

# 生醫材料導論

# Introduction of Biomaterials

## 天然高分子

### Nature polymer

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生醫材料暨組織工程所



# Nature polymers

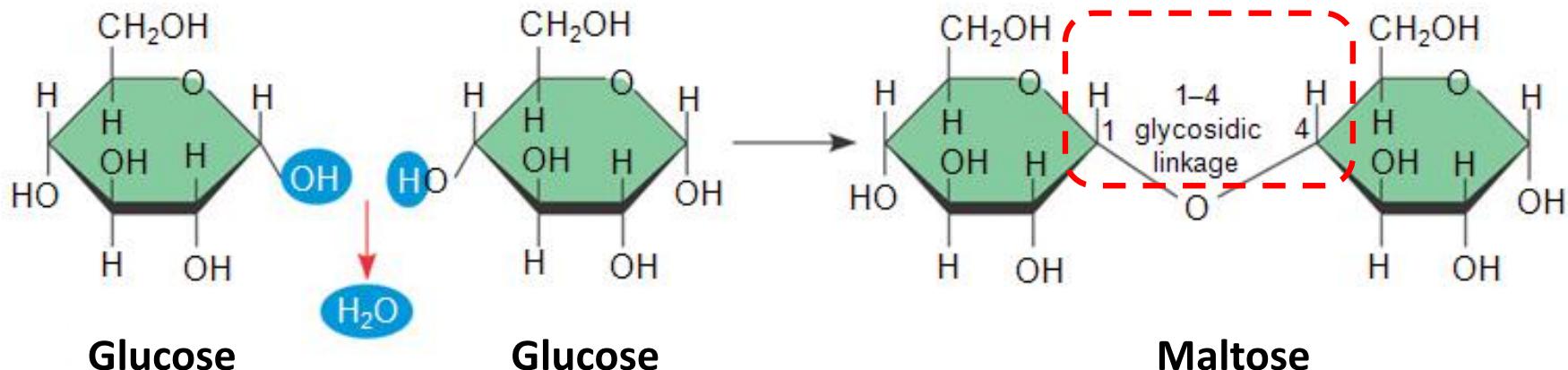
- Nature polymers are derived from renewable resources, namely from plants, animals, and microorganisms and are, therefore, widely distributed in nature.
  - Immunogenicity (enzymatic/hydrolytic degradation)
  - Lot-to lot variability
- Exhibit large diversity of unique rather than complex structure.
  - Structural complexity
- Properties varies, including pseudoplastic, gelation, water binding, biodegradability...
  - Inadequate biomechanical properties (chemical modification)

# Major nature polymers

- **Polysaccharides (多醣類 )**
  - **Alginate** 海藻膠
  - **Chitin** 甲殼素 / **chitosan** 幾丁聚醣
  - **Hyaluronic acid** 玻尿酸
- **Proteins and other polyamides**
  - **Collagen** 膠原蛋白/**gelatin** 明膠
  - **Elastin** 彈性蛋白
  - **Proteoglycans** 蛋白聚醣
  - **Laminin** 層粘連蛋白

# Poly-saccharides

## Disaccharides



## Mono-saccharides

- Glucose
- Fructose
- Galactose

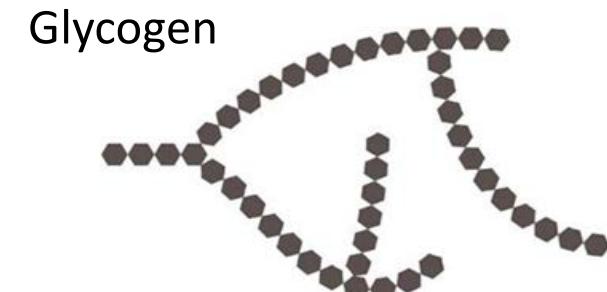
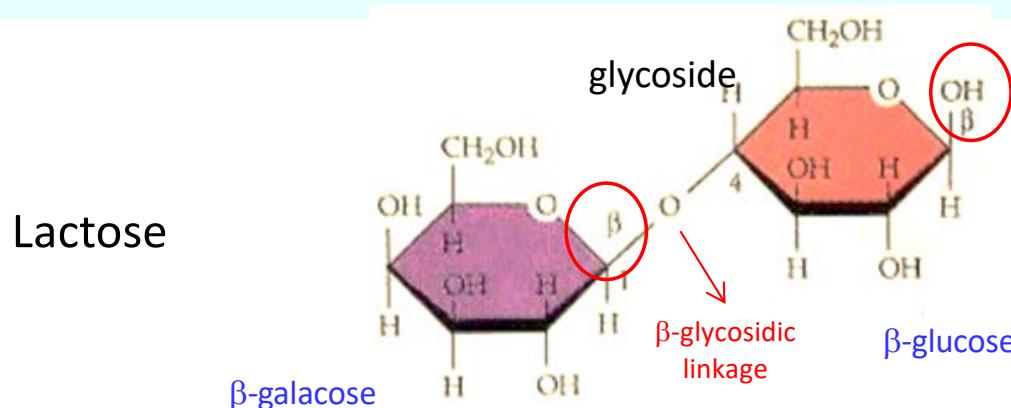
## Di-saccharides

- Maltose (glucose + glucose)
- Sucrose (glucose + fructose)
- Lactose (glucose + galactose)

- Disaccharides form when mono-saccharides combine in a **condensation** reaction.
- Enzymes are used to break down disaccharides in the body. People who lack the enzyme **lactase** cannot break down the sugar **lactose**

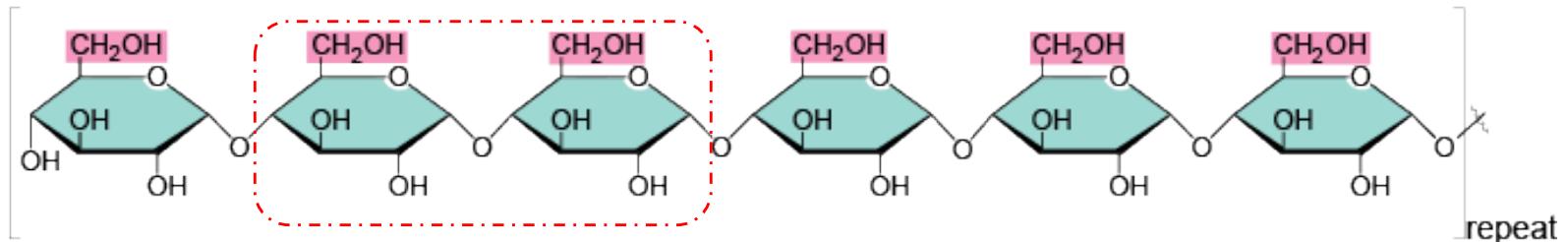
# Polysaccharides

- Known as **glycans**, consist of monosaccharides linked together by O-glycosidic linkage (> 10 sugars)
- Can be homopolysaccharides (only one type of monosaccharide) or heterosaccharides (more than one types of monosaccharides)
- Functions of polysaccharides include **structure integrity** (cellulose, chitin), **energy reserve storage** (starch, glycogen), **biological protection and adhesion** (hyaluronan)
- The glycosidic linkage can be made to any of the hydroxyl groups of monosaccharide, thus the polysaccharide chain forms linear as well as branched polymers.

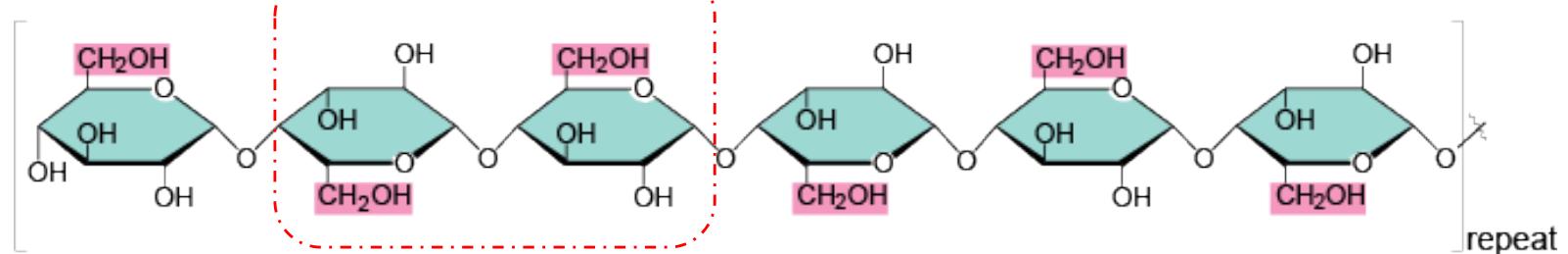


# Polysaccharides

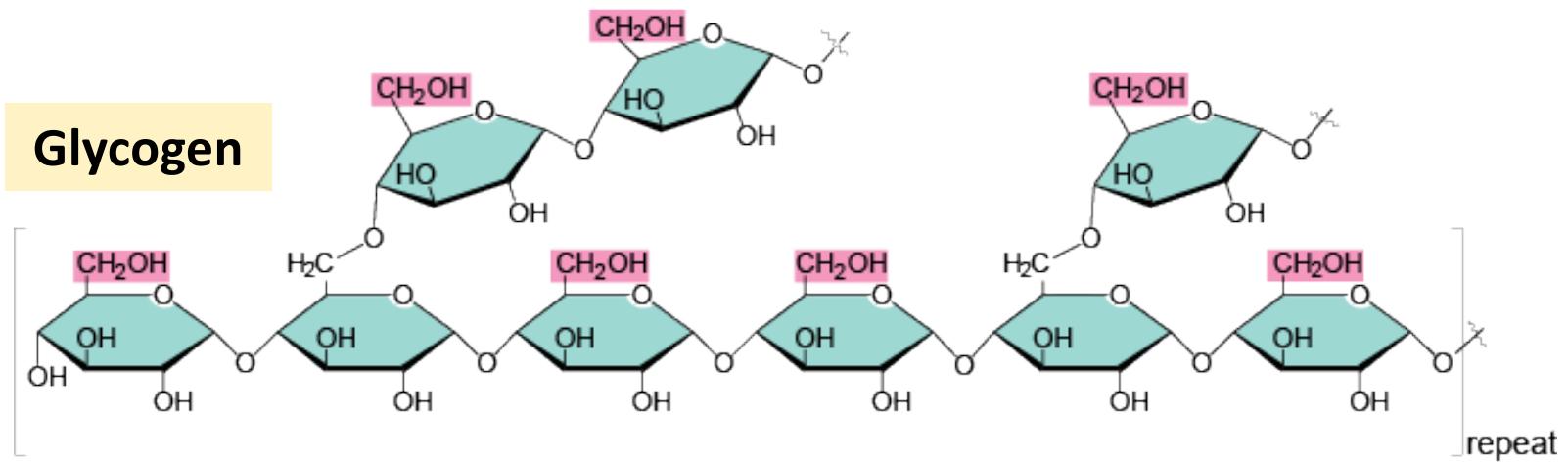
## Starch



## Cellulose



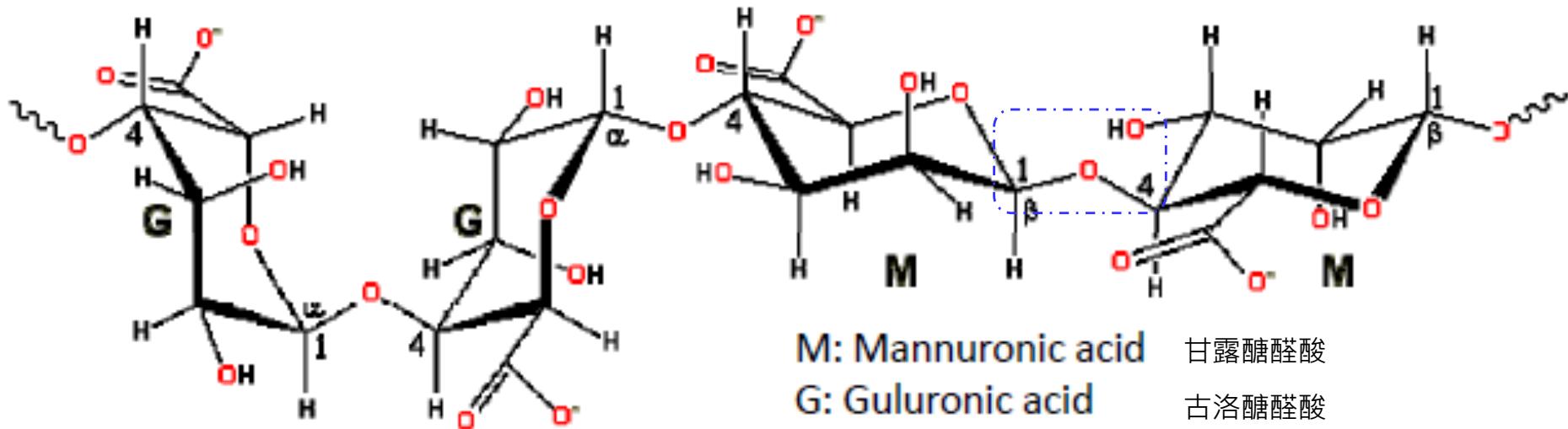
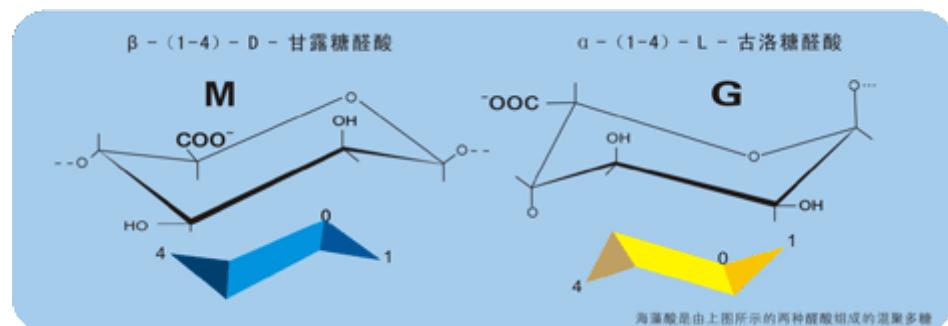
## Glycogen



# Polysaccharides

## Alginate

海藻酸鹽



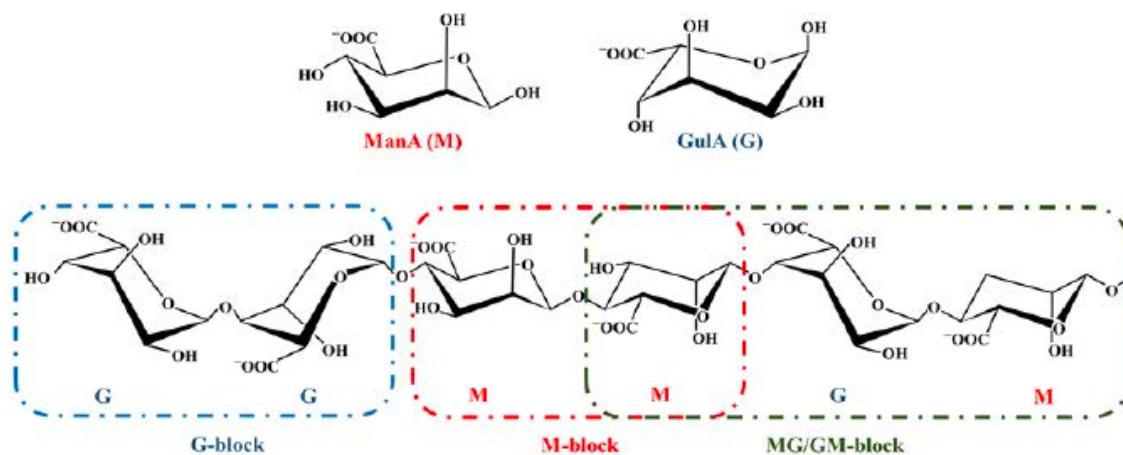
- Alginate are naturally occurring polysaccharides that can be found in all species of **brown algae**.
- Alginate are linear unbranched polymers containing  **$\beta-(1, 4)$ -linked D-mannuronic acid (M)** and  **$\alpha-(1, 4)$ -linked L-guluronic acid (G)** residues.

# Alginic

# Polysaccharides

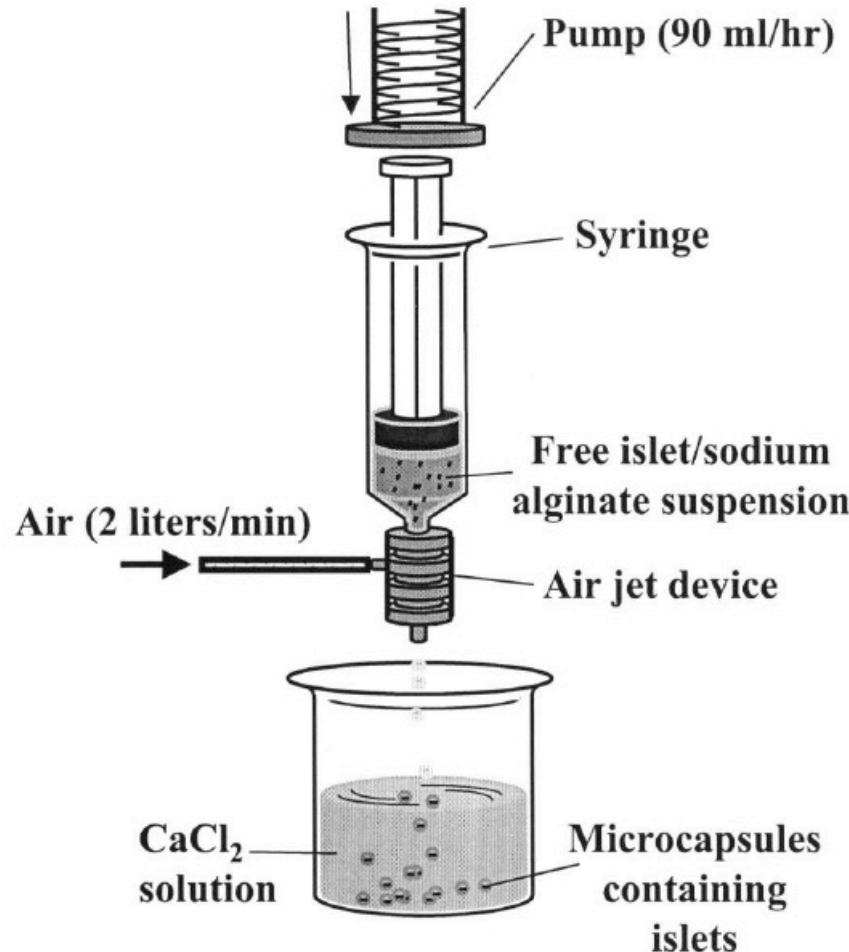


- Alginates are not random copolymers but, according to the **source algae**, consist of blocks of similar and strictly alternating residues (that is, **MMMMMM**, **GGGGGG** and **GMGMGMGM**)
- Therefore, it can be prepared with a wide range of MW to suit application (50 kDa ~100,000kDa).
- G-blocks of alginic are believed to participate in intermolecular cross-linking with divalent cations (e.g.,  $\text{Ca}^{2+}$ ) to form hydrogels.
- **MG ratio** : Stiffness GG> MM> GM ;

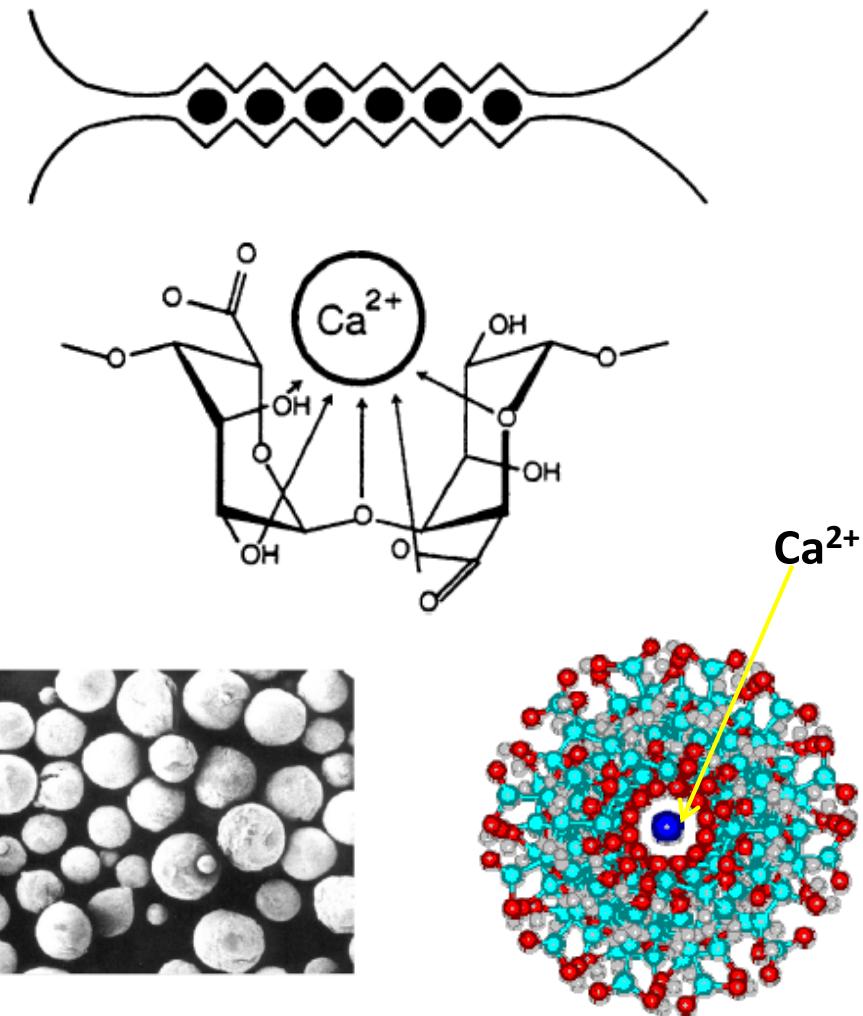


# Calcium Alginate

海藻酸鈣



# Polysaccharides



- \* A divalent cation ( $\text{Ca}^{2+}$ ) to form ionic bonds between the carboxylic groups of neighboring strands, inducing chain-chain association.

# Calcium Alginate

海藻酸鈣

# Polysaccharides



# Polysaccharides

## Alginic acid

- Is foreign to mammalian cells, alginic acid are **not naturally broken down enzymatically *in vivo*.**
- Poorly controlled degradation
  - Modifying polymer molecular weight, composition (M:G) or partial oxidation to adjust degradation kinetics of alginic acid.
- **Biological inert** – Cells do **not naturally adhere to alginic acid**, which had fostered investigations in the attachment of ECM protein/peptide.
  - Adhesion protein (laminin, fibronectin and collagen) have been coupled to alginic acid to promote cell adhesion on alginic acid.

# Chitin/Chitosan

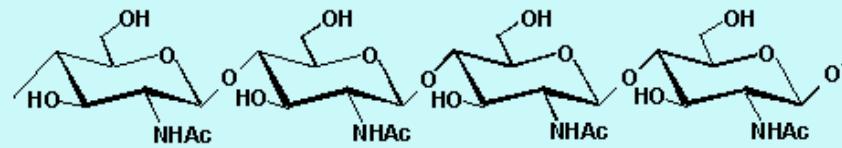
## What is Chitin/Chitosan?

*Chitosan* is a modified carbohydrate polymer derived from the *Chitin* component of the shells of crustacean, such as crab, shrimp and cuttlefish.



Decalcification in dilute aqueous *HCl* solution  
Deproteination in dilute aqueous *NaOH* solution  
Decolorization in 0.5% *KMnO<sub>4</sub>* aq. and *Oxalic acid* aq. or sunshine

Chitin



Deacetylation in hot concentrated *NaOH* solution (40-50%)

Chitosan

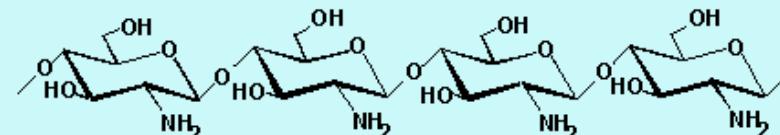
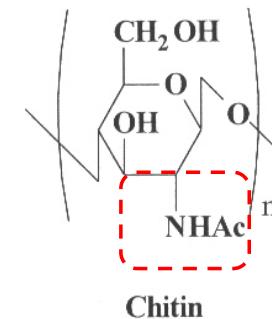


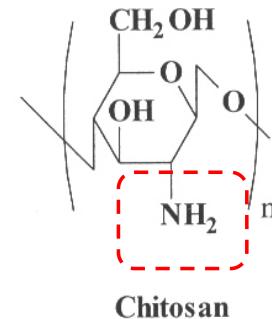
Fig. 2. Preparation of chitin and chitosan

幾丁質

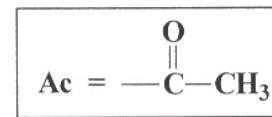


Chitin

幾丁聚糖

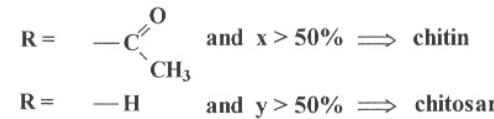
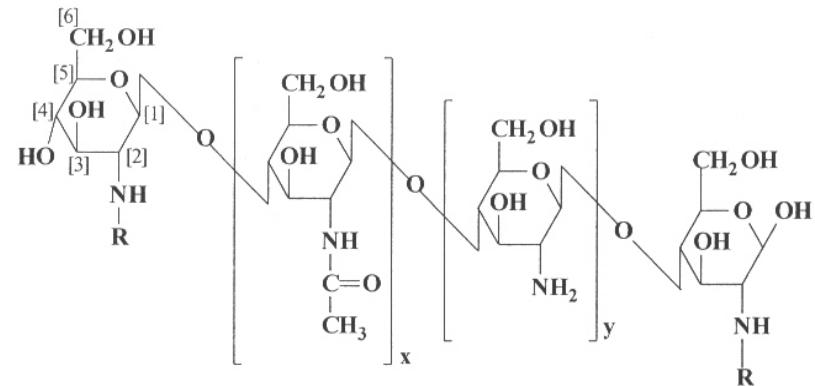


Chitosan



N-acetyl-D-glucosamine

Figure 1.1: Idealized representation of chitin and chitosan



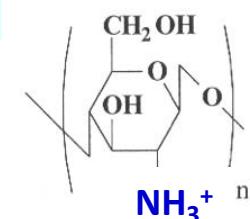
Deacetylation degree (DD)

Figure 1.2:

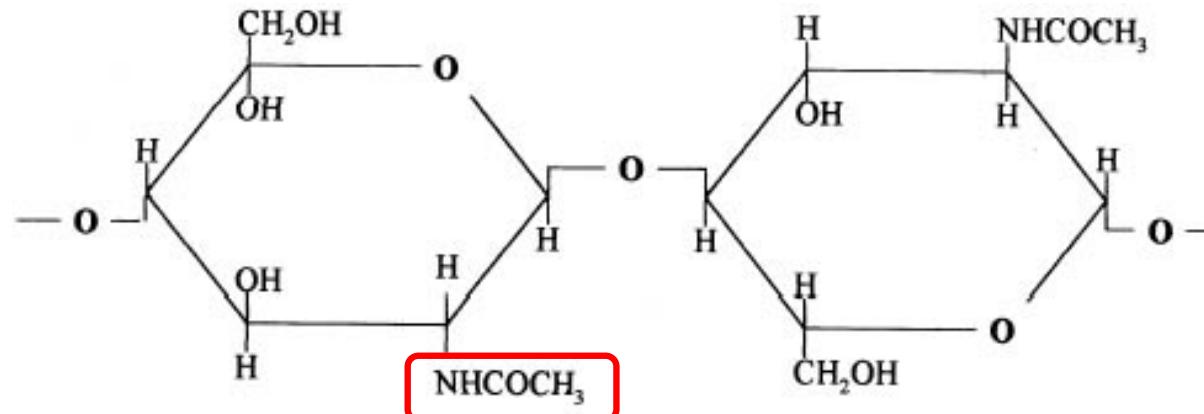
Chemical structural representation of chitin and chitosan depicting the co-polymer character of the biopolymers

# Chitosan

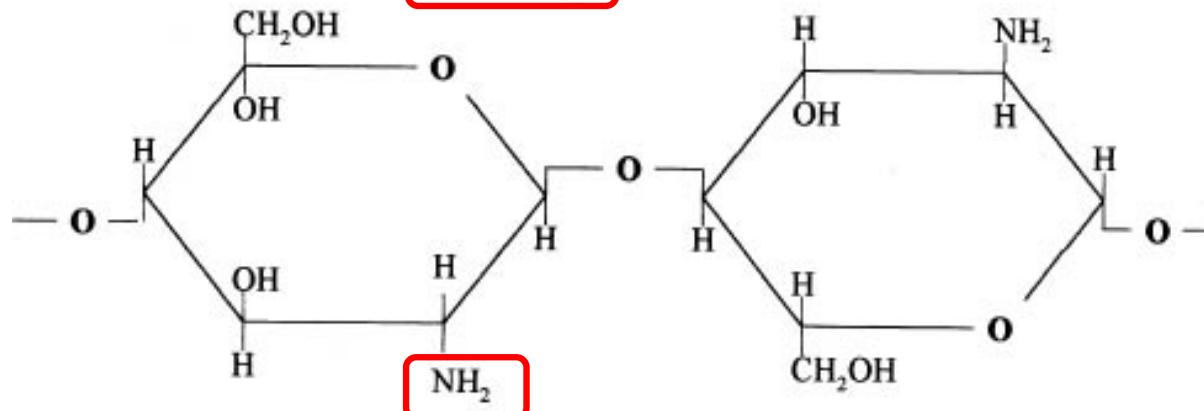
- A **polycationic copolymer** of N-acetyl-glucosamine and N-glucosamine
- Obtained by alkaline deacetylation of chitin (> 50%)
- Soluble in dilute acidic solution (pKa value of 6.3-7.0) as a result the **amino groups become protonated**.
- Can be metabolized by human enzymes such a **lysozyme**, and thus considered **biodegradable**.
- Due to the cationic nature of chitosan, combination with a **negative charged polymer** will result in an ionic bound network.



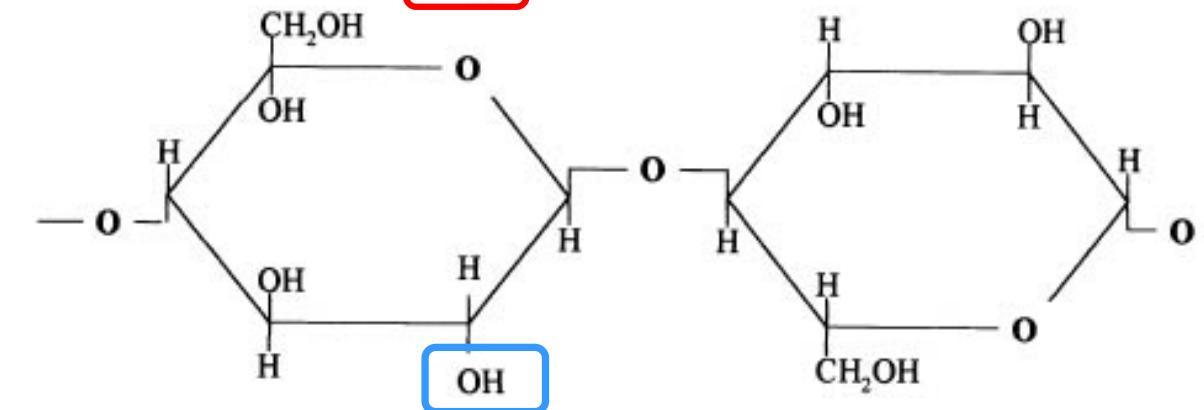
# Chitosan



Chitin



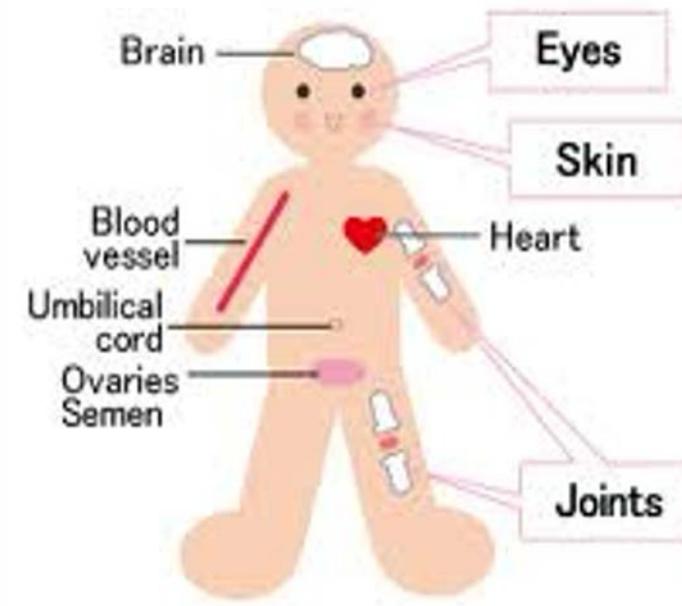
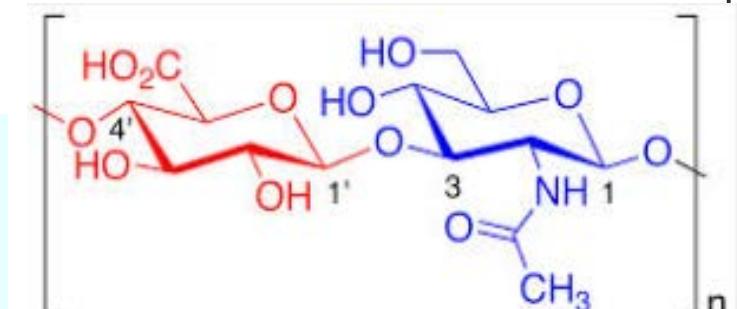
Chitosan



Cellulose

# Hyaluronic acid (Hyaluronan)

- Discovered by Meyer and Palmer in 1934.  
*(vitreous –Hyalos)*
- A **negatively charged** high molecular weight (HMW) polysaccharide (0.2-10million Dalton) composed of repeating disaccharide units of **glucuronic acid** and **N-acetyl glucosamine**.
- Functions as a core molecule for the binding of keratin sulfate and chondroitin sulfate in forming aggrecan in cartilage.
- The main source of lubrication for joints.
- Plays a role in cellular processes like cell proliferation, morphogenesis, inflammation, and wound repair.



# Hyaluronic acid



- HA can be cleaved by an enzyme called **hyaluronidase**, showing the cells in host posses the ability to clean the material while the neo-tissue is being formed.
- The viscosity, ability to **retain water**, hydrodynamic characteristics are critical for the maintenance of both **cartilage homeostasis and biomechanical stability**.
- Provide the binding sites to **cell surface receptor, CD44**, which presents on mesenchymal stem cell and chondrocytes, **help cell adhesion and regulate the cell functions**.
- Hyaluronic acid in collagen gels **helps chondrocytes migration and proliferation** that contributes the cell distribution in the scaffold and also up-regulates the expression of chondroitin sulfates.

# Hyaluronic acid

- Is a “device” not a drug, a visco-supplement.
- A device which may prolong and improve function and decrease pain.
- Attract water to improve articular cartilage and synovial fluids “shock absorbing” capability.

600–800 kDa



500-730 kDa



5 times

6,000 kDa

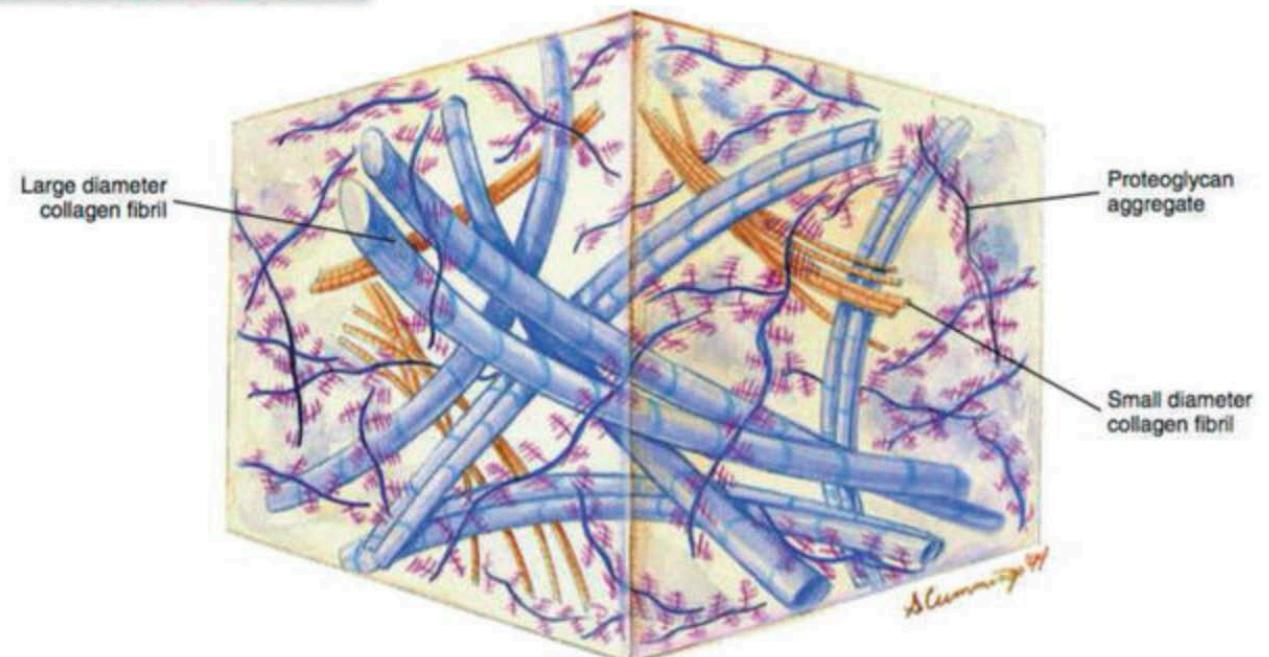
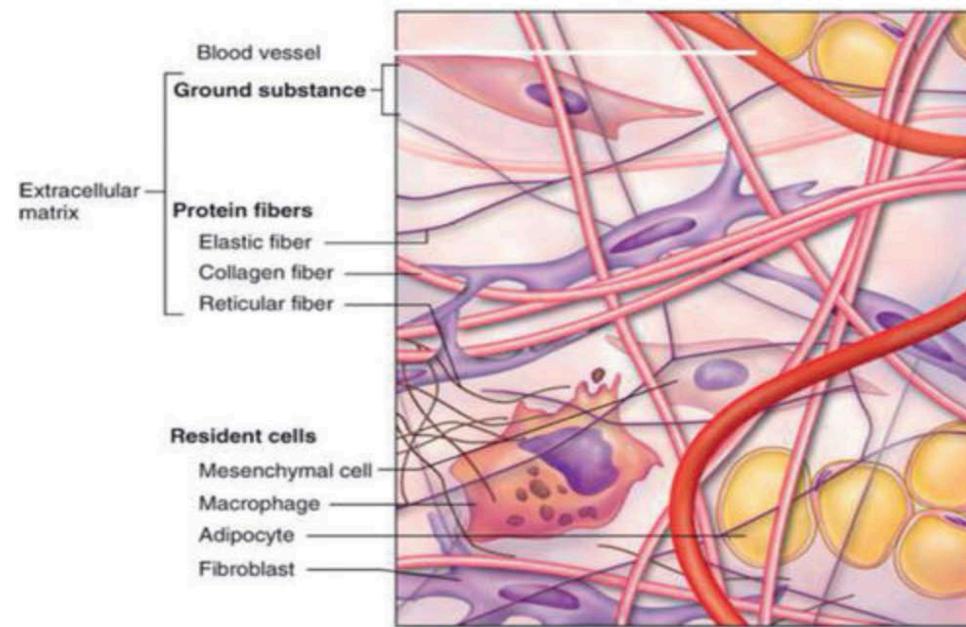


3 times

# Polysaccharides

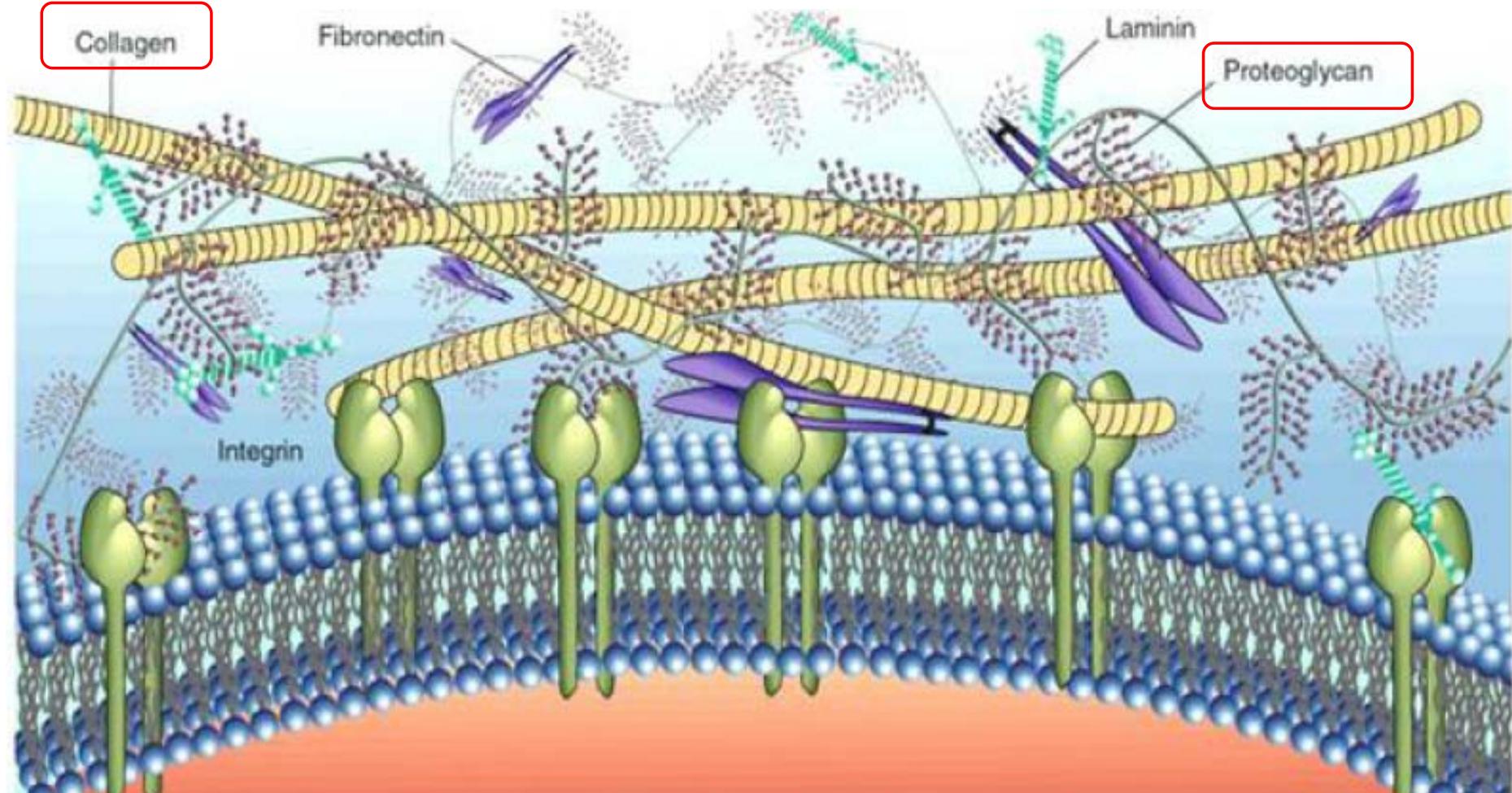
Origin	Polysaccharides	Occurrence/function	Monosaccharide unit
Plant	Starch 漲粉	Energy storage materials in higher plants	Homopolysaccharide, neutral, branched
	Cellulose 纖維素	Structure polysaccharide in cell wall, protection	Homopolysaccharide, neutral, linear
	Arabinogalactan	Secreted after trauma of plant to protect	Heteropolysaccharide, neutral, branched
Algal	Alginate	Main structure in cell wall in brown algae	Heteropolysaccharide, anionic, linear
	Agarose 瓣脂糖	Provide mechanical support at tidal area	Heteropolysaccharide, neural, linear
	Carrageenans 鹿角菜膠	Main structure in red algae	Heteropolysaccharide, anionic, linear
Animal	Chitin, chitosan	Exoskeleton	
	Hyaluronic acid	ECM protein	Heteropolysaccharide, anionic, linear
Microbe	Dextran 葡聚醣	Extracellular polysaccharide	Homopolysaccharide, neutral, branched
	Gellan Gum	Extracellular polysaccharide	Heteropolysaccharide, anionic, linear
	Pullulan	Extracellular polysaccharide	Homopolysaccharide, neutral, branched

# Extracellular Matrix (ECM)



# Extracellular Matrix (ECM)

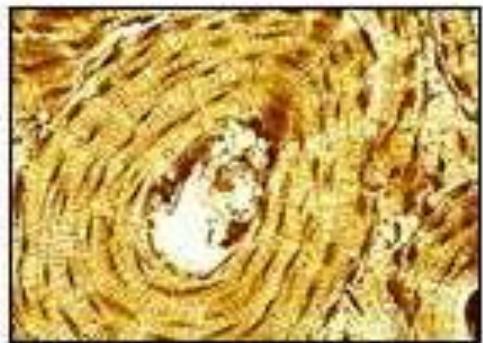
## Cell and ECM



# Extracellular Matrix (ECM)

- Most of the **cells** in multicellular organisms are **organized into cooperative assemblies** called **tissues**, which in turn are associated in various combinations to form larger functional units called **organs**.
- The cells in tissues are usually **in contact with a complex network** of secreted extracellular macromolecules referred to as the **extracellular matrix**.
- In vertebrates the major types of tissues  
*Nerve, Muscle, Blood, Lymphoid, Epithelial, and Connective tissues.*
- **Connective tissues** and **epithelial tissues** represent two extremes in which the, **structural roles** played by the matrix and by cell-cell adhesions are radically different.

# Extracellular Matrix (ECM)



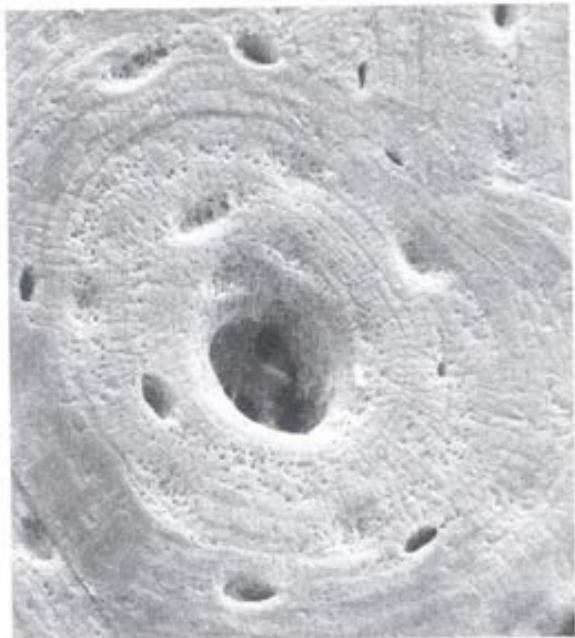
Osseous tissue



Hyaline cartilage

Cartilage cell

Fibroblast



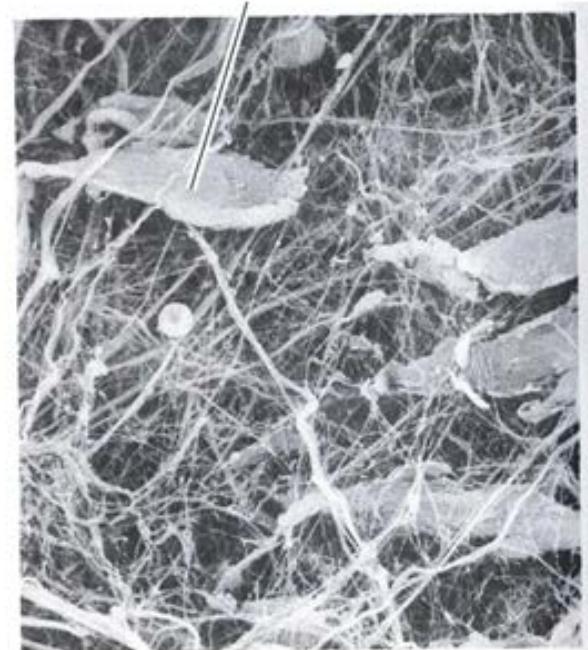
(a) Bone

20  $\mu\text{m}$



(b) Cartilage

20  $\mu\text{m}$



(c) Connective tissue

20  $\mu\text{m}$

# Extracellular Matrix (ECM)

Three classes molecular of ECM (animal cells)

## ➤ Structure protein

*Strength and flexibility*

- Collagen

- Elastin

## ➤ Protein-polysaccharide complex

*Provide matrix in which the structural molecules are embedded*

- Proteoglycans

## ➤ Adhesive glycoproteins

*Attach cells to the matrix*

- Fibronectins

- Laminins

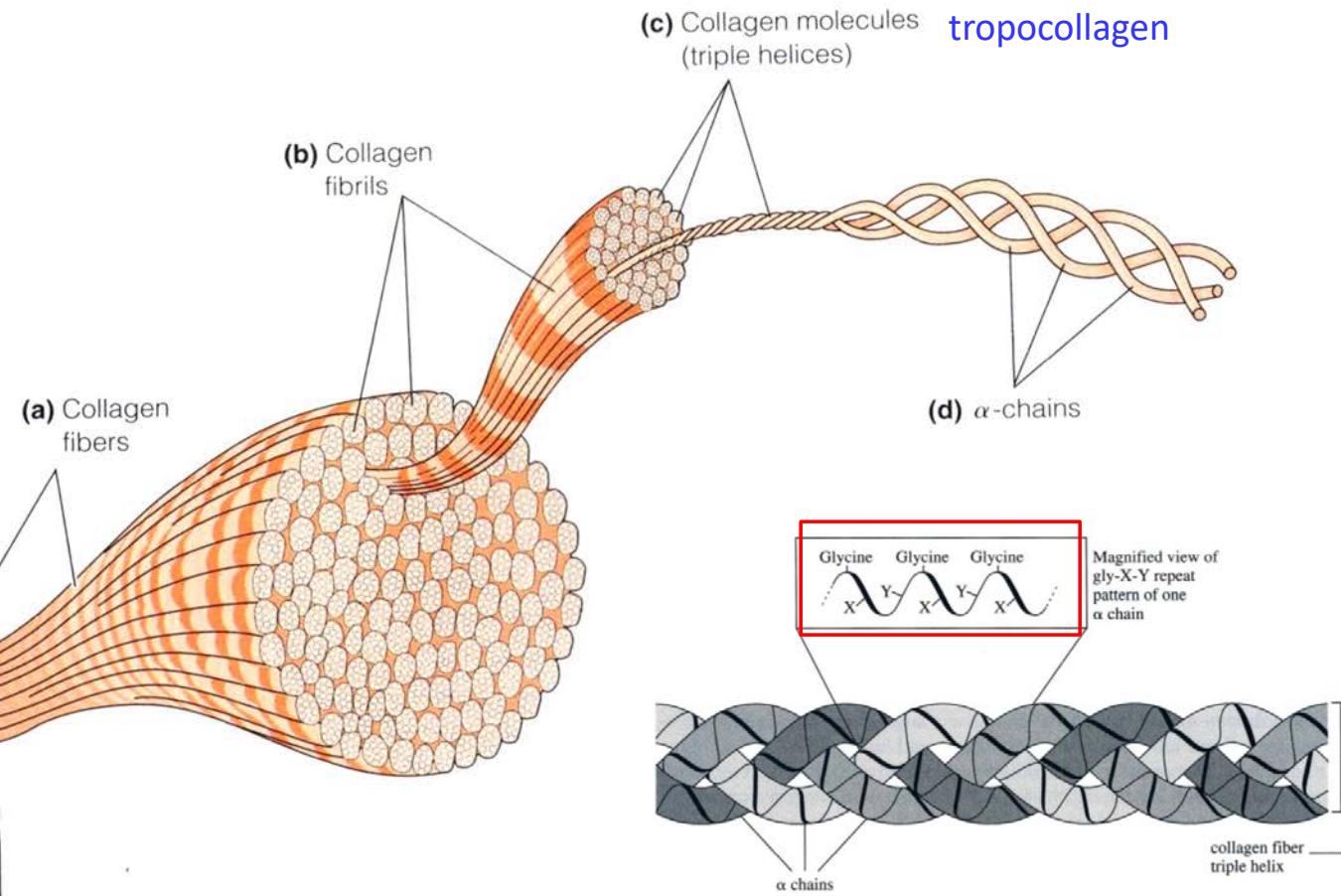
Table 11-1 Extracellular Structures of Eukaryotic Cells

Kind of Organism	Extracellular Structure	Structural Fiber	Components of Hydrated Matrix	Adhesive Molecules
Animals	Extracellular matrix (ECM)	Collagens and elastins	Proteoglycans	Fibronectins and laminins
Plants	Cell wall	Cellulose	Hemicelluloses and extensins	Pectins

# Collagen

膠原蛋白

- 20-30% of total body protein
- Secreted by several type of connective-tissue cells (fibroblasts)



**Figure 11-2 The Structure of Collagen.** (a) Collagen fibers as seen by SEM. (b) A collagen fiber contains many fibrils, each of which is a bundle of collagen molecules, also called tropocollagen. (c) Each collagen molecule is a triple helix consisting of (d) three entwined

$\alpha$  chains. The repeating bands visible on the fibers in the SEM in part a reflect the regular but offset way in which collagen molecules associate laterally to form fibrils; see Figure 11-3 for details of collagen assembly.

# Collagen

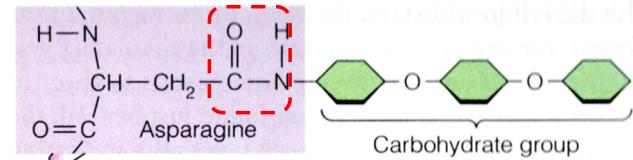
## ➤ Collagen molecular

- 270 nm in length
- 1.5 nm in diameter

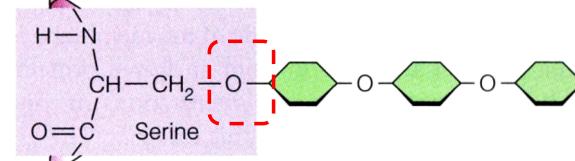
### Primary amino acid sequence of collagen

-Gly-Pro-Met-Gly-Pro-Ser-Gly-Pro-Arg-  
-Gly-Leu-Hyp-Gly-Pro-Hyp-Gly-Ala-Hyp-  
-Gly-Pro-Gln-Gly-Phe-Gln-Gly-Pro-Hyp-  
-Gly-Glu-Hyp-Gly-Glu-Hyp-Gly-Ala-Ser-  
-Gly-Pro-Met-Gly-Pro-Arg-Gly-Pro-Hyp-  
-Gly-Pro-Hyp-Gly-Lys-Asn-Gly-Asp-Asp-

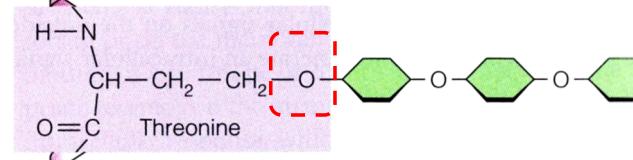
Gly-X-Y



(a) N-linked (to amino group of asparagine)

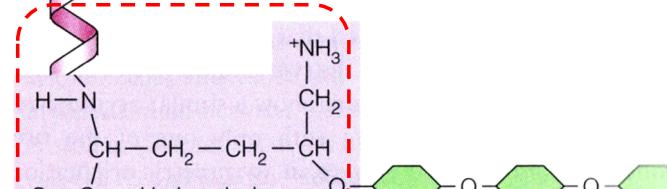


Serine



Threonine

(b) O-linked (to hydroxyl group of serine or threonine)



Hydroxylysine

(c) O-linked (to hydroxyl group of hydroxylysine or hydroxyproline)

## ➤ Collage fiber

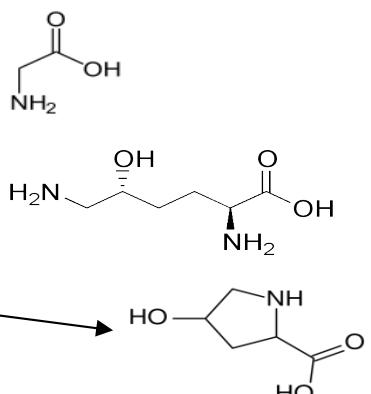
*Take a load of about 9 kg to tear a collagen fiber (1 mm) in diameter*

- Enormous physical strength
- Responsible for the mechanical strength of protective and supporting tissues such as skin, bone, tendon and cartilage.

## ➤ Collagen

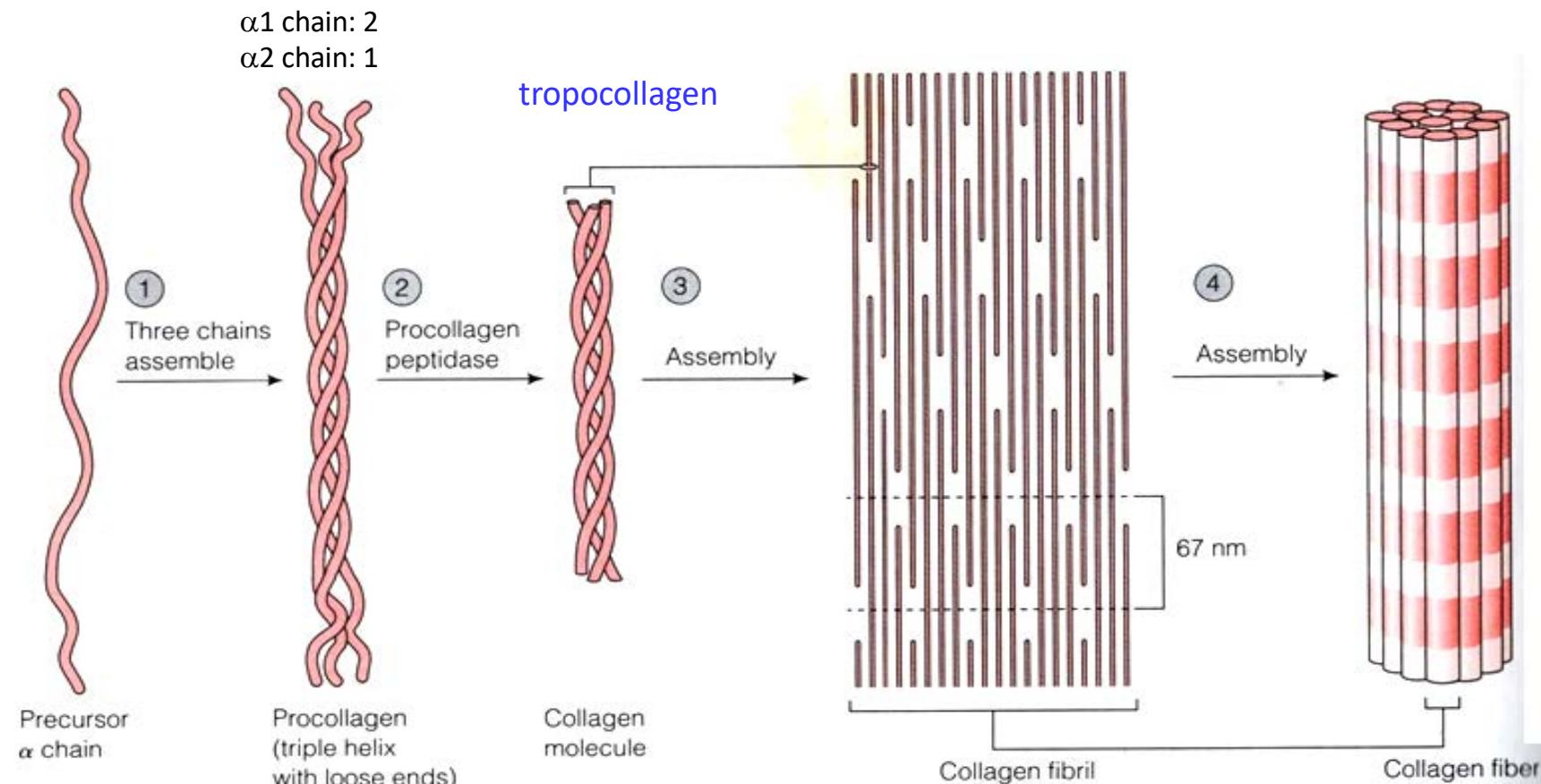
Rigid triple helix of three intertwined polypeptide chain

- Glycin
- Hydroxylysine →
- Hydroxyproline



# Collagen

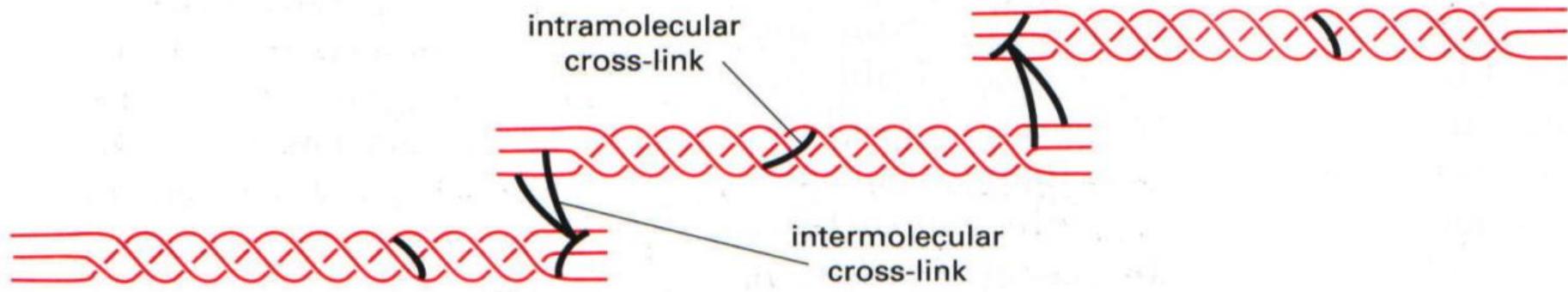
## Collagen precursor : Procollagen



**Figure 11-3 Collagen Assembly.** ① Collagen precursor chains are assembled in the ER lumen to form triple-helical procollagen molecules. ② After secretion from the cell, procollagen is converted to collagen in a peptide-cleaving reaction catalyzed by the enzyme procollagen peptidase. ③ The molecules of collagen molecules, also

called tropocollagen, then bind to each other and self-assemble into collagen fibrils. ④ The fibrils assemble laterally into collagen fibers. In striated collagen, the 67-nm repeat distance is created by packing together rows of collagen molecules in which each row is displaced by one-fourth the length of a single molecule.

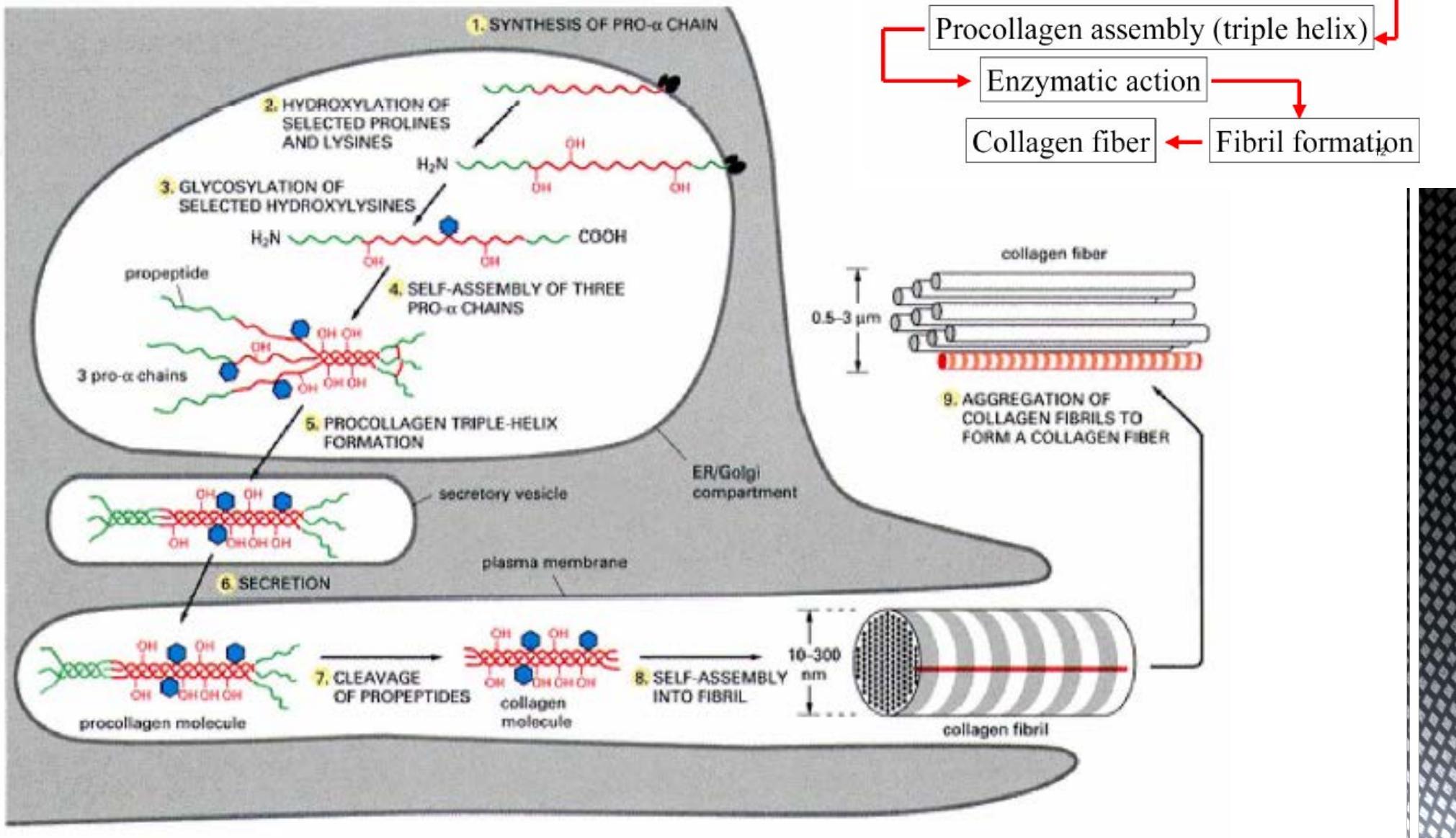
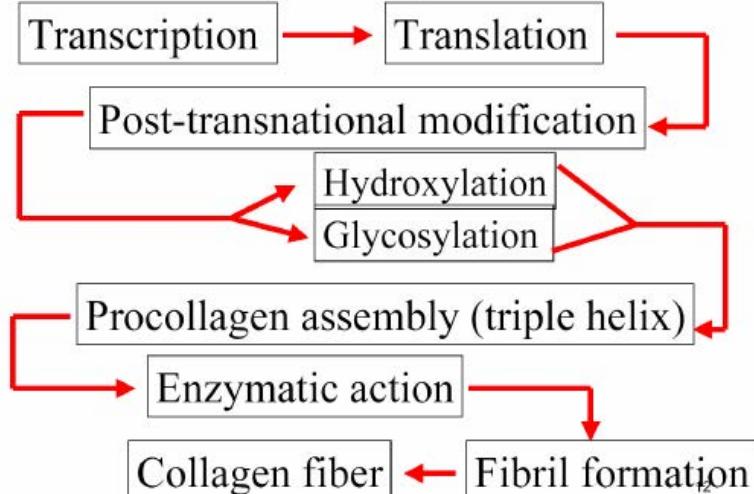
# Collagen



- The covalent intramolecular and intermolecular cross-links formed between modified **lysine side chains within a collagen fibril**.
- The crosslinks are formed in several steps:
  1. Lysine and hydroxylysine residues are de-aminated by the extracellular enzyme lysyl oxidase to yield highly reactive aldehyde groups.
  2. The **aldehydes** then react spontaneously to form covalent bonds with each other or with other **lysine or hydroxylysine residues**.
- Most of the cross-links form between the short nonhelical segments at each end of the collagen molecules.

# Collagen

## Collagen Biosynthesis



# Collagen

## Collagen type

**Table 19–4** Some Types of Collagen and Their Properties

	Type	Molecular Formula	Polymerized Form	Tissue Distribution
<b>FIBRIL-FORMING (FIBRILLAR)</b>	I	$[\alpha 1(I)]_2\alpha 2(I)$	fibril	bone, skin, tendon, ligaments, cornea, internal organs (accounts for 90% of body collagen)
	II	$[\alpha 1(II)]_3$	fibril	cartilage, intervertebral disc, notochord, vitreous humor of the eye
	III	$[\alpha 1(III)]_3$	fibril	skin, blood vessels, internal organs
	V	$[\alpha 1(V)]_2\alpha 2(V)$	fibril (with type I)	as for type I
	XI	$\alpha 1(XI)\alpha 2(XI)\alpha 3(XI)$	fibril (with type II)	as for type II
<b>FIBRIL-ASSOCIATED</b>	IX	$\alpha 1(IX)\alpha 2(IX)\alpha 3(IX)$ with type II fibrils	lateral association	cartilage
	XII	$[\alpha 1(XII)]_3$ with some type I fibrils	lateral association	tendon, ligaments, some other tissues
<b>NETWORK-FORMING</b>	IV	$[\alpha 1(IV)]_2\alpha 2(IV)$	sheetlike network	basal laminae
	VII	$[\alpha 1(VII)]_3$	anchoring fibrils	beneath stratified squamous epithelia

Note that types I, IV, V, and XI are each composed of 2 or 3 types of  $\alpha$  chain, whereas types II, III, VII, and XII are composed of only 1 type of  $\alpha$  chain each. Only 9 types of collagen are shown, but about 15 types of collagen and about 25 types of  $\alpha$  chain have been defined so far.

# Collagen

## Gene mutation

### ➤ Type I collagen mutations

cause **osteogenesis imperfecta**, characterized by ***weak bones*** that easily *fracture*.



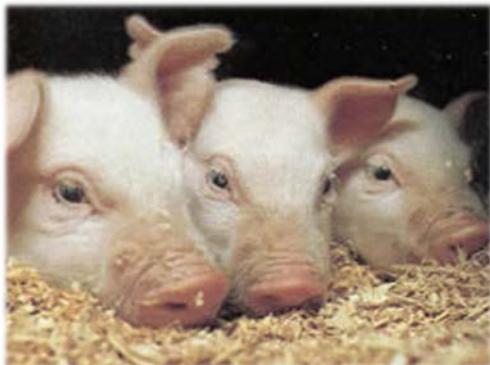
### ➤ Type II collagen mutations

cause **chondrodysplasias**, characterized by ***abnormal cartilage***, which leads to *bone and joint deformities*

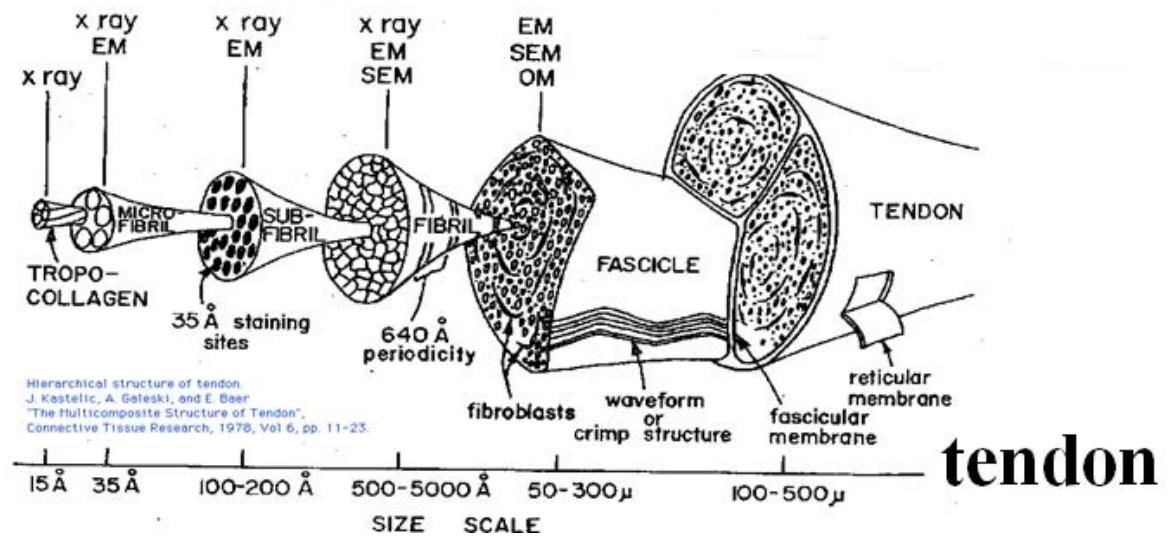


# Collagen

## Type I Collagen Isolation



Skin of porcine from a slaughterhouse



Minced  
Defatted

Swollen

Digested

Precipitated

## **Skin, tendon**

peeled off muscle, fat and all remains of surrounding connective tissue



## **Mince Defatted**

with acetone for 30 min at R.T., twice

## **Cleaned**

with deionized water, twice

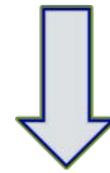


## **Swollen**

Soaked in 10% NaCl  
at 4°C for 24h

## **Swollen**

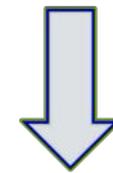
Soaked in citrate buffer solution (pH=4.5) for 24h



## **Digested**

with **pepsin** in 0.5M (pH=2) HCl  
for 24h at 4°C

The weight ratio (Skin/ tendon):pepsin/ HCl  
= 50:1:250



## **Precipitated**

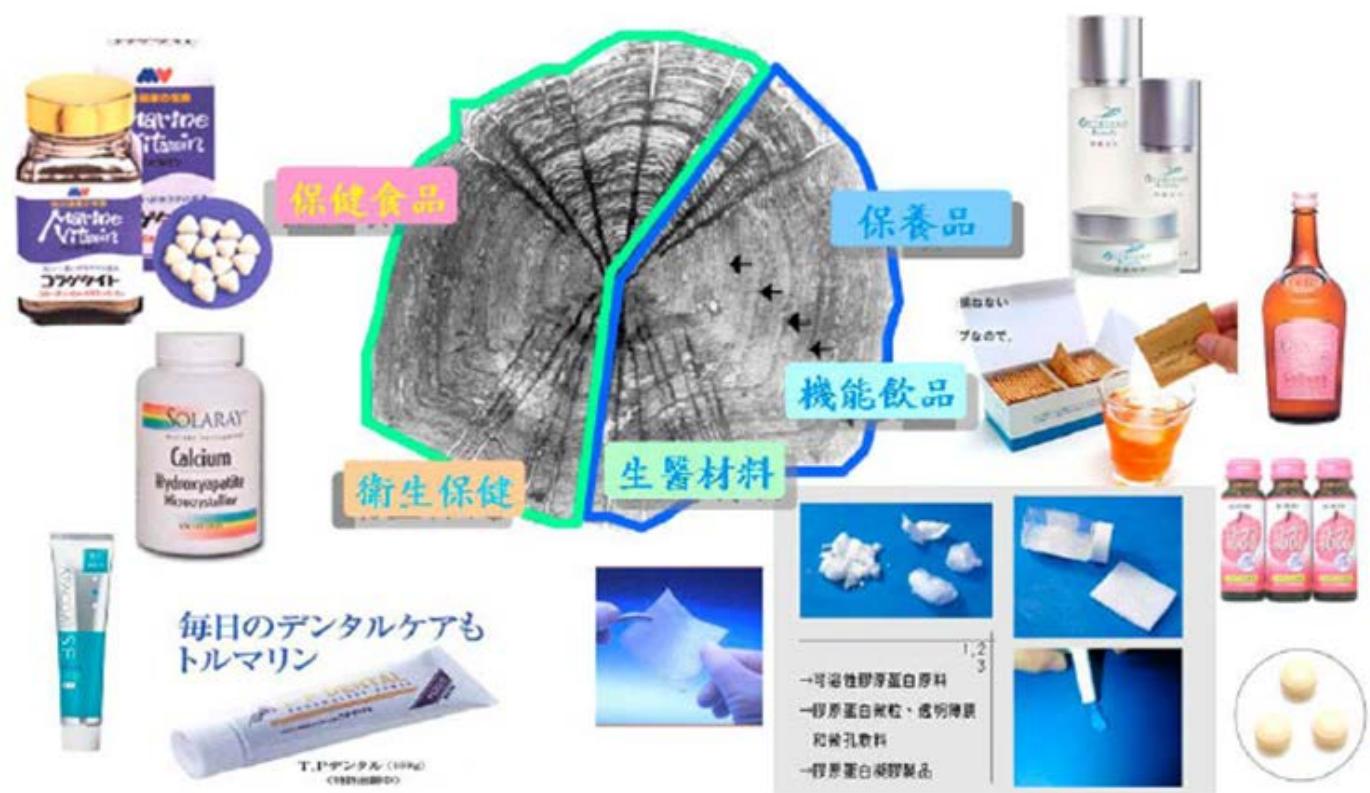
with 5% NaCl solution

# Collagen

# Fish scale

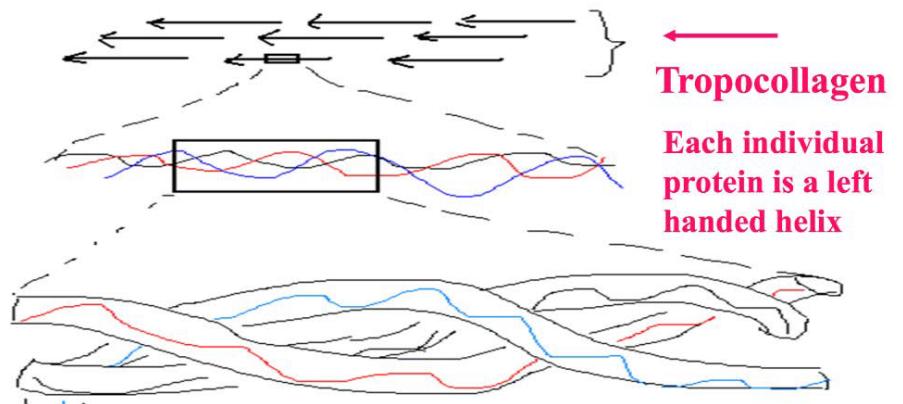


- Hydroxyapatite (50%)
  - Collagen (45%)



# Gelatin

明膠

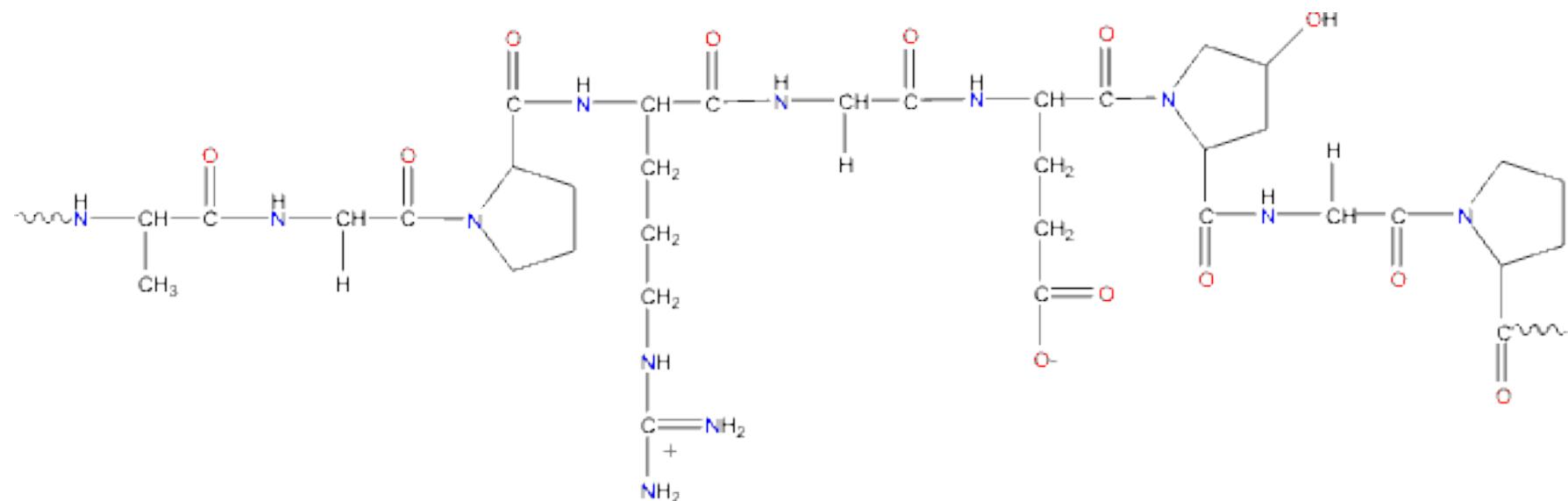


- Obtained by controlled hydrolysis of the fibrous insoluble collagen.
- The **triple-helical structure of tropocollagen is preserved in gelatin**, where it can immobilize water to form gels.
- It has a high content of **glycine, proline, and hydroxyproline**  
*(Gly-A-B)-(Gly-Pro-Hydro)-*
- Biocompatible and nontoxic to tissues
- It has been used in many application in different manners  
*Arg-Gly-Asp (RGD)*

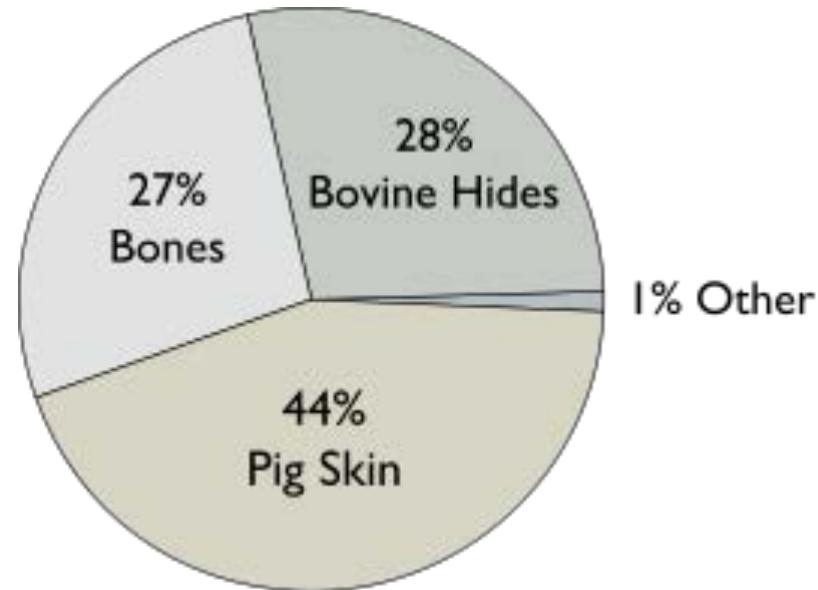
# Gelatin

Gly-X-Y

Ala-**Gly**-Pro-Arg-**Gly**-Glu-4Hyp-**Gly**-Pro-



# Gelatin



- Natural
- Inexpensive
- Low immunogenic
- Biocompatible
- Biodegradable
- Pharmaceutical application
- Provide functional group for ligand conjugate  
(COOH, NH<sub>2</sub>)

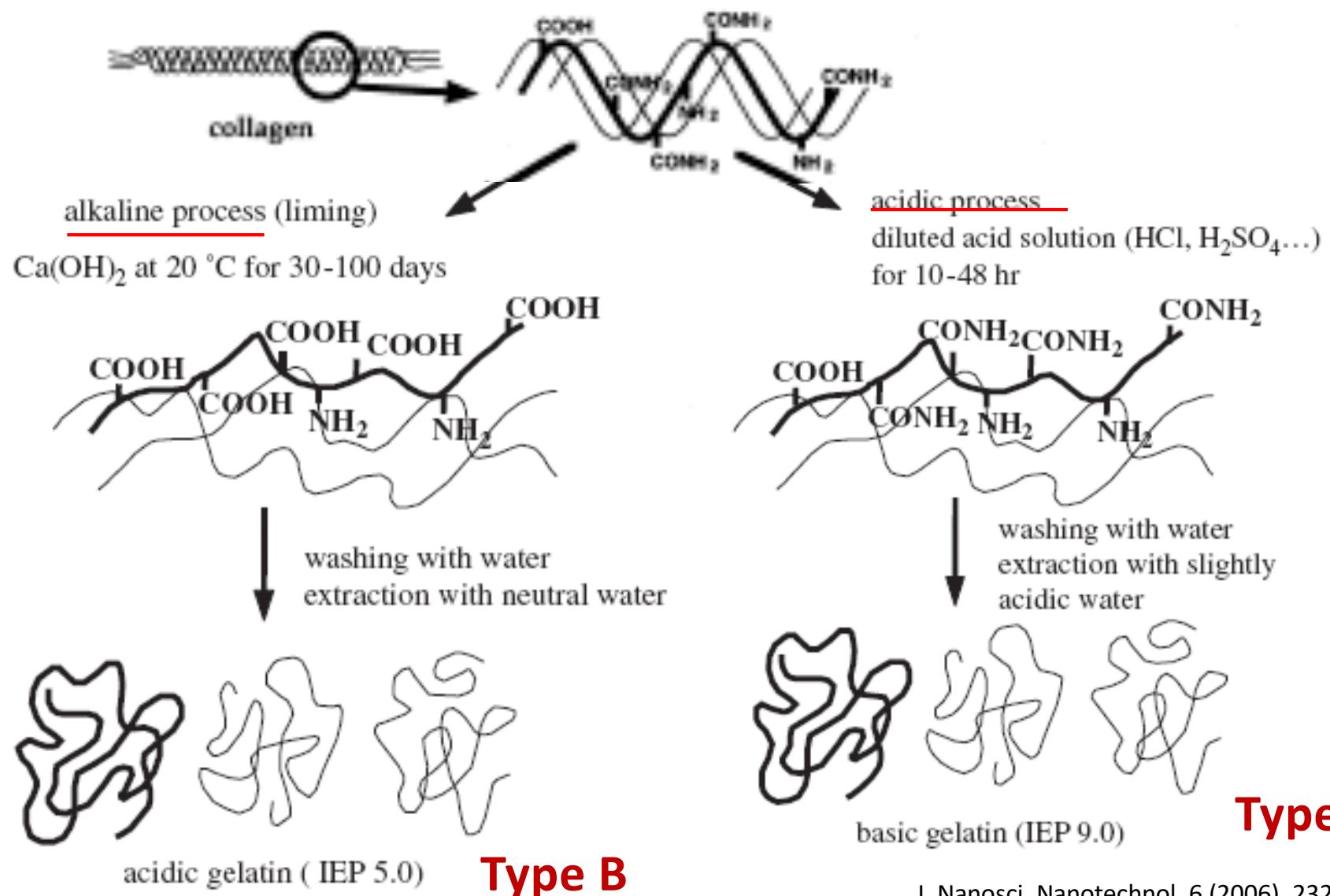
*Collagen 1 g: 35 US\$*

*Gelatin 100 g: 31 US\$*



# Gelatin

## Process for prepared gelatin



# Gelatin

## Gelatin composition

- Type A gelatin has 78-80 millimoles of free carboxyl groups per 100 g of protein and a pI of 7.0-9.0
- Type B has 100-115 millimoles of free carboxyl groups per 100 g of protein and a pI of 4.7-5.2

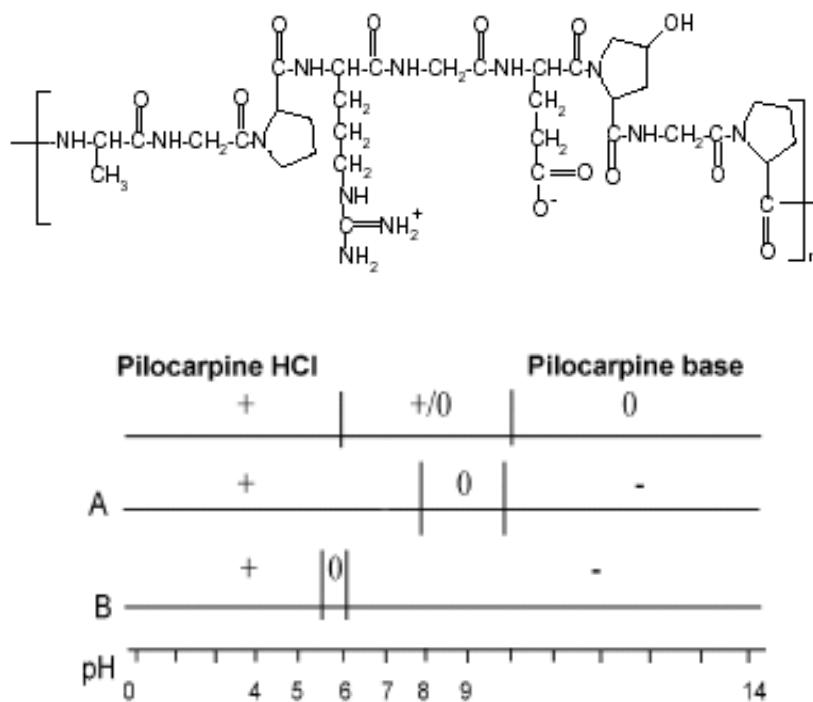


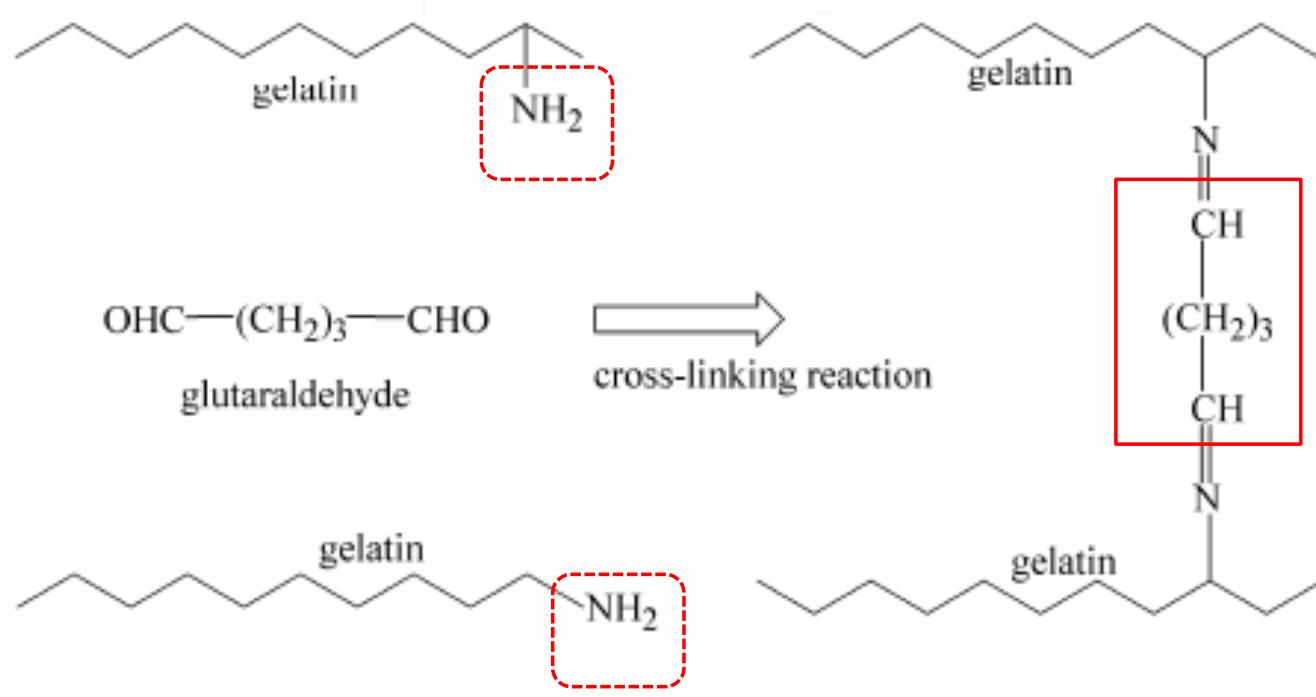
Fig. 1. Electrical charge of pilocarpine HCl and gelatin type A and B in function of the pH value.

GELATIN	
AMINO ACID COMPOSITION (Approximate): <sup>2</sup>	
Amino Acid	Content (%)
Alanine	8.700 - 9.600
Arginine	8.600 - 9.300
Aspartic Acid	5.500 - 6.800
Cystine	0.100 - 0.200
Glutamic Acid	10.200 - 11.700
Glycine	26.000 - 27.000
Histidine	0.600 - 1.000
Hydroxylysine	0.760 - 1.500
Hydroxyproline	12.600 - 14.400
Isoleucine	1.400 - 1.700
Leucine	3.200 - 3.600
Lysine	4.100 - 5.900
Methionine	0.600 - 1.000
Phenylalanine	2.200 - 2.600
Proline	14.800 - 17.600
Serine	3.200 - 3.800
Threonine	1.900 - 2.200
Tryptophan	0.000 - 0.003
Tyrosine	0.490 - 1.100
Valine	2.500 - 2.700

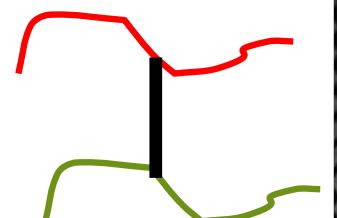
-COOH : 18.5%

# Gelatin

## Cross-linking

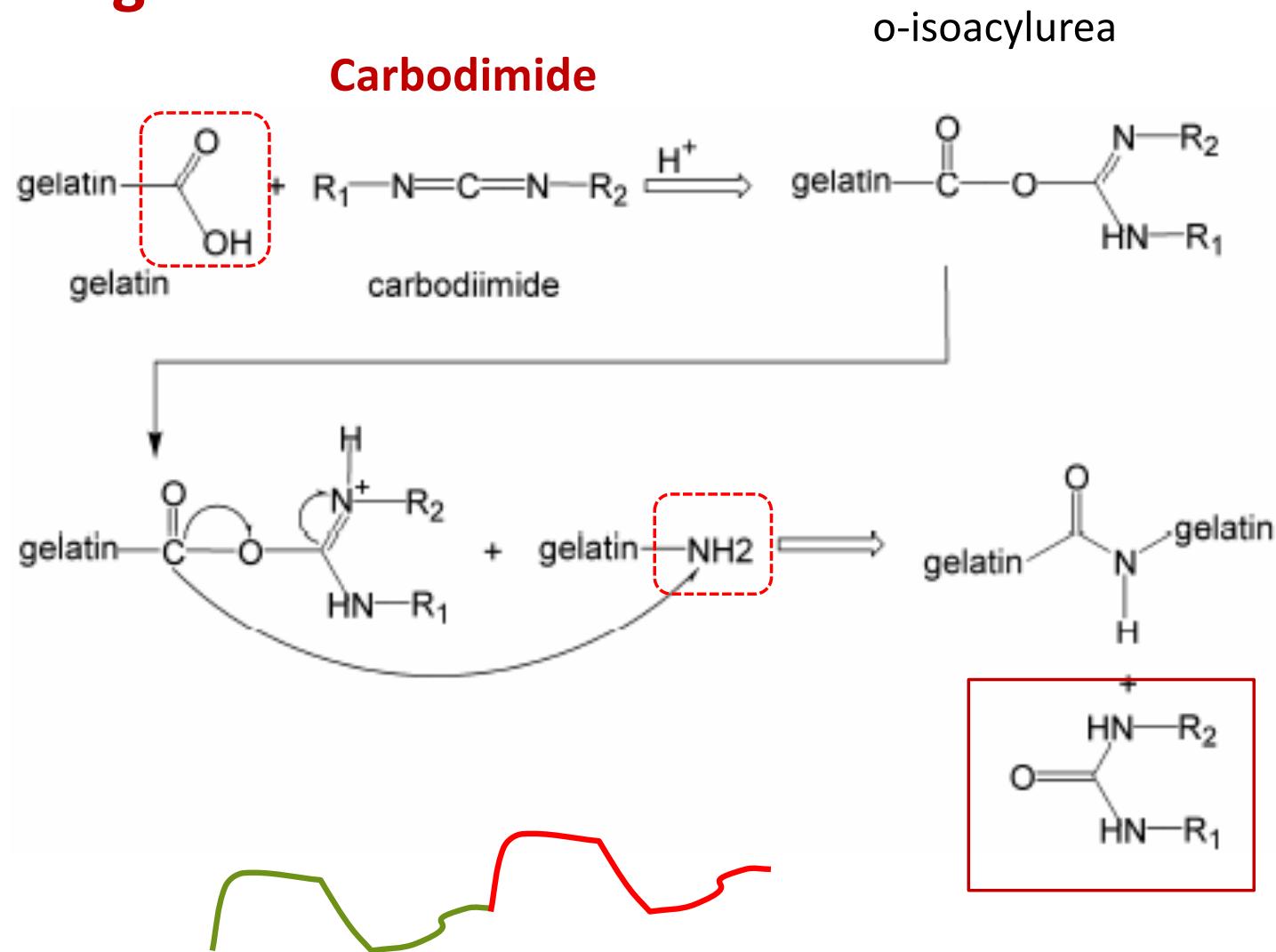


Glutaraldehyde



# Gelatin

## Cross-linking



# Collagen vs. Gelatin

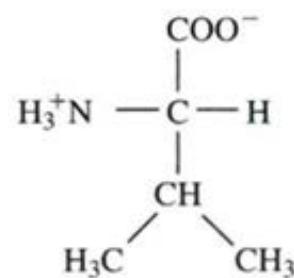
	Collagen (medical grade)	Collagen -like (cosmetic grade)	gelatin (food grade)
級別	生醫材料級原料 (膠原蛋白)	化妝品級原料 (類膠原蛋白)	食品級原料 (明 膠)
分子構造	1、完整的分子結構 2、具三股螺旋體構造 3、可交聯聚合成膠原纖維 4、具天然生物體之生物活性及功能	1、大部份具完整分子結構 2、部份三股螺旋體展開 3、無法交聯聚合成膠原纖維 4、天然生物體之生物活性較差尚具部分生物功能	1、分子結構呈現不規則 2、缺乏三股螺旋體結構 3、呈現非膠原蛋白生物反應 4、缺乏膠原蛋白的生物功能
應用範圍	生物醫學材料	化妝品原料 外敷用 醫學材料	食品原料 部分用於化妝品原料
國際價格	新台幣約 4,000 萬元 /kg	新台幣約 50~60 萬元 /kg	新台幣約 1,200~1,800 元 /kg

# Elastin

- Elastin forms fibers that allow large elastic deformation at low stresses and that are responsible for the resiliency and extensibility of the ECM.
- Elastin fiber : elastin + auxiliary protein/lysyl oxidase

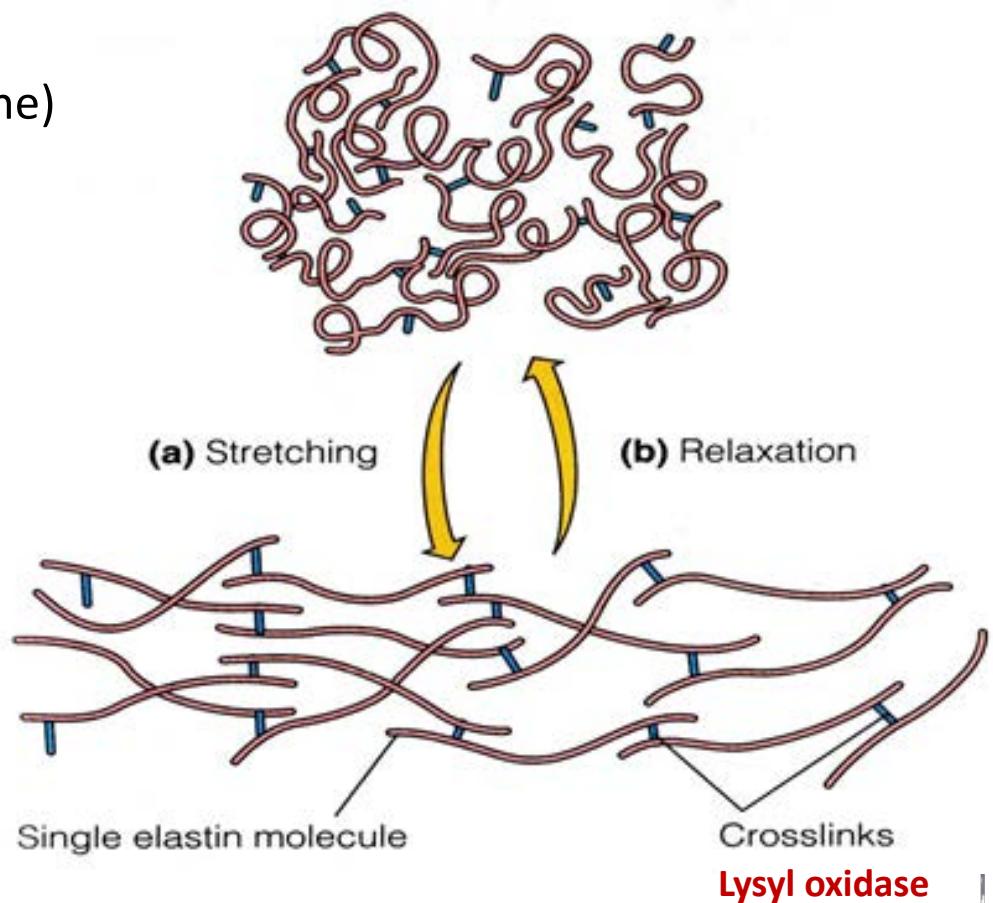
~ 85% hydrophobic amino acid (~ 15 % Valine)

- proline, glycine



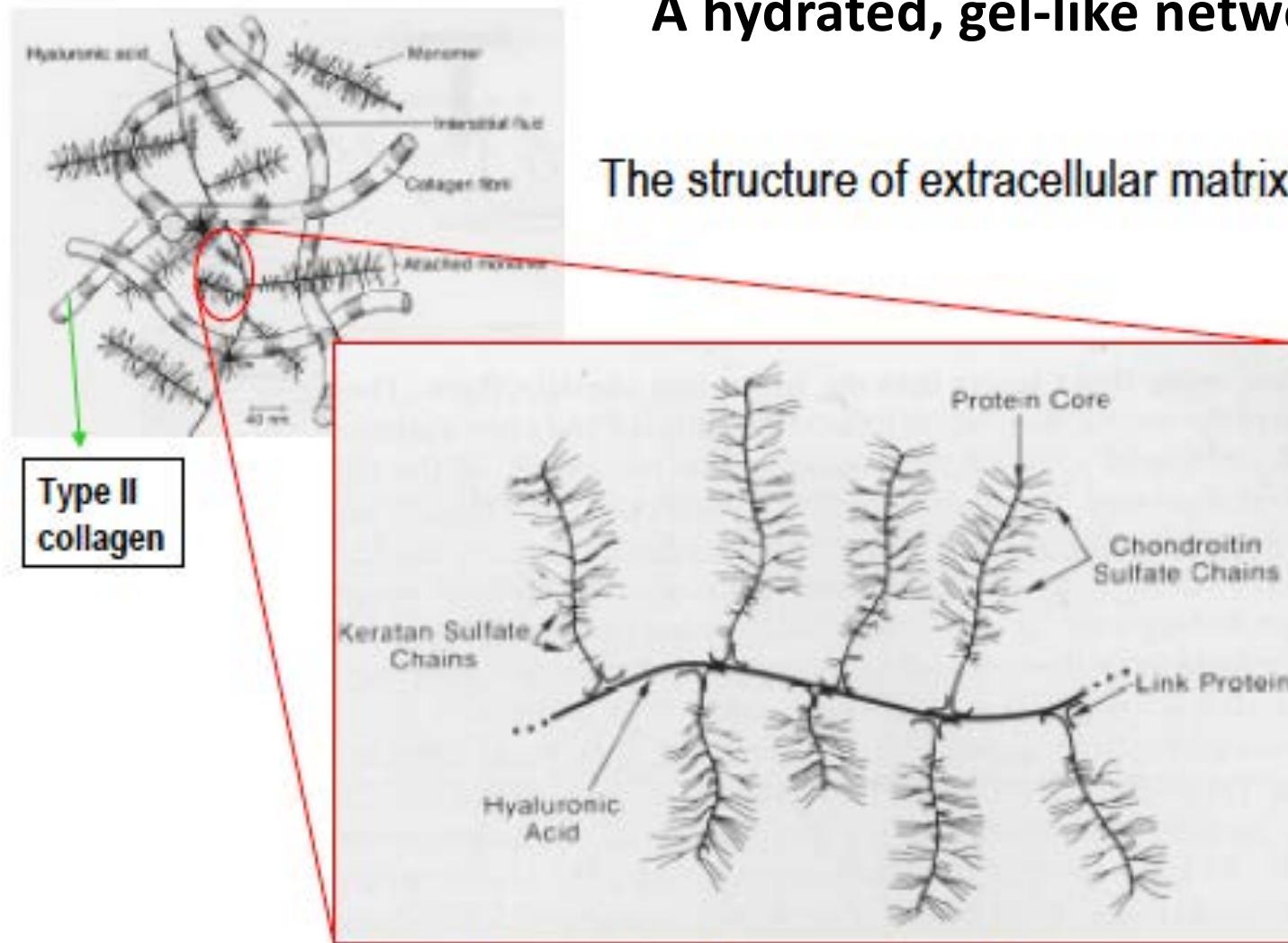
Elastin is not like collagen to be used in tissue engineering because:

- It has strong tendency to be **calcified** upon implantation.
- The purification of elastin is not easy



# Collagen and Elastin fibers are embedded in a matrix of proteoglycans

A hydrated, gel-like network



- Proteoglycans  
蛋白聚糖
- Glycoprotein  
糖蛋白

The proteoglycan aggregate

# Proteoglycans

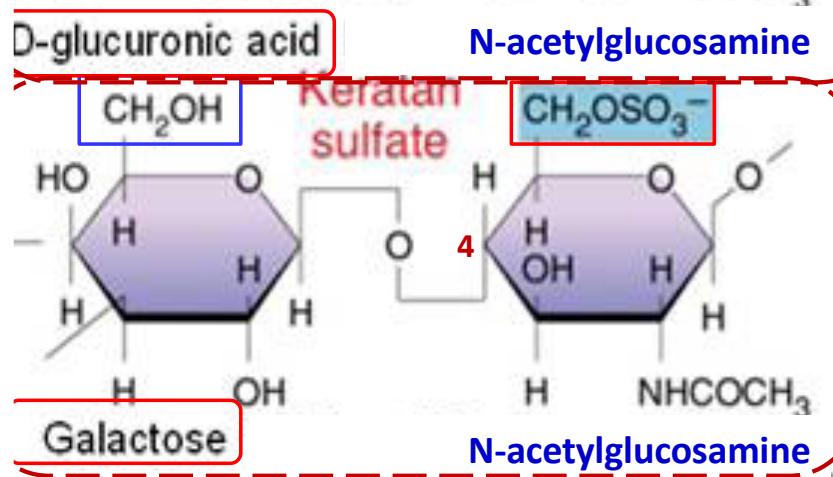
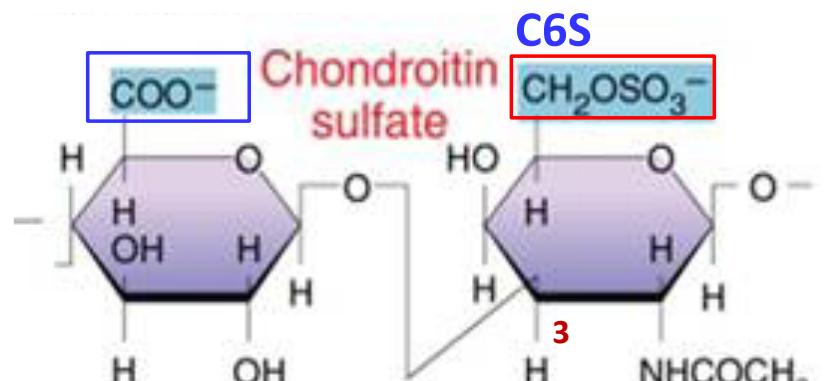
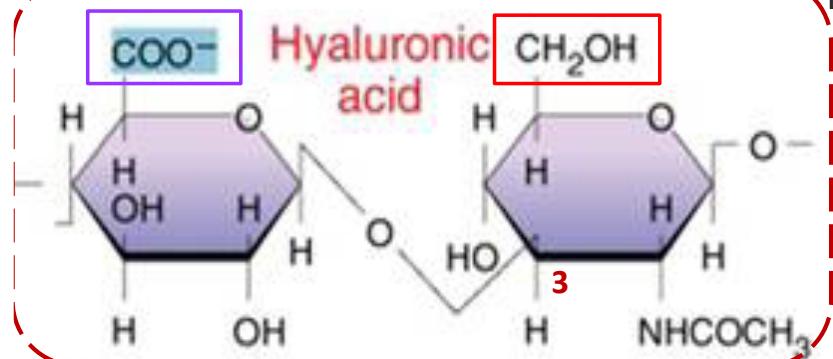
## ➤ Proteoglycans 蛋白聚糖

- Mainly carbohydrate(glycan) with small amounts of attached protein.
- A larger number of **glycoaminoglycans (GAG)** are attached to a single protein molecule called glycoprotein.
- Molecular weight : 0.25~3 million
- Carbohydrate content: 95%
- Are linked directly to collagen fiber

- **Glycoaminoglycans (GAG)** 葡萄糖胺聚糖

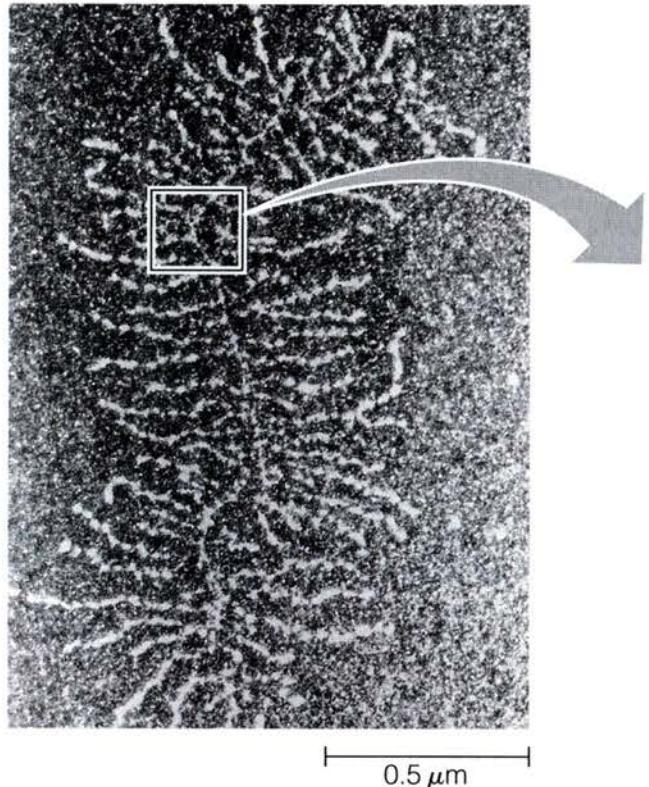
- Repeating disaccharide units
- Long polysaccharide chains, consisting of **two monosaccharides** or **monosaccharide derivatives** in strictly alternating order

## Glycoaminoglycans (GAG)

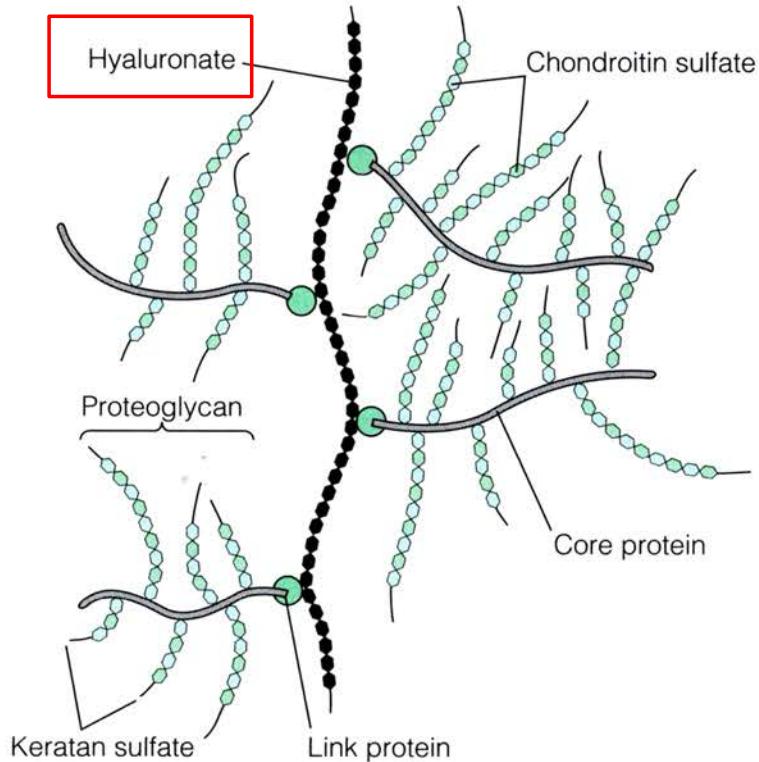


# Proteoglycans

## In cartilage



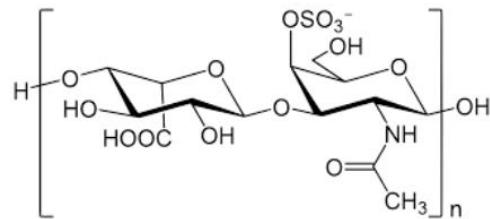
Aggrecan (cartilage) : CS + KS



**Figure 11-6 Proteoglycan Structure in Cartilage.** In cartilage, many proteoglycans such as the one shown in Figure 11-5 associate with a hyaluronate backbone to form a complex that is readily visible with an electron microscope. (**Left**) A hyaluronate-proteoglycan complex isolated from bovine cartilage (TEM). (**Right**) A diagram of a small portion of the

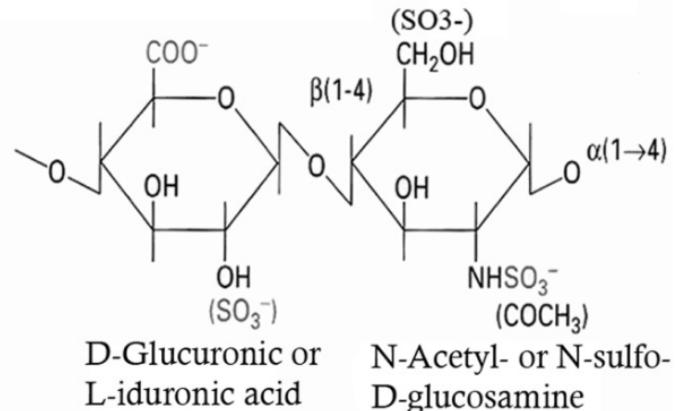
structure showing core proteins of proteoglycans attached by means of link proteins to a long hyaluronate molecule. Short keratan sulfate and chondroitin sulfate chains are linked covalently along the length of the core proteins, as in Figure 11-5b. Proteoglycans have a carbohydrate content of about 95%.

# Proteoglycans



Dermatan sulfate

## Heparin/heparan sulfate (n=15-30)

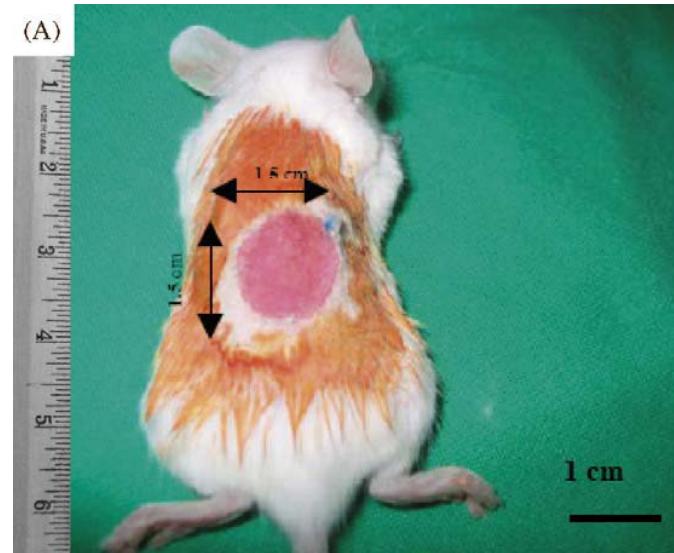


## Variant GAG & tissue distribution

	GAG	Sulfate	Tissue distribution
透明質酸	hyaluronic acid	0	<input type="checkbox"/> Connective tissue, <b>skin</b> , <b>cartilage</b> , <b>vitreous body</b> , synovia
硫酸軟骨素	chondroitin sulfate	0.2-2.3	<input type="checkbox"/> <b>Cartilage</b> , <b>cornea</b> , bone, <b>skin</b> , aorta vessel
硫酸皮膚素	dermatan sulfate	1.0-2.0	<input type="checkbox"/> <b>Skin</b> , blood vessel, heart valve
硫酸乙醯肝素	hetaran sulfate	0.2-3.0	<input type="checkbox"/> Lung, aorta, cell membrane
肝素	heparin	2.0-3.0	<input type="checkbox"/> Lung, liver, <b>skin</b> , mast cell
硫酸角質素	keratin sulfate	0.9-1.8	<input type="checkbox"/> <b>Cartilage</b> , <b>cornea</b> , intervertebral disk

# Gelatin-C6S-HA membrane

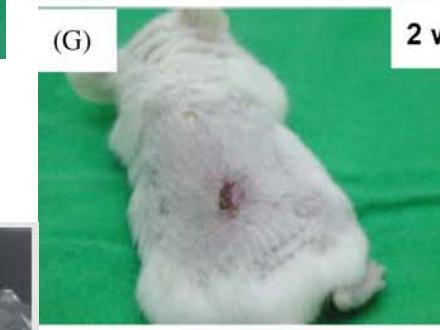
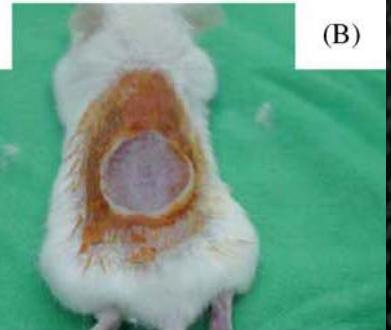
keratinocytes and dermal fibroblasts (K&FB) cells



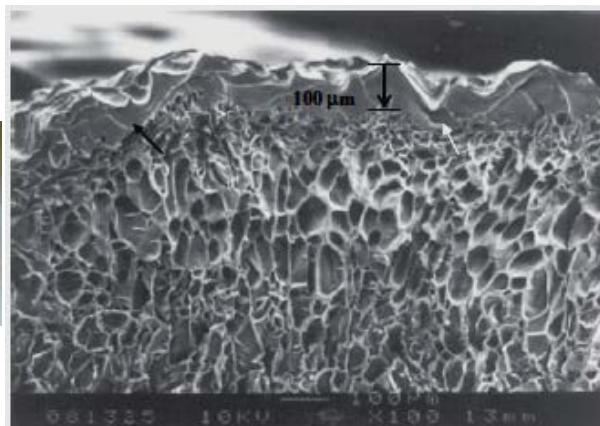
**K& F cells/Scaffold**



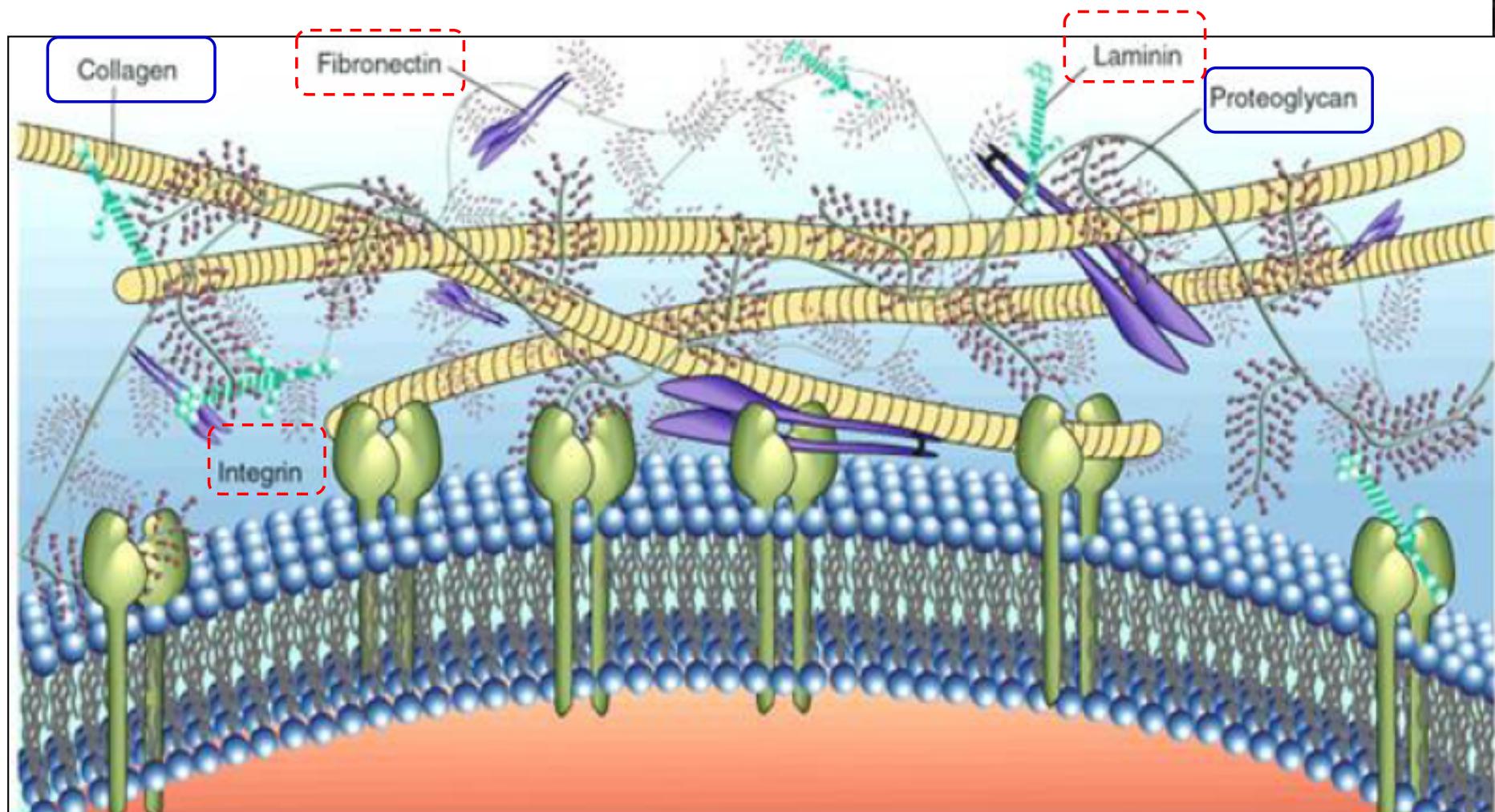
**Scaffold only**



Gelatin-C6S-HA membrane



# Cell and ECM



# Glycoproteins

## Fibronectin

- Proteoglycans and adhesive glycoprotein anchor cells to the extracellular matrix. (*5% carbohydrate*)
- Direct links between the ECM and the plasma membrane by AG that bind proteoglycans and collagen molecules to each other and to receptors on the membrane surface

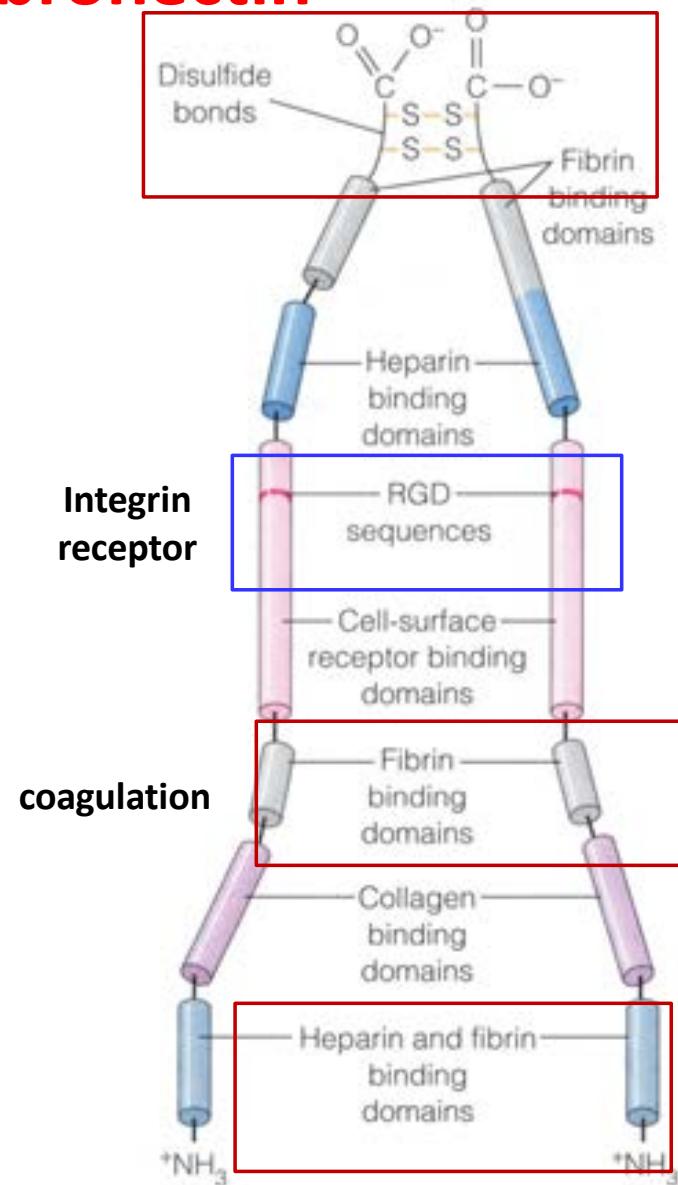
Fibronectins, laminins



Binding to the receptor,  
a transmembrane protein - **integrins**

# Glycoproteins

## Fibronectin



- Fibronectins bind cells to the matrix and guide cellular movement
- Two very large peptide subunits that are linked near their carboxyl ends by a pair of **disulfide bonds**

ECM : Collagen I, II, IV

Heparin

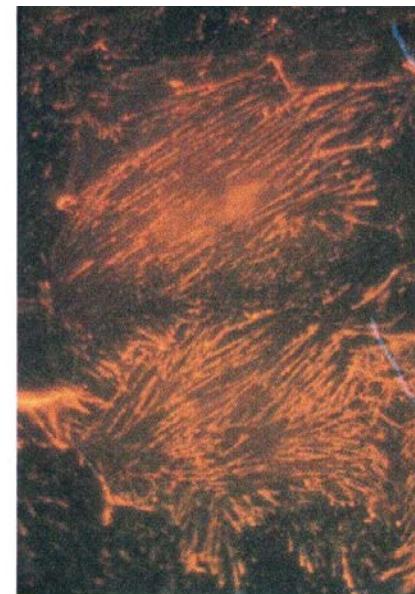
Fibrin

Cell surface receptor:

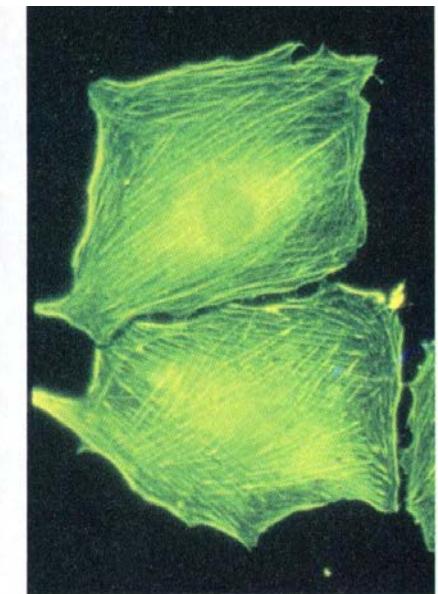
RGD (arginine- glycine- aspartate)

# Glycoproteins

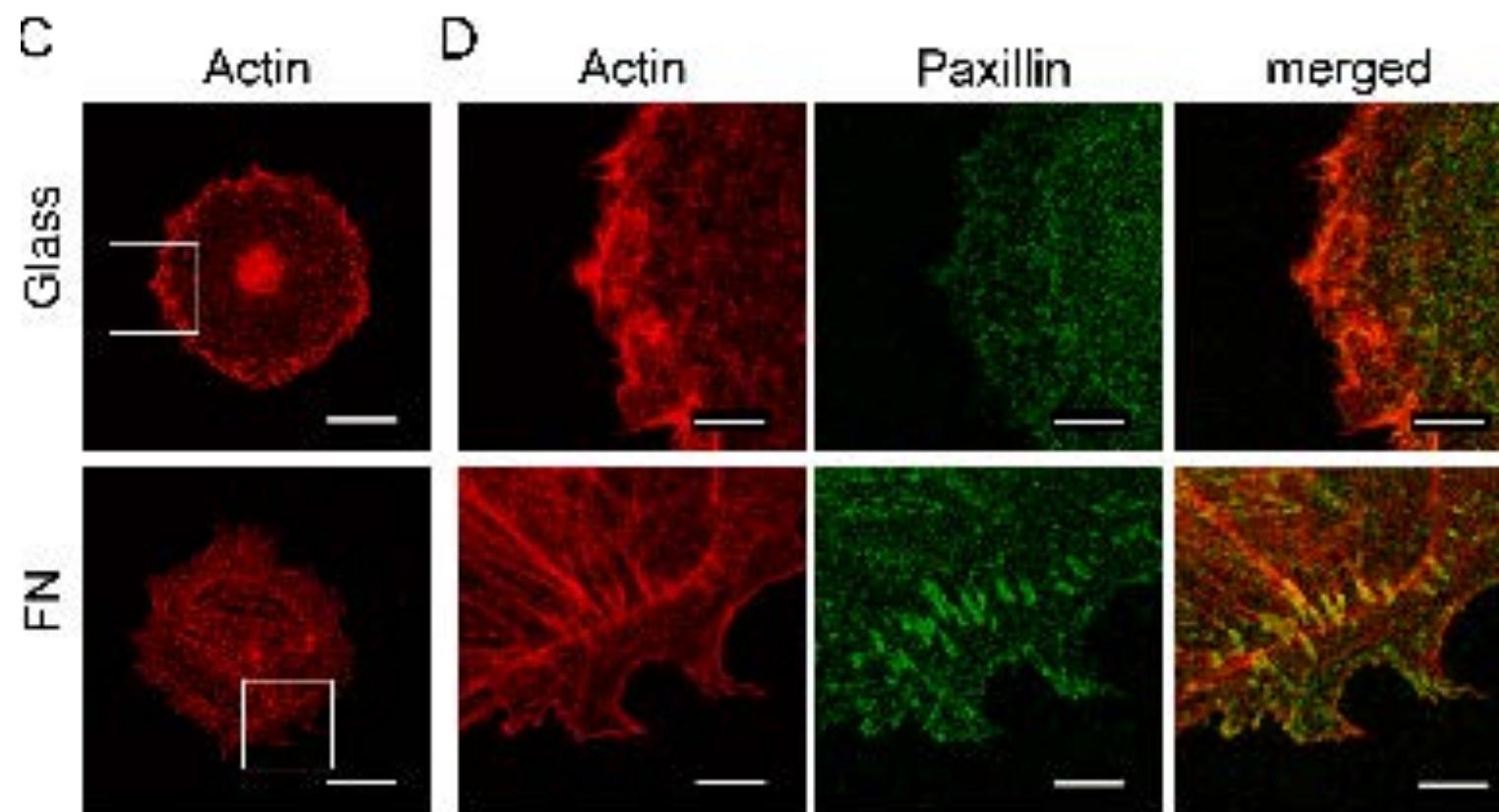
## Fibronectin



(a) Fibronectin network



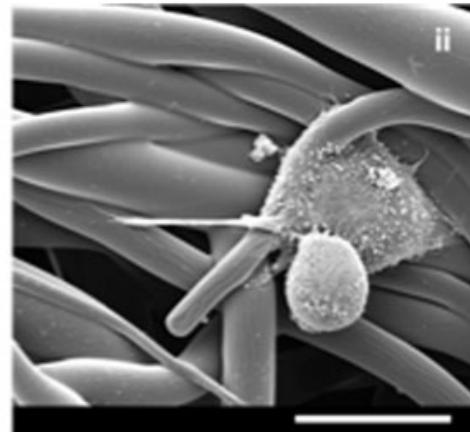
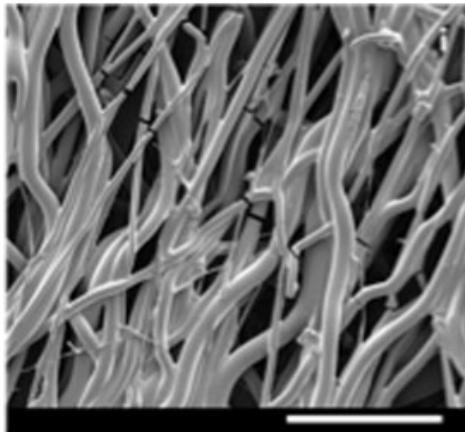
(b) Actin microfilaments  
(part of the extracellular)



**Matrix and the**  
cence micrographs  
ent antibodies specific  
extracellular  
ofilaments (part of the  
s).

# Fibronectin coating on scaffold

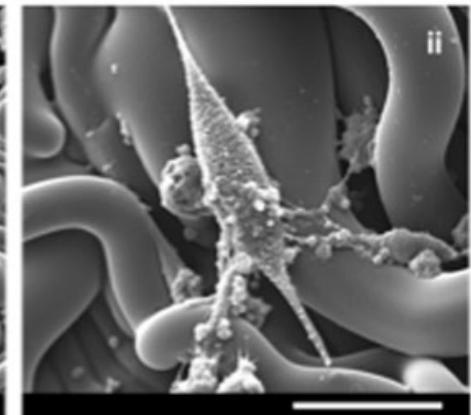
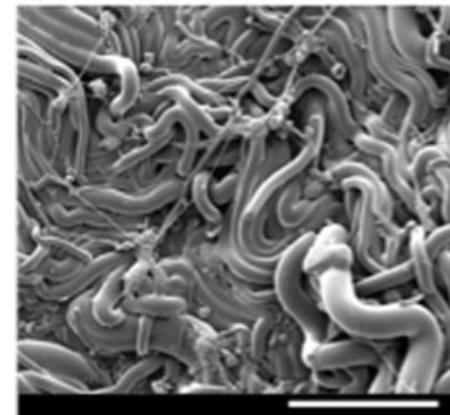
Periodontal ligament cells (PDL)



untreated PLGA

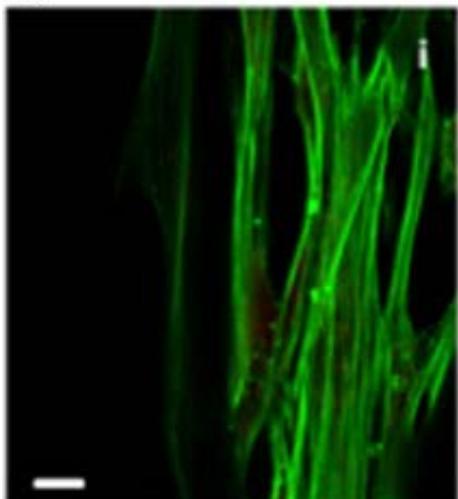
PDL cells cultured on scaffold for 24hr

**B**

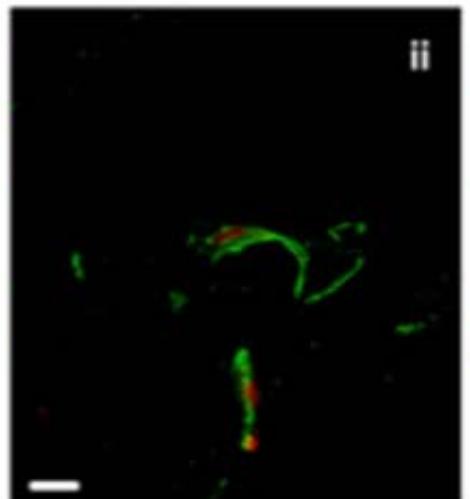


PLGAH001-FN coating

**C**

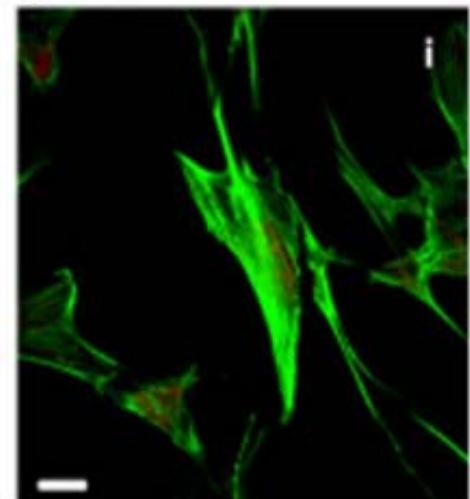


superior

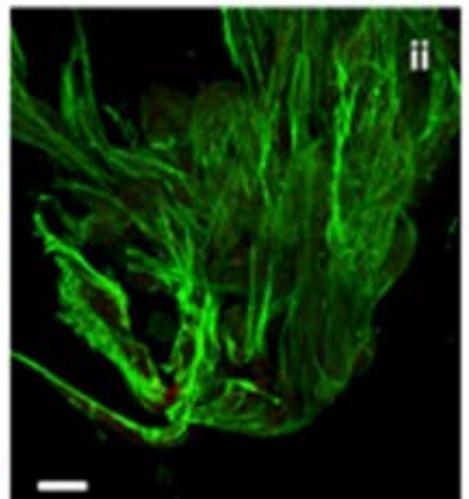


inferior

**D**



superior

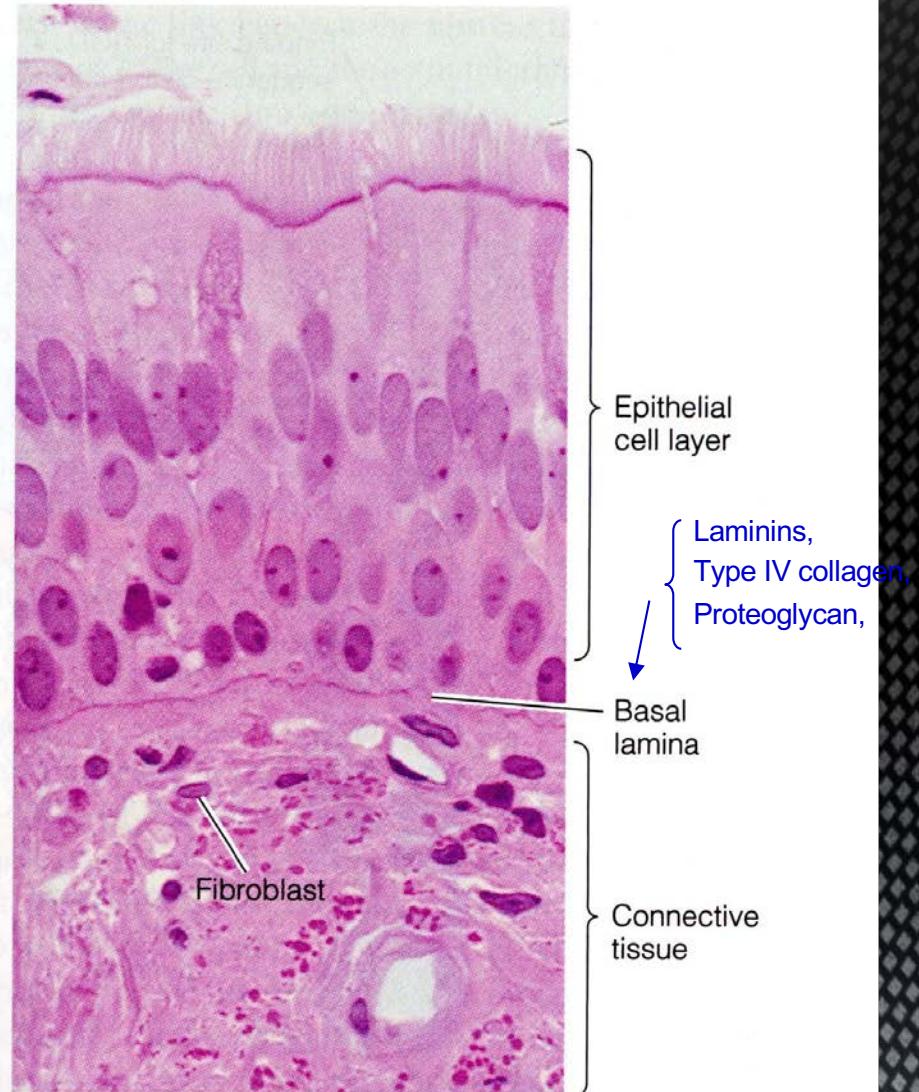


inferior

# Glycoproteins

## Laminin

- Mainly in basal laminae, a thin sheet of specialized extracellular material, that underlies epithelial cells, thereby *separating them from connective tissues*.
- As a structural support that maintains tissue organization and as a permeability barrier that regulates the movement of molecules as well as cells
- Prevents the passage of underlying connective tissue cells into the epithelium.



**Figure 11-9 The Basal Lamina.** The basal lamina is a thin sheet, typically about 50 nm, of matrix material that separates an epithelial cell layer from underlying connective tissue (TEM).

# Glycoproteins

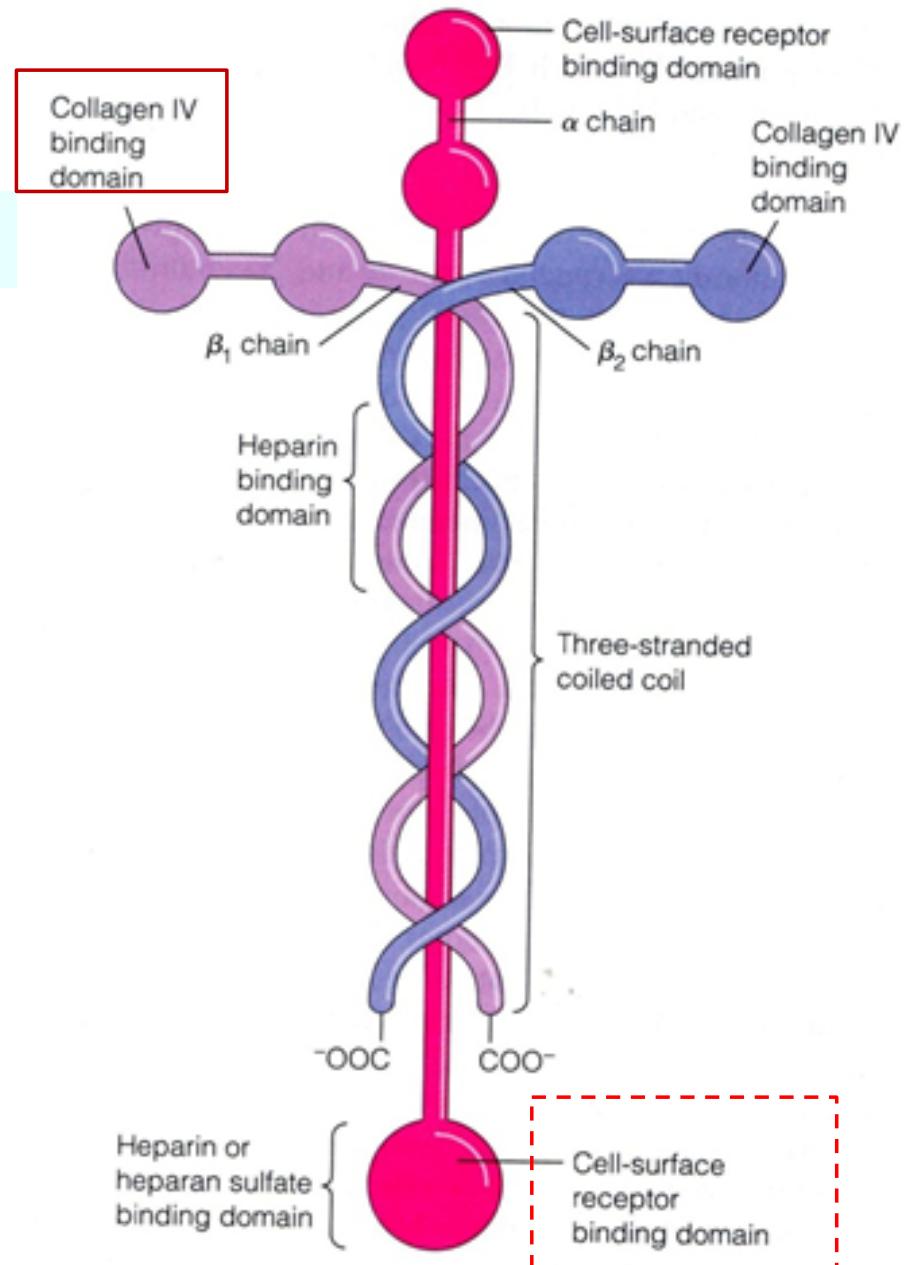
## Laminin

➤ Consists of three long polypeptide

- $\alpha$ ,  $\beta_1$ ,  $\beta_2$

➤ Binding domain

- Type IV collagen
- Heparin
- Heparin sulfate
- Entactin



Component	Location	Function
Collagen	Widely distributed	Key component of tissue architecture, provide tensile strength, cell-matrix interaction, matrix-matrix interaction
Elastin	Highly elastic tissues (lung, blood vessels, skin)	Key component of tissue architecture, provide elasticity
Proteoglycan	Widely distributed	Cell-matrix interaction, matrix-matrix interaction, cell proliferation, cell migration
Hyaluronan	Widely distributed	Cell-matrix interaction, matrix-matrix interaction, cell proliferation, cell migration
Laminin	Basement membrane	Basement membrane component, cell migration
Fibronectin	Widely distributed	Component of tissue architecture, cell-matrix interaction, matrix-matrix interaction, cell proliferation, cell migration
Fibrinogen	Blood, wound healing site	Cell proliferation, cell migration, hemostasis
Various adhesion molecules	Widely distributed	Mediate cell adhesion to matrix, mediate transmembrane signals