminogroup – elimination of a positive charge
- Attachment of a sulphate on OH C-4 or C-6 (ester bond), or on nonacetylated amino group – increase of a negative charge

Glycosaminoglycans

Characteristics

- high number of acidic groups
  - $-COO^-$ (uronic acids)
  - $-OSO_3^-$ (amino sugars with sulphate groups)

- highly negative charge at physiological pH (polyanions)



Glycosaminoglycans

Characteristic (cont.)

- chains repel each other and in solution tend to straighten
- negatively charged groups bind cations – Na^+, K^+
- osmotically active
- strongly hydrophilic (1 g proteoglycans/50 g of water)
  - occupy larger volume when compared with proteins
- in low concentrations form hydrated gel
  - determine the turgor of extracellular matrix
- act as a filter allowing the diffusion of small molecules (e.g. ions, water) and prevents the diffusion of proteins and movement of cells

Glycosaminoglycans

Types of glycosaminoglycans

Seven types (groups) of GAG

- differ in occurrence of monosaccharides, type of glycoside bond, grade and localisation of sulphate groups

Groups of glycosaminoglycans

Chondroitin-4-sulphate

- cartilage
- bone
- vascular wall
- aorta
- cornea
- dentin, cement
- gingiva, periodontal ligaments

Repeating disaccharide

GLUCURONATE

+ N-ACETYLGALACTOSAMINE-4-sulphate

Chondroitin-6-sulphate

- embryonal connective tissue
- heart valves
- cartilage
- bone
- vascular wall, aorta
- cornea
- predentin, cement
- periodontal ligaments

Repeating disaccharide

GLUCURONATE

+ N-ACETYLGALAKTOSAMINE-6-sulphate

Groups of glycosaminoglycans

Chondroitin-4-sulphate Chondroitin-6-sulphate

Both are the most abundant GAG in the body

Both bind collagen and firmly connect the fibrils.

Depletion of chondroitinsulphate in the cartilage is the main cause of osteoartritis.

Groups of glycosaminoglycans

Keratansulphate

- intervertebral disc
- bone
- cornea
- predentin, cement
- periodontal ligaments

Repeating disaccharide

GALACTOSE +
N-ACETYLGLUKOSAMIN-6-sulphate

No uronic acid !!

Dermatansulphate

- predominantly in skin
- vessels, heart valves
- tendons
- lungs
- gingiva, periodontal ligament
- cement

Repeating disaccharide

IDURONATE
+ N-ACETYLGALAcTOSAMIN-4-sulphate

Differs from chondroitin-4-sulphate only by inverse configuration on C-5 in glucuronate, changed by epimeration to iduronate.

Groups of glycosaminoglycans

Heparin

- deposited intracellularly in granules of mastocytes along arteries in the liver, lungs and skin
- anticoagulant effect

Heparansulphate

- extracellularly deposited in basal membranes and cell surfaces
- larger than heparin
- gingiva, periodontal ligaments, cement

Repeating disaccharides

IDURONAT-2-SULPHATE + N-SULPHO-GLUCOSAMIN-6-SULPHATE

Groups of glycosaminoglycans

Hyaluronic acid (hyaluronate)

Repeating disaccharide

GLUCURONATE + N-acetyl-GLUCOSAMIN

Both monosaccharide units are glucose derivatives.

They do not contain any sulphate groups.

- Characterized by abnormal length (up to 25 000 disaccharide units - Mr 10^6 – 10^7)
- Polysaccharide chain is coiled to levorotatory helix stabilized by intramolecular hydrogen bonds.

Groups of glycosaminoglycans

Hyaluronic acid (hyaluronate)

Occurrence

- proteoglycan aggregates
- vitreous body
- synovial fluid (lubricating function)
- umbilical cord
- production increases during wound healing
- gingiva, periodontal ligaments
- cement

Groups of glycosaminoglycans

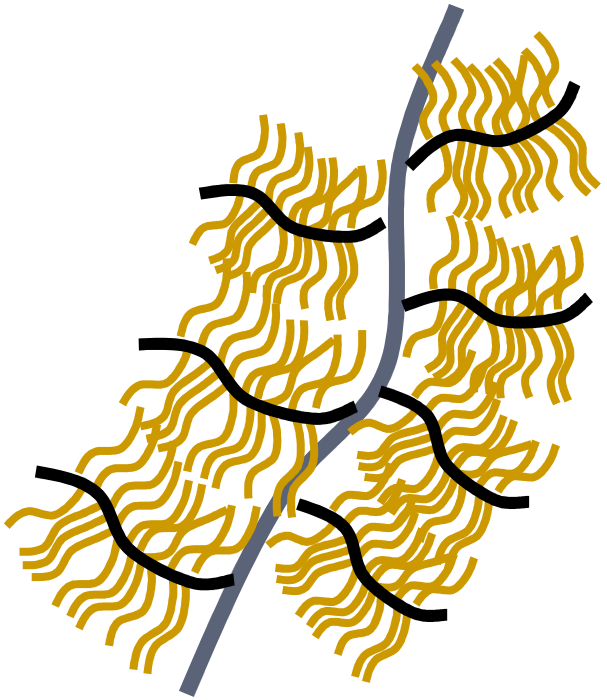
Hyaluronic acid (hyaluronate)

Hyaluronate unlike other GAG is not bound covalently to any core protein.

X

Hyaluronate forms with other proteoglycans aggregates.

Proteoglycans are attached noncovalently to hyaluronate by the N-end domain of the core protein (electrostatic interaction) with the help of link protein.



Proteoglycan
(glycosaminoglycans and core protein)

Glycosaminoglycans

Forms of GAG existence

- part of larger structures (proteoglycans)

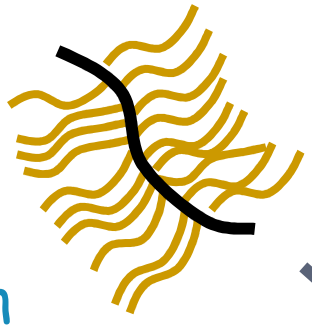
- independent molecules (heparin, hyaluronate)

PROTEOGLYCANS

Proteoglycans are formed by glycosaminoglycans, attached to core protein.

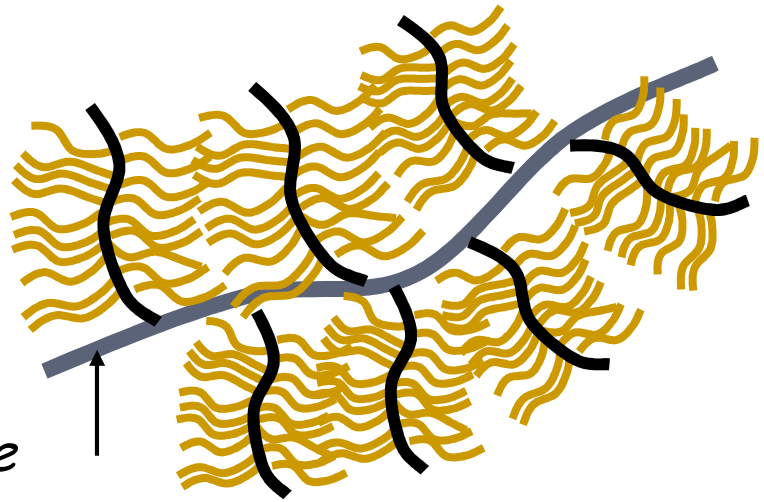
Proteoglycans

Glycosaminoglycan
(non branched saccharide chain)



Proteoglycan
(glycosaminoglycans and core protein)

Proteoglycan aggregate
(proteoglycans and hyaluronate)



Hyualuronate

Proteoglycans

Function of proteoglycans

- increase of the pressure resistance
- sieve for macromolecules – restriction of their diffusion
- lubrication effect
- hydratation of joint cartilages
- adhesion of cells and their migration
- involvement in the development of cells and tissues
- binding of signal molecules
- in bone tissue – binding of calcium salts

Proteoglycans

Glycosaminoglycans (except for hyaluronate) are covalently bound to so called core protein.

Parts of proteoglycans

- Glycosaminoglycans (polysaccharides) 95 %
- Protein 5 %

Proteoglycans

Attachment of glycosaminoglycan chain to core protein:

- O-glycoside bond
  - Through the reaction of -OH group of serine or threonine of the core protein with trisaccharide Xyl-Gal-Gal
- N-glycoside bond
  - Through the reaction of amide nitrogen of asparagine

Proteoglycans

- Proteoglycans are characterized by structural diversity:
  - different core proteins
  - different *GAG* chains
  - different length of *GAG* chains
- Proteoglycans differ also in localisation:
  - proteoglycans attached to basal membrane
  - interstitial proteoglycans

Selected proteoglycans

Proteoglycan	Typ GAG	Function
Versican	chondroitinsulphate dermatansulphate	*forms proteoglycan aggregates with hyaluronate* • *cartilage, gingiva*
Aggrecan	chondroitinsulphate keratansulphate	
Decorin	chondroitinsulphate dermatansulphate	• *binds to collagen* • *belongs to a group of small proteoglycan rich in leucine* • *gingiva*
Perlecan	heparansulphate	• *present in basal membrane* • *long core protein* • *forms a barrier limiting penetration of macromolecules through the basal membrane*

Selected proteoglycans

Proteoglycan	Occurrence in tissues of oral cavity
Versikan	periodontal ligaments, cement
Aggrecan	
Decorin	periodontal ligaments, cement, dentine
Perlecan	development of different tissues

ADHESION GLYCOPROTEINS

Ensure specific interactions between cells and molecules of extracellular matrix.

Adhesion glycoproteins

- Functions of adhesion glycoproteins
  - attachment of cells to extracellular matrix
  - organization of the compounds of extracellular matrix

- Long flexible molecules with several binding sites for:
  - collagen
  - other matrix proteins
  - polysaccharides
  - cell receptors (integrins – cell adhesion receptors)

Adhesion glycoproteins

- Selected representatives of adhesion glycoproteins
  - fibronectin
  - laminin
  - osteonectin
  - chondronectin

Adhesion glycoproteins

- Fibronectin
  - Formed by two subunits arranged to the shape of letter V
  - Binding sites for:
    - collagen,
    - heparansulphate,
    - hyaluronate
    - integrins
  - Functions as a connection of cells in extracellular matrix containig fibrillary collagen

Adhesion glycoproteins

- Laminin
  - Formed by three different chains arranged to the shape of cross
  - High relative molecular mass Mr = 950 000
  - Binding sites for:
    - collagen of type IV
    - heparansulphate,
    - hyaluronate,
    - cell adhesion receptors
  - Adhesion glycoprotein of the basal membrane – connect collagen type IV and other compounds of the membrane