

Components of the extracellular matrix

COMPONENTS OF THE **EXTRACELLULAR MATRIX**

Structure • mechanics • cell adhesion • disease

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Learning objectives

By the end, explain how matrix molecules shape tissue behavior.

Identify

Classify the three major ECM families

Explain mechanics

Distinguish tensile strength, recoil, compression

Explain adhesion

Connect glycoproteins, receptors and cytoskeleton

Interpret disease

Link molecular defects to clinical consequences

Three major molecular families

Matrix functions arise from three complementary classes.

FIBROUS PROTEINS

Collagen: Tensile strength
Elastin: Recoil



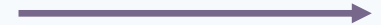
HYDRATED GELS

Proteoglycans / hyaluronan
Compression resistance



ADHESIVE MOLECULES

Fibronectin / laminin
Cells $\leftrightarrow$ ECM connections



Each family addresses a different physical demand

A tissue must resist pulling, recover shape and withstand compression.

- Tensile loads are resisted by collagen-rich structures.
- Recoil depends on elastin-containing fibers.
- Hydrated gel dissipates compressive forces.

Tension

Collagen network

Elastic recoil

Elastin fibers

Compression

Proteoglycan gel

Adhesion

ECM glycoproteins

Interstitial matrix and basement membrane differ

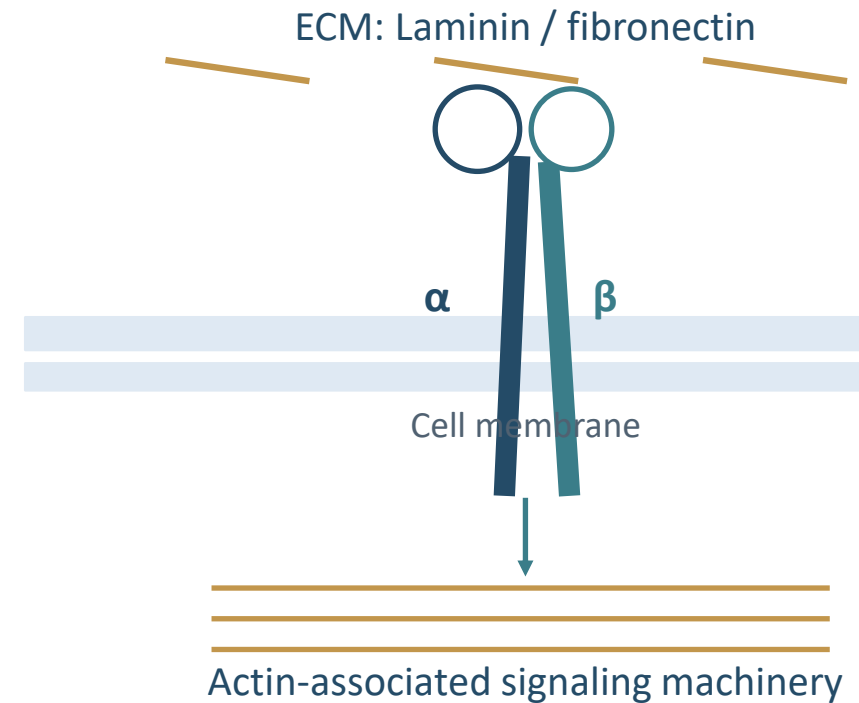
ECM composition reflects its anatomical location.

Dimension	Interstitial matrix	Basement membrane
Architecture	Three-dimensional gel and fibers	Organized planar mesh
Dominant components	Collagens, elastin, fibronectin, GAGs	Type IV collagen and laminin
Relation to cells	Stromal intercellular spaces	Specialized interface with cells
Role	Support / cushioning	Adhesion / specialized surface

Cells are connected to their surrounding matrix

Integrin contacts translate ECM architecture into cellular responses.

- Cells engage fibronectin and laminin through integrins.
- Integrins connect extracellular ligands with cytoskeletal elements.
- These contacts can regulate shape, migration and growth.

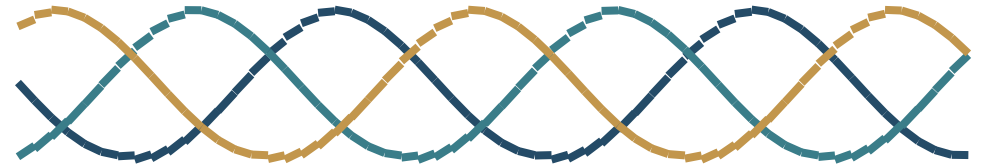


Collagen is a three-chain triple helix

Three polypeptide chains form a rope-like structural protein.

- Three separate polypeptide chains intertwine.
- The triple helix provides the molecular building block.
- Different collagen types have distinct tissue roles.

Three intertwined polypeptide chains



Triple-helix schematic

Fibrillar collagen types

Some collagens assemble into long fibrils that bear tension.

- Types I, II, III and V are examples of fibrillar collagens.
- Linear fibrils constitute much of connective tissue.
- Fibrillar organization differs from planar basement membrane collagen.

Type I

Fibrillar

Type II

Fibrillar

Type III

Fibrillar

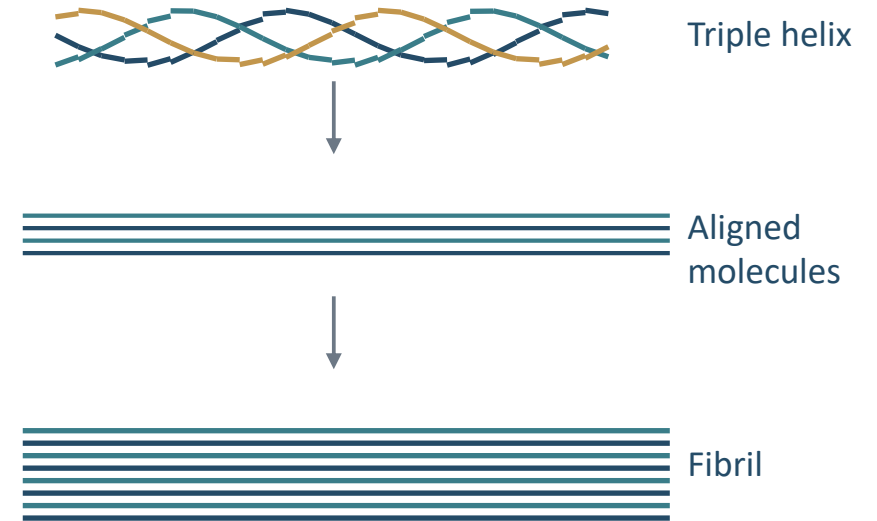
Type V

Fibrillar

From molecule to load-bearing fibril

Molecular alignment yields tissue-scale tensile structures.

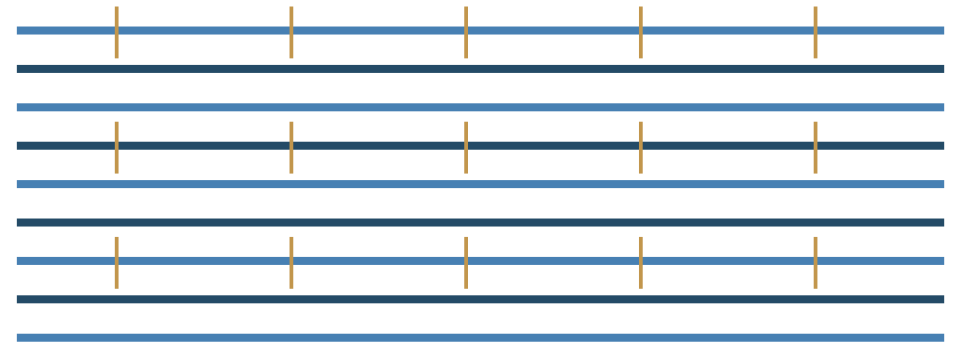
- Triple helices pack into aligned assemblies.
- Lateral associations stabilize fibrillar structures.
- Fibrils provide a scaffold for supportive tissue.



Lateral bonding creates tensile strength

Collagen fibers resist stretch because aligned helices are linked.

- Interchain hydrogen bonds stabilize fibrillar assembly.
- Covalent lateral cross-links contribute to high tensile strength.
- This produces mechanical resistance without elastin-like recoil.



Parallel collagen molecules with lateral links

Where fibrillar collagens dominate

Fibrillar networks support multiple connective tissues.

- Fibrillar collagens occur in bone, tendon, cartilage and skin.
- They also support blood vessels.
- They accumulate in healing wounds and scars.

Bone / tendon

Load bearing

Skin / vessels

Structural integrity

Cartilage

Fibrous framework

Scar

Repair scaffold

Collagen and elastin solve different load problems

High tensile resistance does not imply elastic recovery.

Property	Fibrillar collagen	Elastin-rich fiber
Principal property	Resistance to tensile force	Stretch and recoil
Structural basis	Aligned, cross-linked helices	Elastic core with cross-links
Response to release	Limited recoil	Return toward baseline
Key examples	Tendon / scar	Large arteries / skin

Why collagen cross-links matter

A useful fiber requires both strong molecules and strong lateral connections.

- Covalently linked helices distribute force.
- Loss of structural integrity compromises tissue strength.
- Clinical consequences depend on the affected tissue.

Triple-helical collagen molecules



Lateral covalent bonds stabilize fibrils



Tensile strength of connective tissue

Vitamin C supports collagen integrity

Hydroxylation during collagen formation depends on ascorbate.

- The source highlights vitamin C–dependent lysyl hydroxylation.
- Defective collagen processing weakens connective tissue.
- Clinical deficiency is expressed as scurvy.

Vitamin C availability



Appropriate lysine hydroxylation

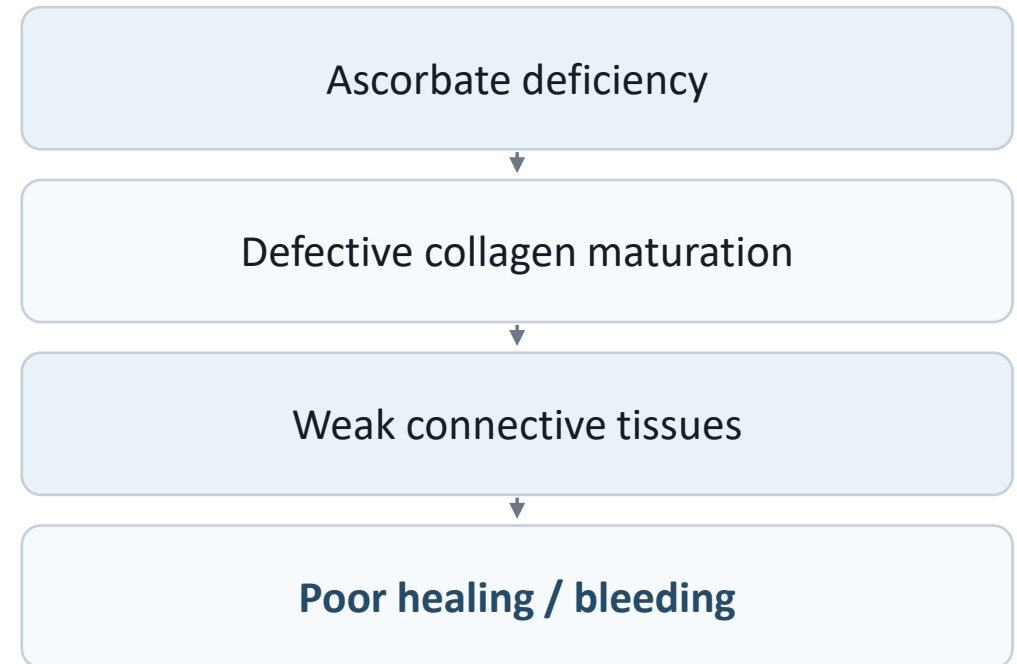


Competent collagen structure / strength

Scurvy: Weakened connective tissue

Vitamin C deficiency impairs tissue strength and repair.

- Poor wound healing reflects deficient collagen integrity.
- Vessel wall fragility contributes to easy bleeding.
- Skeletal deformities may occur during growth.



Scurvy: Tissue consequences are interconnected

The same ECM defect explains multiple manifestations.

- A fragile vascular matrix predisposes to bleeding.
- Inadequate collagen support undermines wound repair.
- Developing skeletal tissues are vulnerable in children.

Vessels

Easy bleeding

Wounds

Delayed healing

Skeleton

Growth-related deformity

Inherited defects affect collagen pathways

Disorders can arise from collagen or collagen-processing gene defects.

- Mutations in collagen proteins compromise the final matrix.
- Mutations in enzymes affecting processing may also weaken it.
- Examples named in the source include osteogenesis imperfecta and some Ehlers–Danlos syndromes.

Structural protein / processing-gene defect



Abnormal collagen matrix



Tissue-specific inherited disorder

Osteogenesis imperfecta: A collagen association

Osteogenesis imperfecta exemplifies genetic collagen dysfunction.

- The source links collagen mutations to osteogenesis imperfecta.
- Its inclusion illustrates how a systemic matrix defect affects skeletal integrity.
- Specific genotype–phenotype relationships require the dedicated genetics section.

Molecular level

Collagen mutation

Tissue level

Altered supportive matrix

Clinical framing

Skeletal fragility

Ehlers–Danlos syndromes: Matrix diversity

Some Ehlers–Danlos syndromes arise from collagen-pathway defects.

- Collagen and lysyl hydroxylase mutations are named mechanisms.
- The disease family is genetically and phenotypically heterogeneous.
- Do not assume every Ehlers–Danlos subtype has the same defect.

Structural genes

Some syndromes

Processing enzymes

Some syndromes

Teaching caution

Subtypes differ

Not every collagen forms a classical fibril

Nonfibrillar collagens organize interfaces and modulate fibrils.

- Type IV collagen forms planar basement membrane networks.
- Fibril-associated collagens regulate collagen interactions.
- Type VII collagen provides anchoring fibrils under stratified epithelium.

Type IV

Planar network

Type IX

FACIT interaction

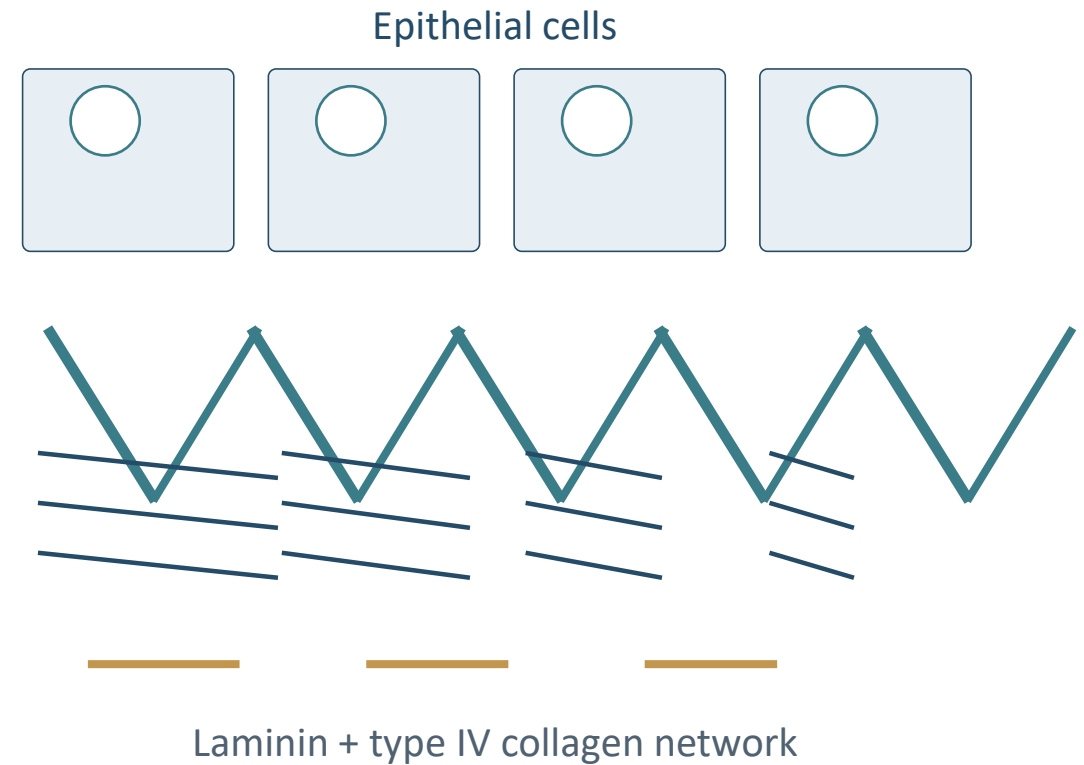
Type VII

Anchoring fibrils

Type IV collagen: Basement membrane network

Basement membranes depend on an organized collagen IV framework.

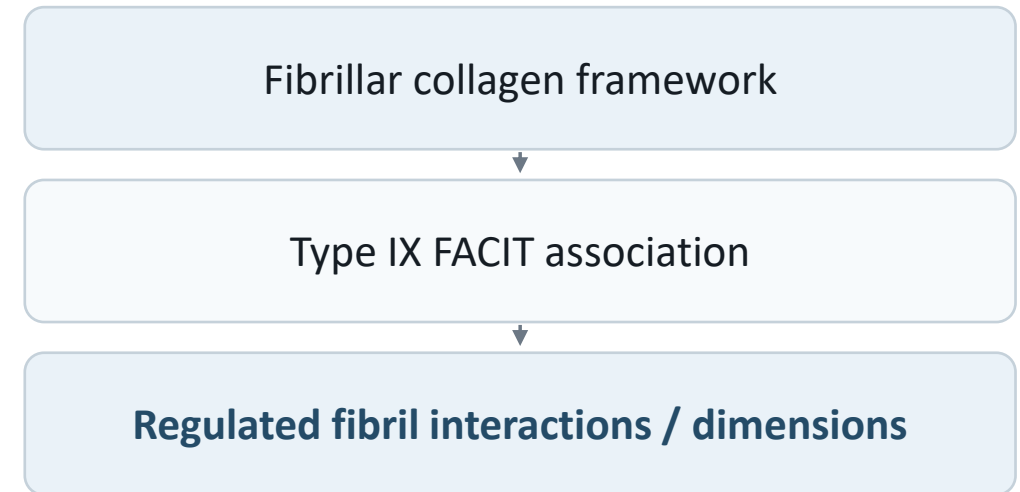
- Type IV collagen is nonfibrillar.
- It contributes to a flat, lamellar ECM network.
- Laminin is a key associated basement-membrane glycoprotein.



Type IX collagen: A FACIT example

Fibril-associated collagen can regulate other fibrils.

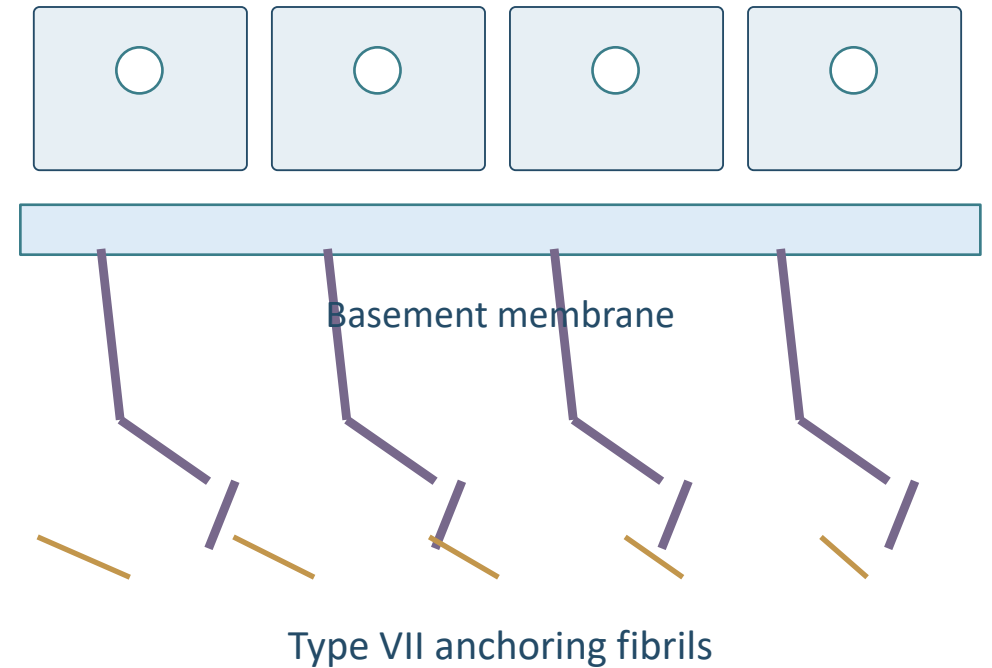
- FACIT = fibril-associated collagen with interrupted triple helices.
- Type IX collagen is a source example in cartilage.
- These collagens influence fibril diameters and collagen interactions.



Type VII collagen: Epithelial anchorage

Anchoring fibrils help retain stratified squamous epithelium.

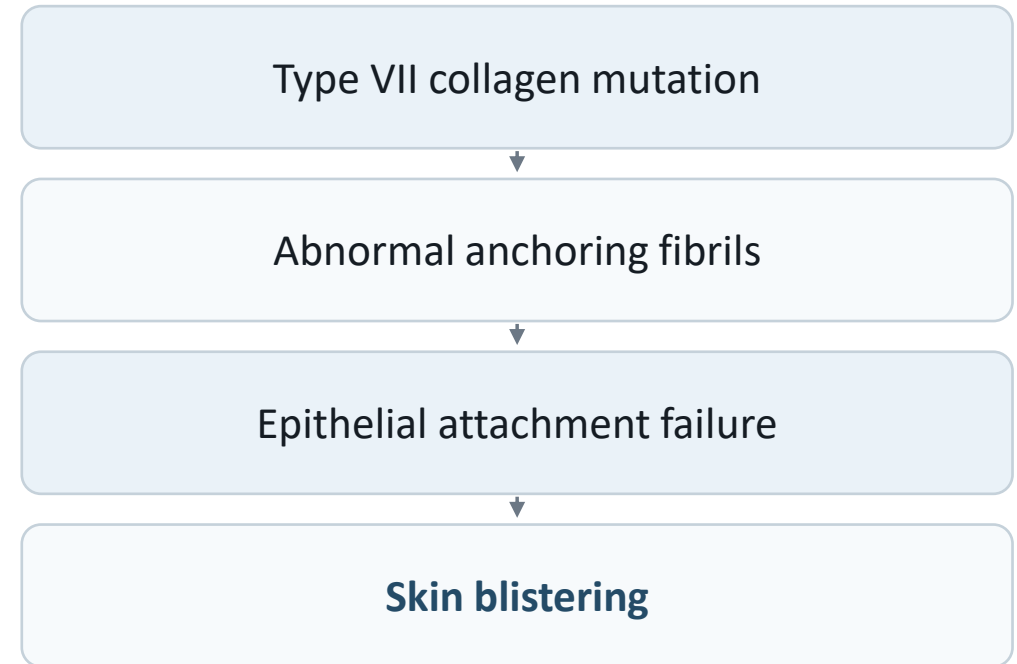
- Type VII collagen forms anchoring fibrils.
- These fibrils preserve epithelial structural attachment.
- Defects can lead to inherited blistering skin disorders.



A blistering phenotype can reflect failed anchorage

Epithelial separation follows loss of structural attachment.

- Type VII collagen normally contributes to anchoring fibrils.
- Mutations weaken the epithelial attachment system.
- The source links these defects to blistering diseases.



Compare structural collagen roles

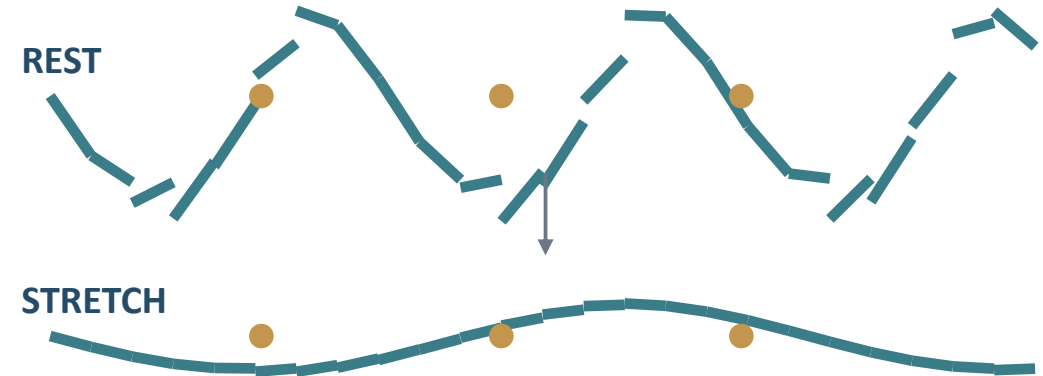
Collagen nomenclature encodes distinct assembly functions.

Example	Architecture	Functional role
Types I / II / III / V	Fibrillar	Tensile support
Type IV	Nonfibrillar network	Basement membrane
Type IX	FACIT	Fibril interactions
Type VII	Anchoring fibrils	Epithelial anchorage

Elastin permits recovery after stretch

Elasticity means return toward baseline after deformation.

- Elastin fibers deform with mechanical stress.
- After force release, fibers recoil toward their resting state.
- This is functionally different from collagen tensile resistance.

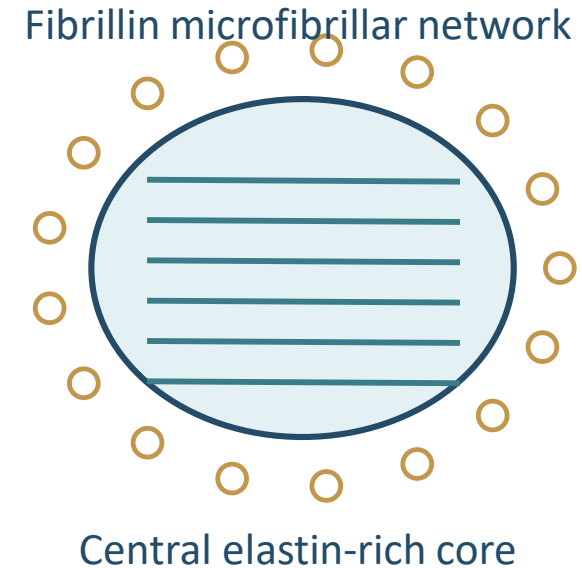


Cross-linked elastin recoils after release

Elastic fibers contain elastin and fibrillin

An elastic fiber has a mechanically active core and associated scaffold.

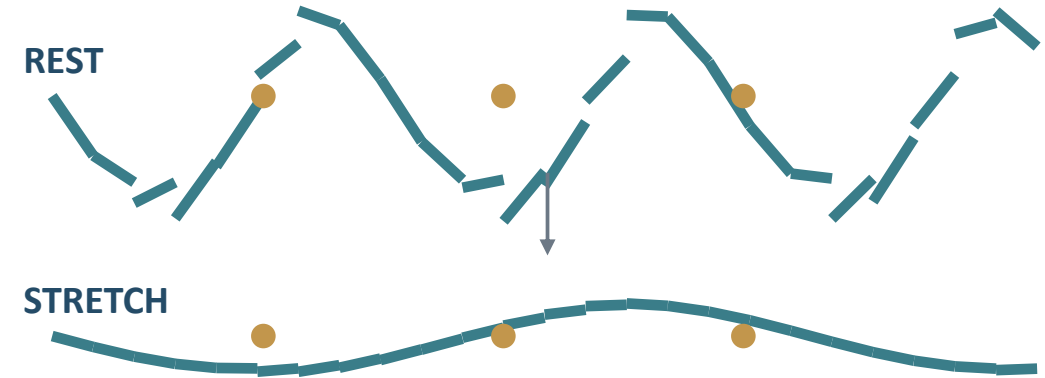
- An elastin-rich central core supports recoil.
- Fibrillin glycoprotein forms an associated meshlike network.
- The composite supports both mechanics and tissue organization.



Stretch and recoil: A reversible cycle

Hydrophobic elastin domains can deform yet recover.

- Cross-links help preserve elastic fiber integrity.
- Stretch extends the structure while cross-links hold it together.
- Release of tension restores the relaxed configuration.

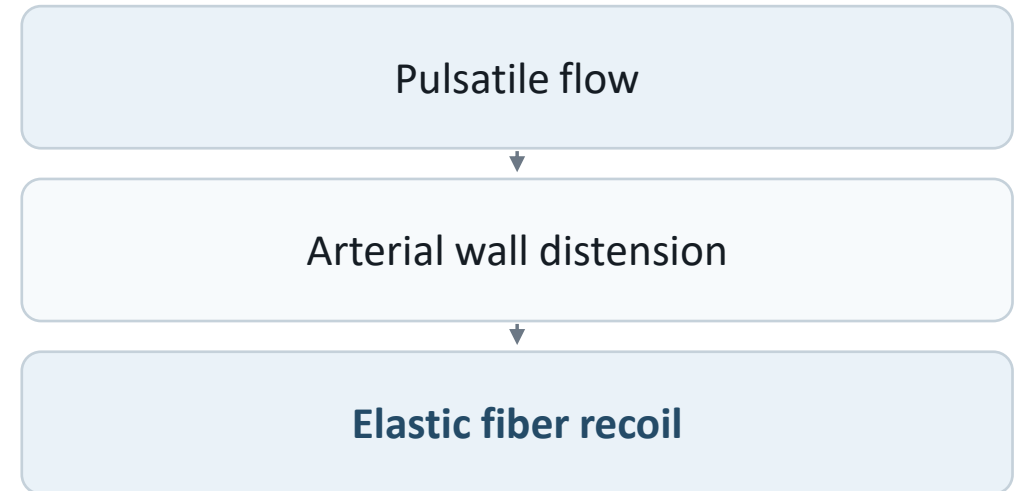


Cross-linked elastin recoils after release

Large arteries require repeated recoil

Arterial walls undergo recurrent pulsatile deformation.

- Large blood vessels repeatedly expand under pulsatile flow.
- Elastic ECM allows return toward baseline configuration.
- Loss of wall integrity may have serious mechanical consequences.



Other elastin-rich mechanical settings

Elasticity also supports valves, skin, ligaments and uterus.

- Cardiac valves must accommodate cyclical motion.
- Skin and ligaments encounter repeated stretch.
- The uterus experiences substantial mechanical deformation.

Valves

Cyclic deformation

Skin

Repeated stretch

Ligaments

Elastic response

Uterus

Tissue distensibility

Fibrillin has mechanical and regulatory roles

Fibrillin is more than passive elastic-fiber support.

- It contributes to the network associated with elastin.
- It influences availability of free transforming growth factor β (TGF- β).
- Both functions are implicated in Marfan syndrome.

Structural role

Elastic-fiber scaffold

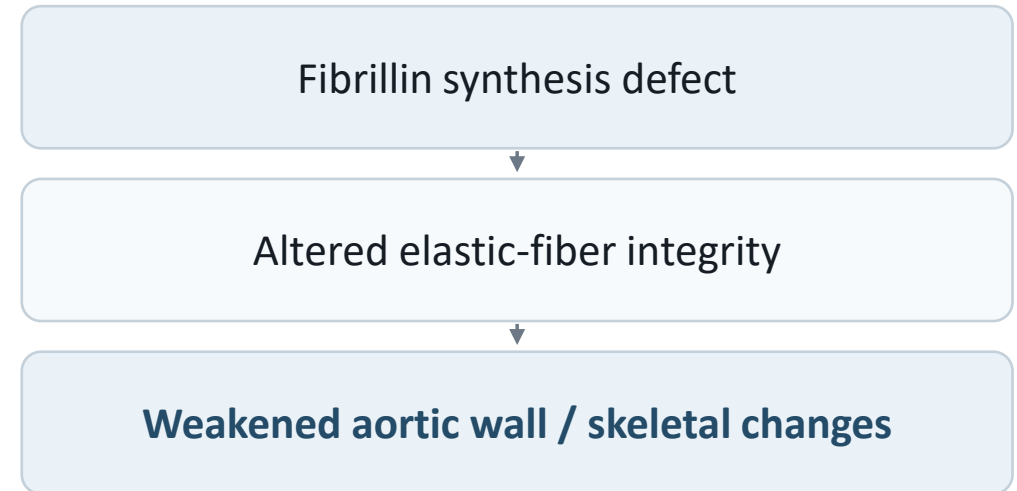
Regulatory role

TGF- β bioavailability

Marfan syndrome: Compromised elastic support

Fibrillin synthesis defects weaken susceptible tissues.

- The source links fibrillin defects with skeletal abnormalities.
- It also highlights weakened aortic walls.
- Altered regulation of free TGF- β contributes to pathogenesis.



Fibrillin influences TGF- β bioavailability

Matrix proteins can control extracellular signaling cues.

- Fibrillin normally influences availability of free TGF- β .
- Perturbation changes matrix-associated signaling regulation.
- This complements the mechanical explanation of Marfan syndrome.

Fibrillin-containing extracellular network



Control of free TGF- β availability



Cellular / tissue responses

Collagen and elastin: Choose the mechanism

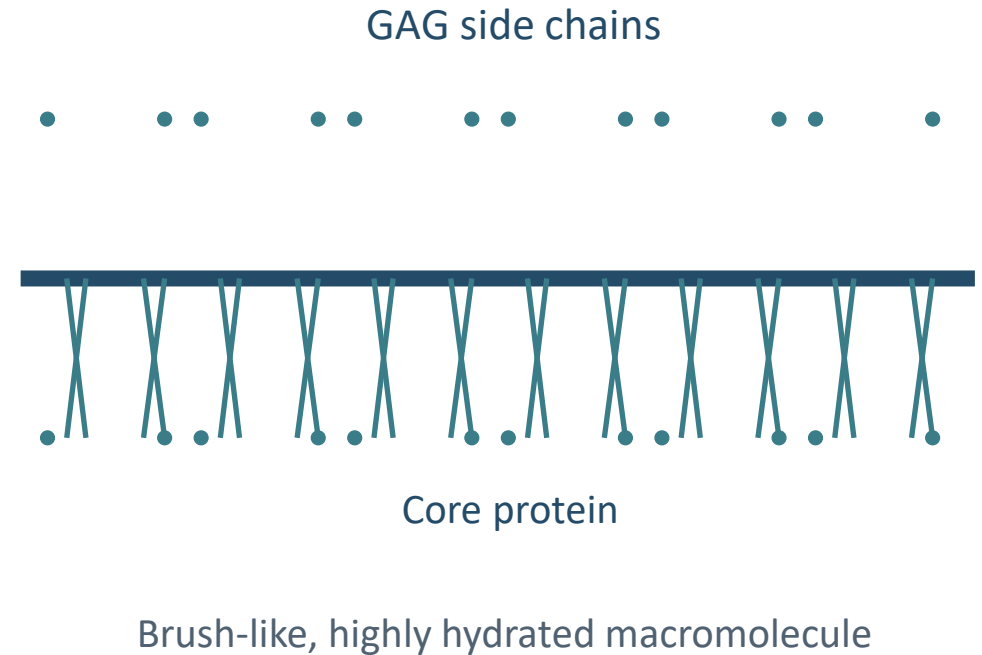
Two fibrous proteins have distinct structural tasks.

Question	Collagen	Elastin
Strong against pulling?	Major role	Not primary explanation
Returns after stretching?	Limited recoil	Major role
Molecular basis	Triple helix + lateral links	Cross-linked hydrophobic domains
Associated disorders	OI / some EDS / scurvy	Fibrillin defects / Marfan

Proteoglycans are core proteins with GAG chains

A core protein carries long carbohydrate side chains.

- Glycosaminoglycans (GAGs) attach to a core protein.
- This highly charged assembly attracts water.
- Proteoglycans form space-filling compressible gels.



Chondroitin and keratan sulfate are GAGs

These long polysaccharides form proteoglycan side chains.

- Chondroitin sulfate is a named GAG example.
- Keratan sulfate is another named GAG example.
- Their sulfated groups contribute to fixed negative charge.

Chondroitin sulfate

GAG side chain

Keratan sulfate

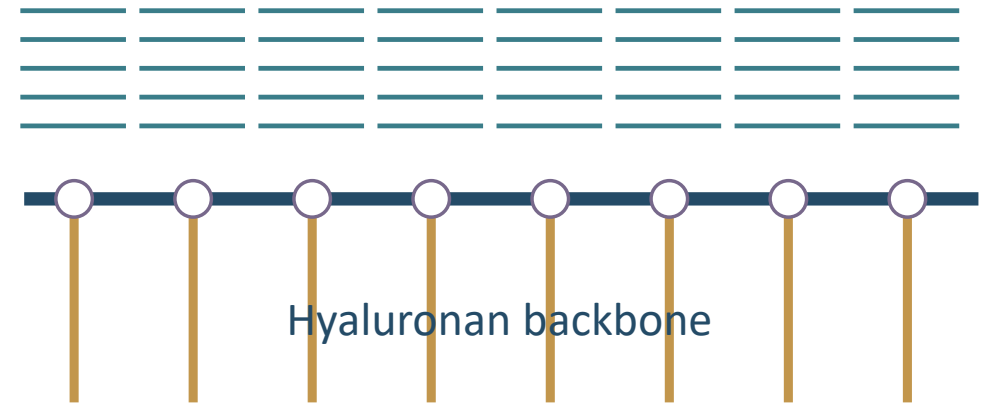
GAG side chain

Hyaluronan organizes large aggregates

Many proteoglycans attach along a long hyaluronan polymer.

- Hyaluronan provides a long assembly backbone.
- Linked proteoglycans give an extended brush-like architecture.
- The aggregate occupies hydrated extracellular space.

Proteoglycan monomers bearing GAG side chains

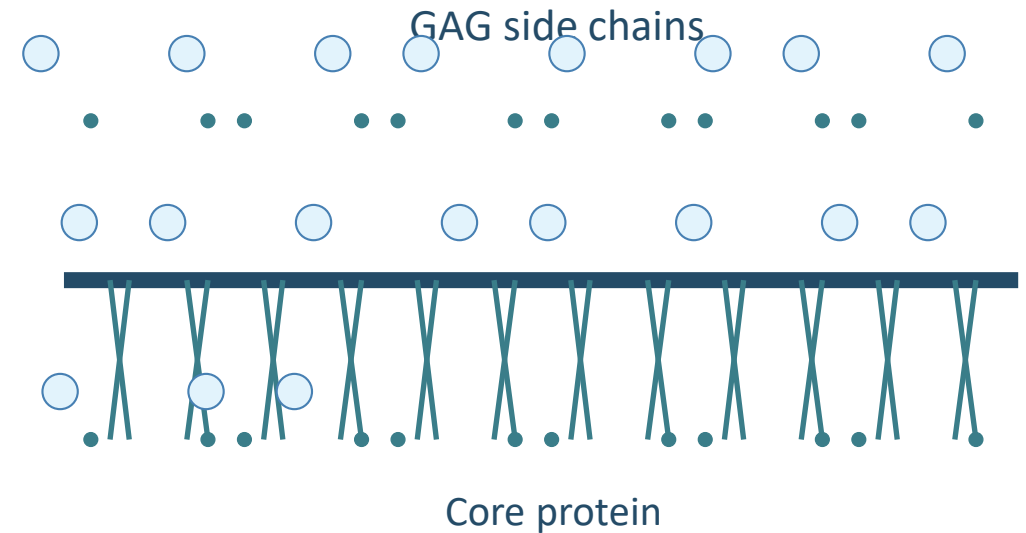


Large aggregate assembled along a continuous polymer

Negative charge creates a water-rich gel

Fixed negative charges recruit ions and osmotically retained water.

- Densely packed sulfated sugars carry negative charge.
- Cations—especially sodium—are attracted to the matrix.
- Water follows osmotically, generating a viscous gel.

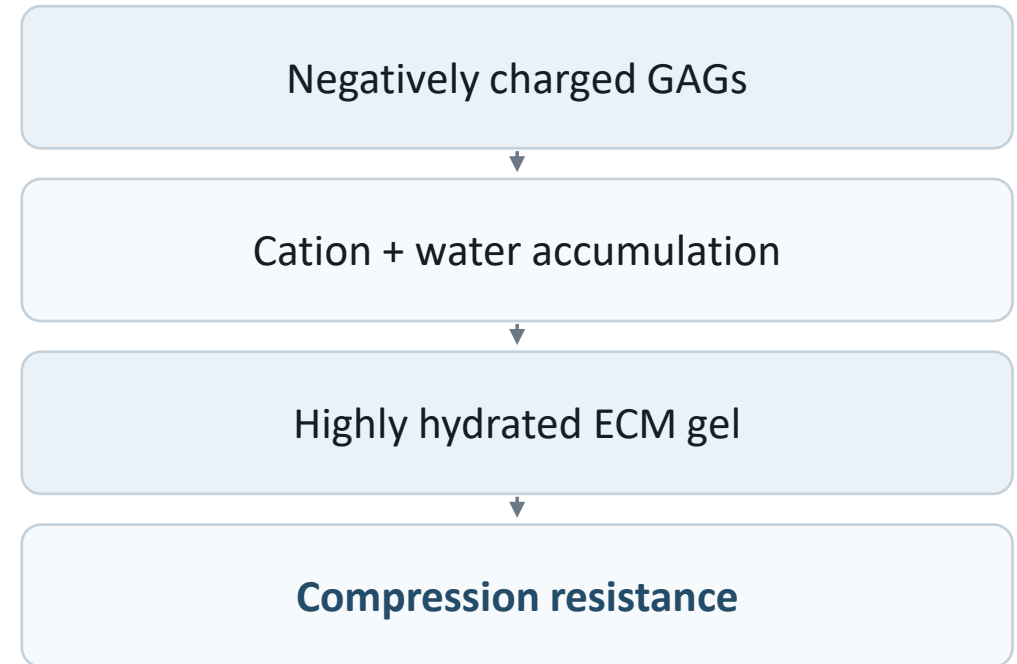


Negative charge attracts Na^+ and water

A hydrated gel resists compression

Compressive loads are buffered by fluid-rich matrix.

- The hydrated matrix behaves as a compressible gel.
- Water content helps oppose local compression.
- The resultant cushioning is distinct from collagen tensile strength.



Cartilage couples cushioning and lubrication

Proteoglycans protect articular surfaces in more than one way.

- Hydrated gels resist compressive loading.
- Proteoglycans also supply lubrication between adjacent bony surfaces.
- This complements the collagen framework of cartilage.

Fibrous framework

Collagen

Hydrated phase

Proteoglycans

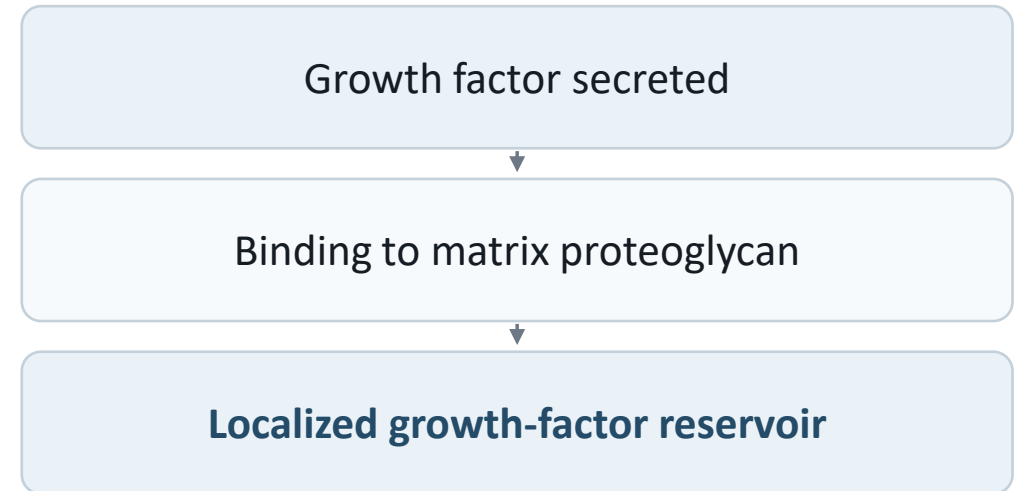
Mechanical result

Cushion + lubrication

Proteoglycans also store signals

The ECM binds factors as well as mechanical loads.

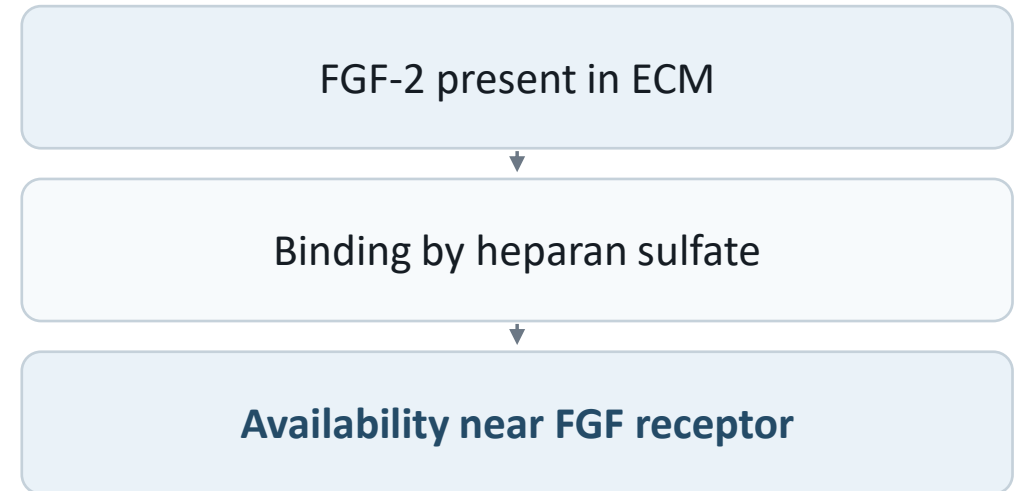
- Proteoglycans bind growth factors secreted into the ECM.
- Examples include FGF and HGF.
- Matrix association can influence local availability of signals.



Heparan sulfate can bind FGF-2

Growth-factor presentation is a matrix-dependent process.

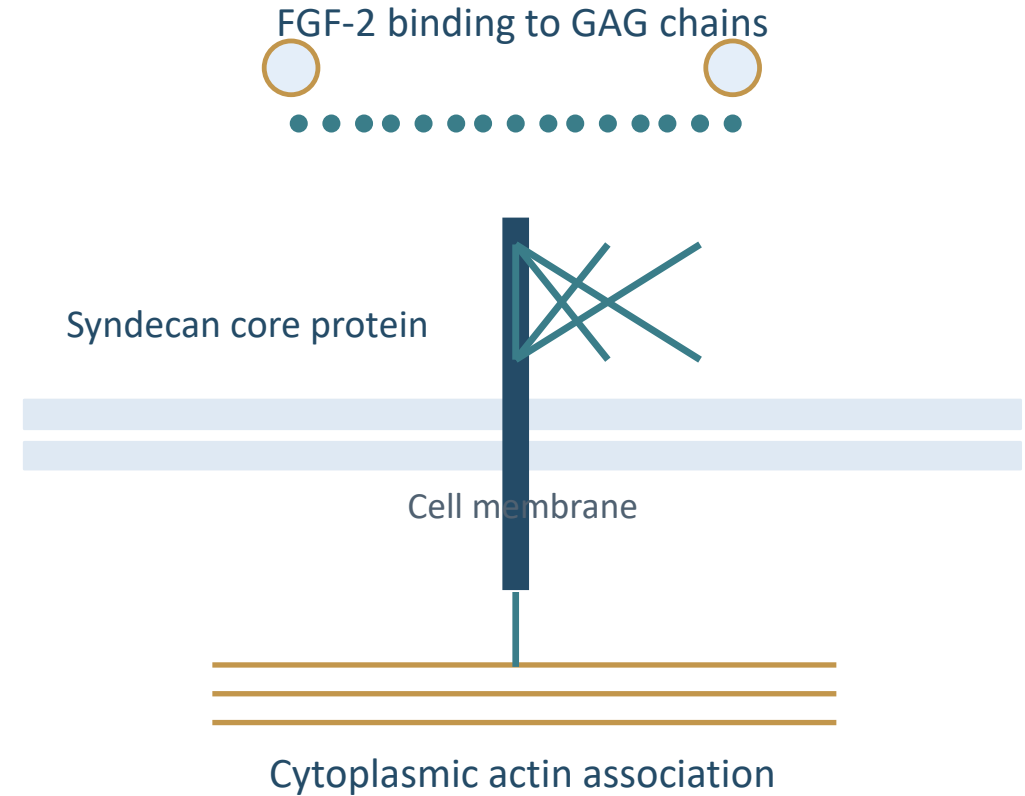
- Heparan sulfate proteoglycans bind basic FGF (FGF-2).
- Matrix binding retains factor near responsive cells.
- Released factors may later interact with cell receptors.



Syndecan is a cell-surface proteoglycan

Not all proteoglycans are embedded only within interstitial matrix.

- Syndecan contains a transmembrane core protein.
- Extracellular GAG side chains interact with growth factors.
- Its intracellular tail associates with actin cytoskeleton.



Syndecan can facilitate FGF-2 signaling

Growth factors released from damaged ECM may be captured at the surface.

- Injury can liberate matrix-associated FGF-2.
- Syndecan side chains bind FGF-2 near the cell surface.
- This facilitates engagement with FGF receptors.

Damaged ECM releases FGF-2



Syndecan GAG chains bind FGF-2



FGF receptor engagement facilitated

Adhesive molecules build molecular bridges

Cell–ECM, ECM–ECM and cell–cell contacts involve distinct proteins.

- Fibronectin is prominent in interstitial ECM.
- Laminin is prominent in basement membranes.
- Integrins are transmembrane adhesion receptors.

Fibronectin

Interstitial ECM

Laminin

Basement membrane

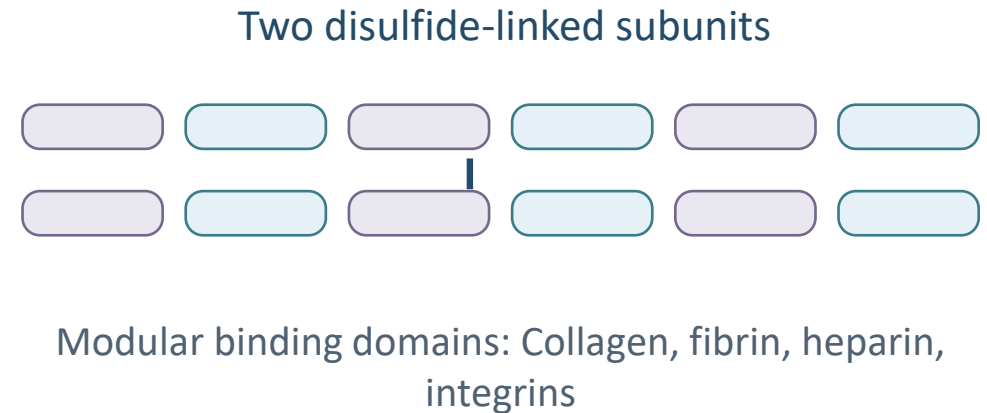
Integrins

Cell-surface receptors

Fibronectin is a modular heterodimer

Fibronectin uses distinct binding domains to join matrix elements.

- Fibronectin is a large disulfide-linked heterodimer.
- Tissue and plasma forms exist.
- Multiple domains recognize different matrix ligands.



Fibronectin binds several partner molecules

Its modular domains permit diverse extracellular connections.

- Fibronectin can bind collagen and fibrin.
- It also binds heparin and proteoglycans.
- Cell binding occurs through integrin receptors.

Collagen

Matrix fiber

Fibrin

Provisional matrix

Heparin / GAGs

Carbohydrate-rich matrix

Integrins

Cell attachment

Fibronectin has tissue and plasma sources

Fibronectin is supplied by multiple cell populations.

- Fibroblasts, monocytes and endothelial cells synthesize it.
- The protein exists in tissue and plasma forms.
- Both forms contribute during wound repair.

Fibroblasts

Matrix-producing cells

Monocytes

Inflammatory lineage

Endothelium

Vascular interface

Fibronectin scaffolds wound repair

The wound matrix provides a platform for sequential repair events.

- Tissue and plasma fibronectin form a wound scaffold.
- This supports subsequent ECM deposition.
- The scaffold also supports angiogenesis and reepithelialization.

Fibronectin-containing scaffold



Subsequent ECM deposition

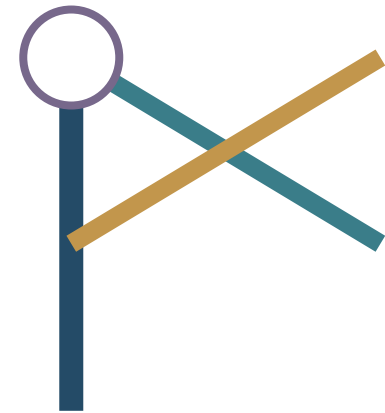


Angiogenesis + reepithelialization

Laminin is a cross-shaped heterotrimer

Its structure creates multiple basement membrane interactions.

- Laminin has three distinct subunits.
- The source describes a cross-shaped architecture.
- It is the most abundant basement membrane glycoprotein.

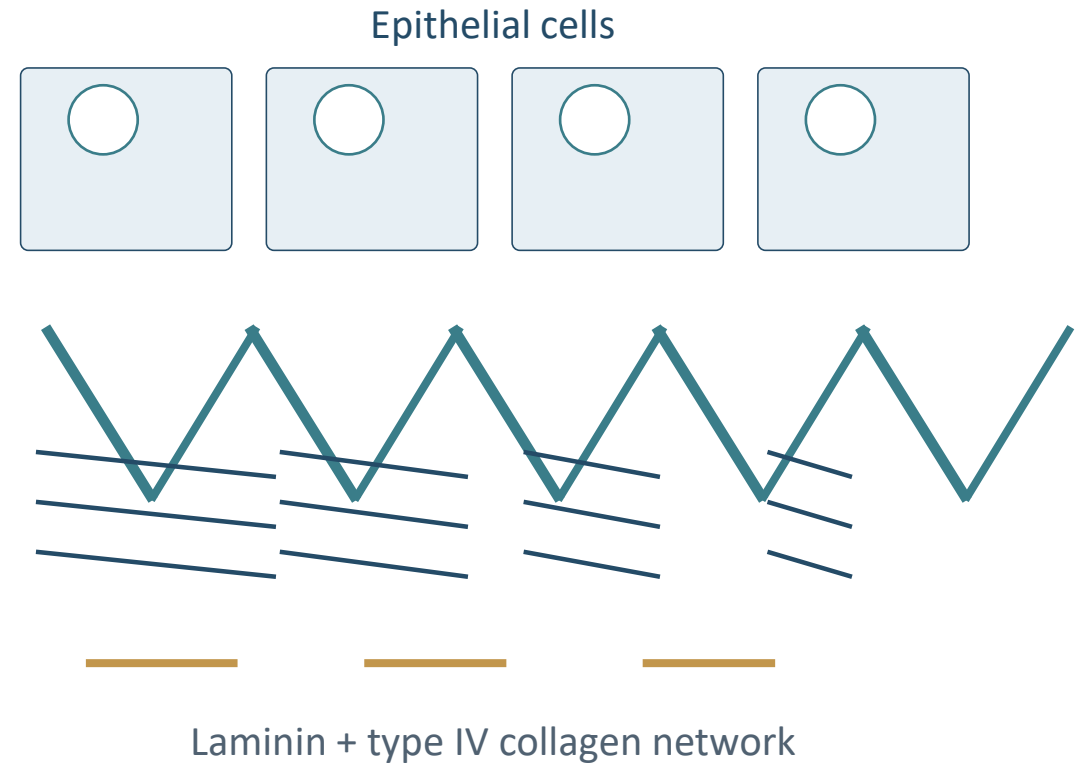


Three-chain cross-shaped heterotrimer

Laminin connects cells with the basement membrane

A laminin network connects cellular adhesion with matrix constituents.

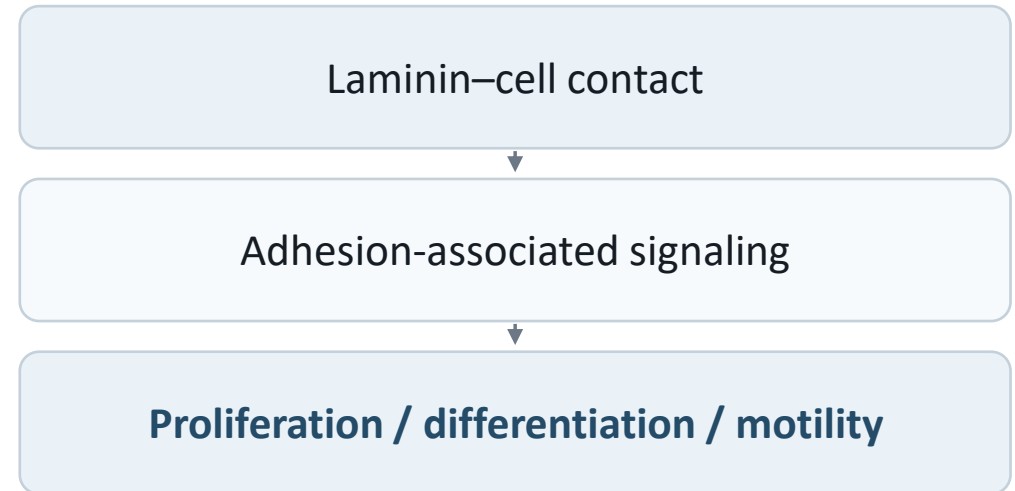
- Laminin interacts with underlying type IV collagen.
- Heparan sulfate is another binding partner.
- It supports cell attachment to the basement membrane.



Laminin also regulates cell behavior

Basement membrane engagement can convey information to cells.

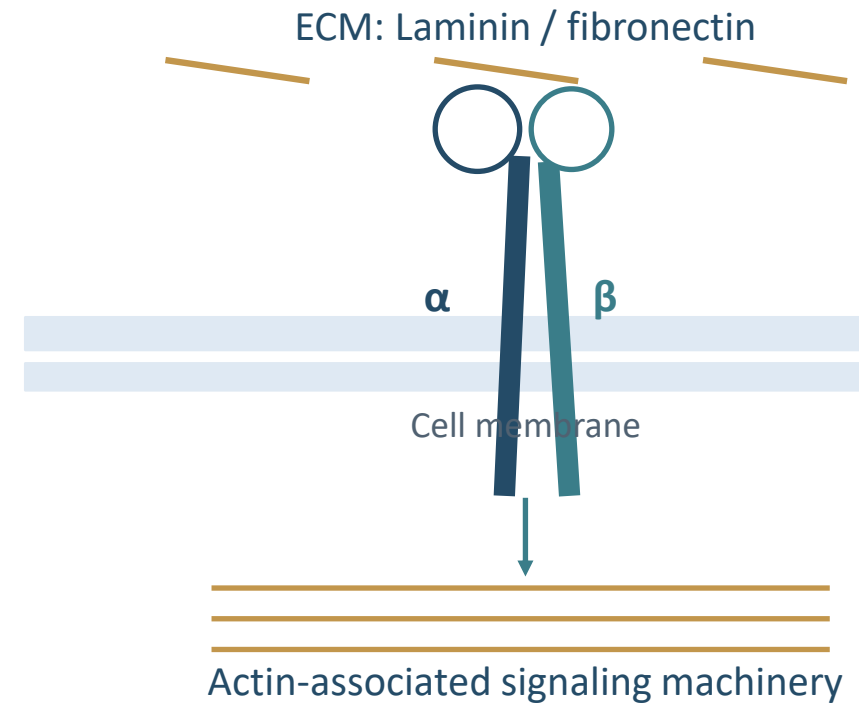
- Laminin has structural adhesion functions.
- It can modulate cell proliferation and differentiation.
- It also influences cell motility.



Integrins are α/β heterodimers

Two different subunits form a transmembrane adhesion receptor.

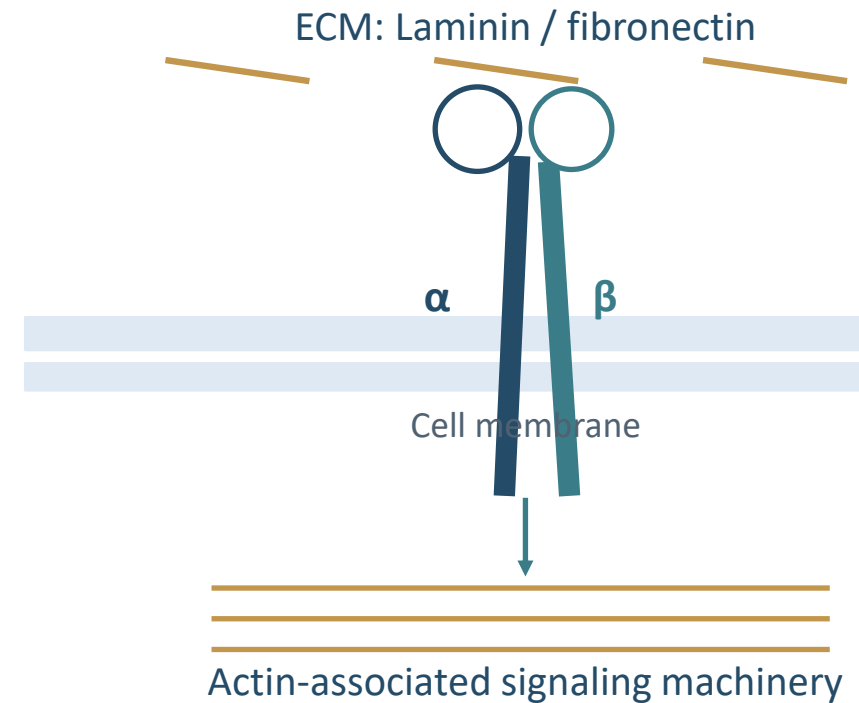
- An α -subunit pairs with a β -subunit.
- Together they bind extracellular ligands.
- They connect cell architecture with the external matrix.



Integrins link ECM to the actin cytoskeleton

The connection is structural and also signaling-active.

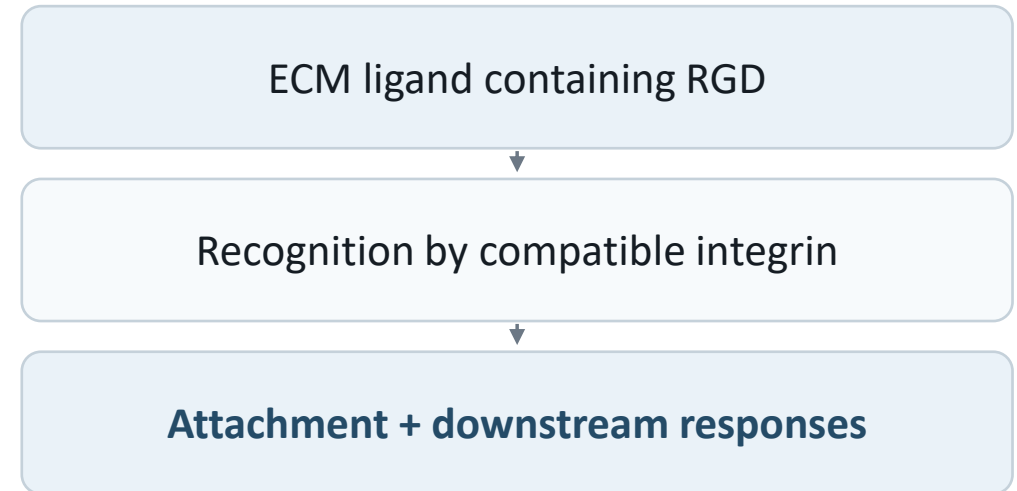
- Extracellular fibronectin or laminin engages integrins.
- Intracellular complexes connect to actin.
- Ligand engagement can initiate signaling cascades.



The RGD motif is a recognition sequence

Arginine–glycine–aspartic acid is abbreviated RGD.

- RGD is a ligand motif recognized by several integrins.
- RGD-mediated interactions enable focal substrate attachment.
- Integrin binding specificity varies among family members.



Integrins coordinate cellular responses

Matrix adhesion can modify behavior rather than merely tether cells.

- Locomotion requires regulated adhesion and detachment.
- Signaling helps control cell shape and differentiation.
- Matrix inputs can influence proliferation.

Motility

Locomotion

Cell architecture

Shape

Cell fate

Differentiation

Growth

Proliferation

Leukocyte adhesion needs integrins

Firm adhesion enables migration at inflammatory sites.

- Leukocyte integrins mediate firm attachment to endothelium.
- They also participate in passage across tissue barriers.
- The source connects this to inflammation and leukocyte migration.

Activated leukocyte adhesion



Firm endothelial interaction



Transendothelial migration

Platelet aggregation also uses integrins

Adhesion receptors participate in hemostatic interactions.

- Integrins are essential in platelet aggregation.
- Thus, the same receptor family participates beyond classical ECM adhesion.
- The detailed platelet pathway is addressed in hemostasis teaching.

Platelet integrin engagement



Cell-cell adhesive bridging

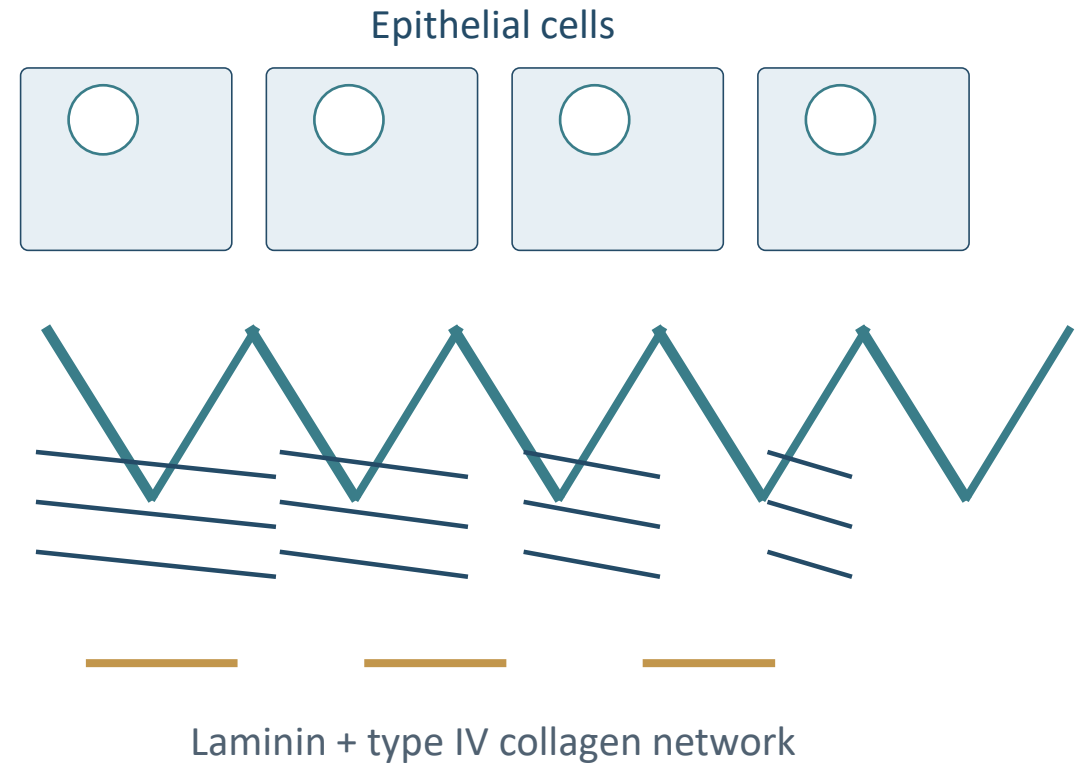


Platelet aggregation

The basement membrane is a coordinated matrix

Type IV collagen, laminin and adhesion receptors work together.

- Type IV collagen creates the network framework.
- Laminin provides cell-associated adhesive linkages.
- Integrins connect these interactions to cells.



Why ECM integrity matters for regeneration

A preserved scaffold guides organized tissue repair.

- Matrix and basement membrane provide a regenerative scaffold.
- Loss of scaffold integrity disrupts organized repair.
- These principles extend the parent ECM section.

Preserved ECM / basement membrane



Cell adhesion and tissue organization



Effective architecture during repair

Application: Impaired wound healing and bleeding

A patient with poor healing and easy bleeding has a nutritional deficiency. Which ECM process is most directly implicated?

A. Vitamin C–dependent collagen maturation

B. Hyaluronan-mediated hydration

C. Laminin basement binding

D. Fibrillin-associated recoil

Discuss the molecular component before revealing the answer.

Application: Nutritional collagen deficiency

Molecular failure produces mechanically fragile tissues.

Vitamin C–dependent collagen maturation

- Scurvy causes impaired collagen integrity.
- Poor tissue support explains bleeding and delayed wound healing.
- Distinguish this from elastin recoil and GAG-based compression.

Application: Aortic wall weakness

An inherited disorder affects elastic-fiber microfibrils and weakens the aortic wall. Which protein is implicated?

A. Fibronectin

B. Fibrillin

C. Type IV collagen

D. Hyaluronan

Discuss the molecular component before revealing the answer.

Application: Elastic-fiber disease

The extracellular defect has mechanical and signaling effects.

Fibrillin

- Fibrillin contributes to elastic-fiber architecture.
- The source links its defect to Marfan syndrome and aortic weakness.
- Fibrillin additionally regulates free TGF- β availability.

Application: Epithelial anchoring failure

An inherited skin disorder causes blistering through failed anchoring fibrils. Which collagen is the relevant example?

A. Type II

B. Type IV

C. Type VII

D. Type IX

Discuss the molecular component before revealing the answer.

Application: Collagen VII anchoring fibrils

The level of matrix organization determines clinical phenotype.

Type VII collagen

- Type VII collagen forms anchoring fibrils.
- These preserve stratified squamous epithelial attachments.
- Its disruption can cause inherited blistering skin disease.

Integrated map: Molecule to function

Identify each molecule by the mechanical or biological task it performs.

Collagen

Triple helix → tensile framework / specialized anchors

Elastin–fibrillin

Recoil and elastic-fiber integrity

Proteoglycans

Hydration, compression resistance, growth-factor depot

Fibronectin / laminin / integrins

Matrix bridges, cell adhesion and signaling

Reference and source boundaries

Primary content drawn from the supplied Robbins chapter extract.

Primary source

Robbins, Cotran & Kumar, 11th ed. (2026), chapter 1

Source location

Components of the ECM, printed pp. 21–23

Additional context

Extracellular Matrix, printed pp. 20–21

Figure policy

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