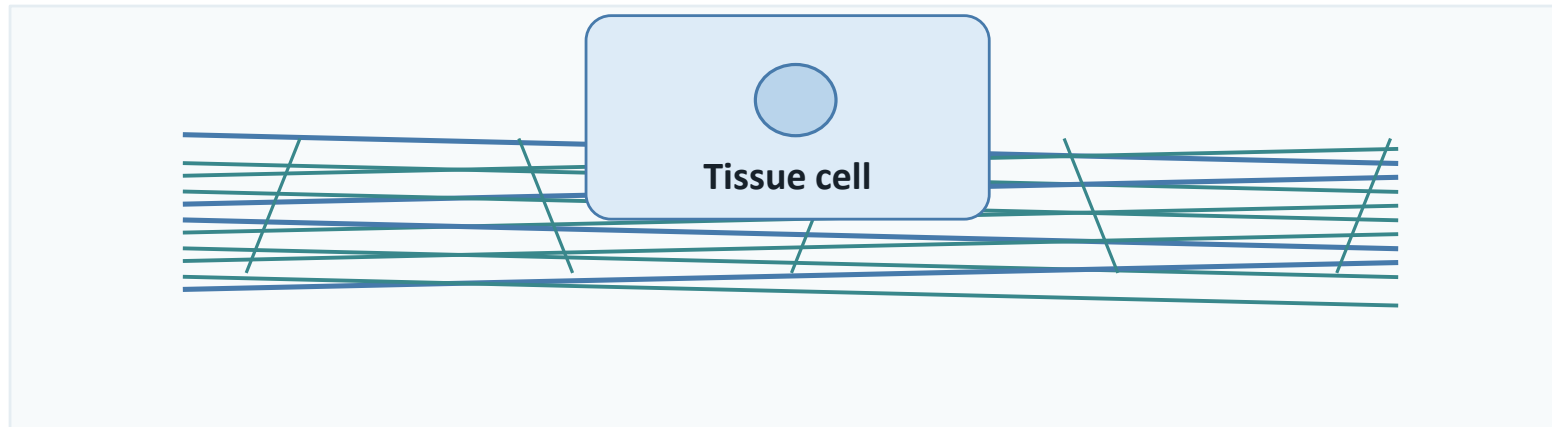


Extracellular Matrix

Tissue architecture · Cell signaling · Repair and remodeling

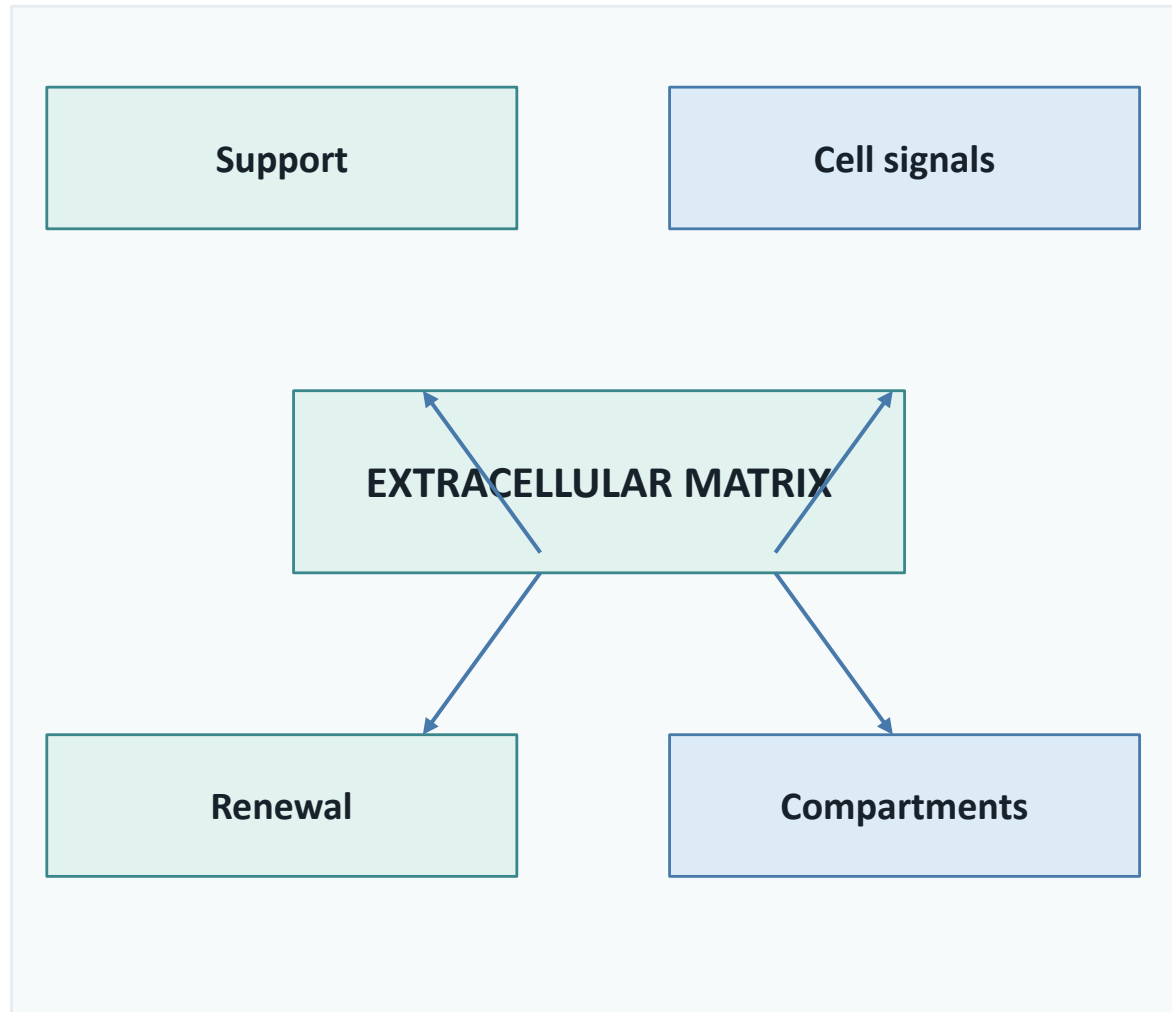


Dr Abu Suraih Sakhri

MBBS, MD (Pathology)

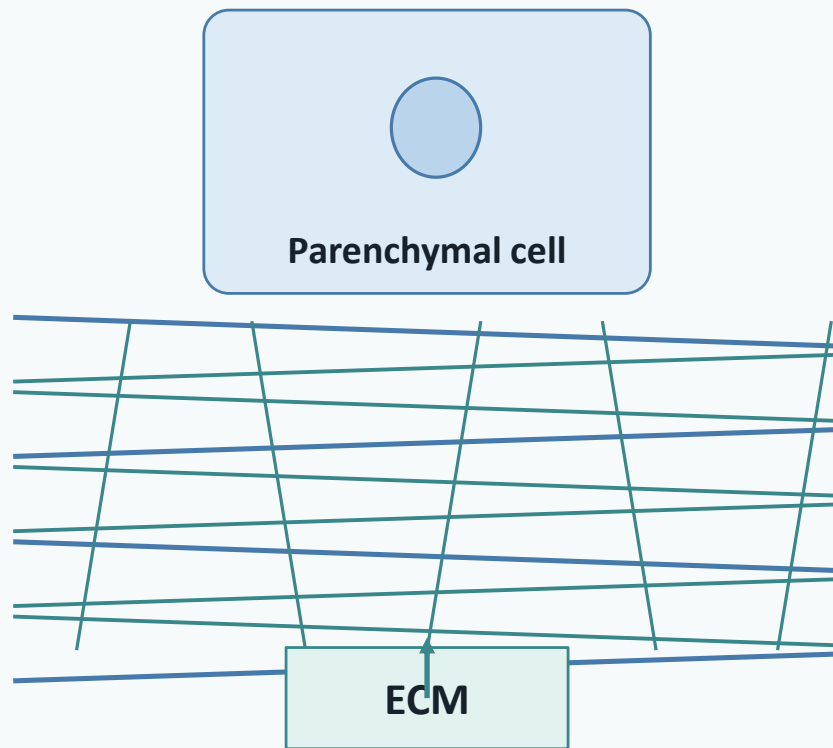
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Learning objectives



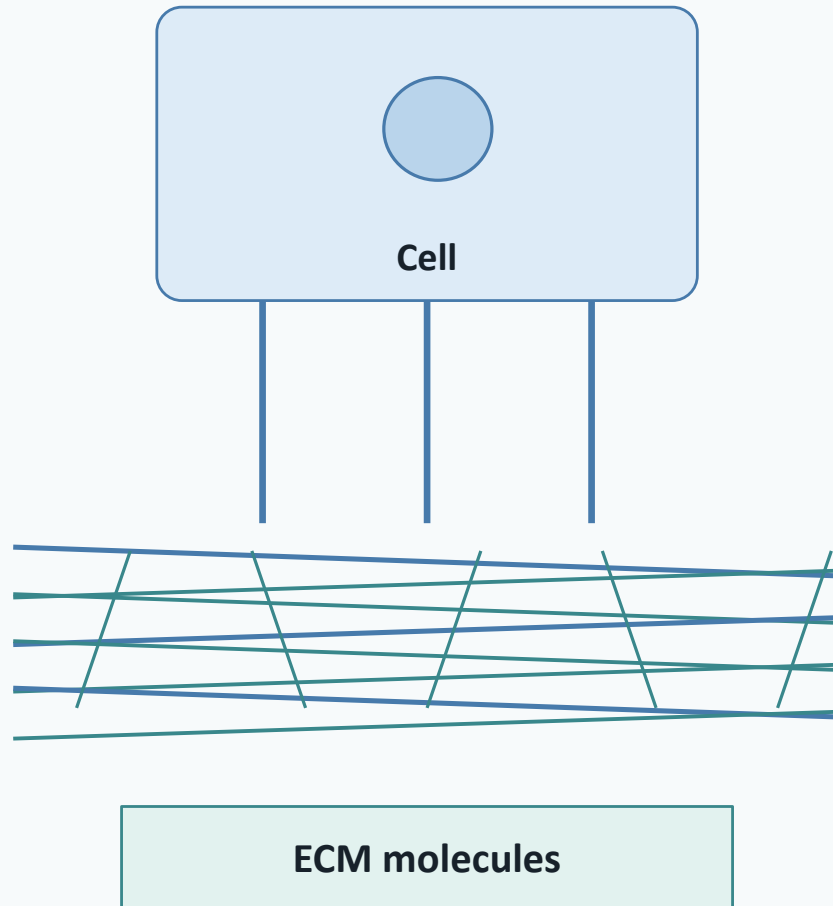
- Describe how extracellular matrix (ECM) provides mechanical and biochemical information.
- Distinguish interstitial matrix from basement membrane by location, structure, and function.
- Explain matrix contributions to signaling, tissue renewal, fibrosis, and invasion.

ECM is a dynamic component of every tissue



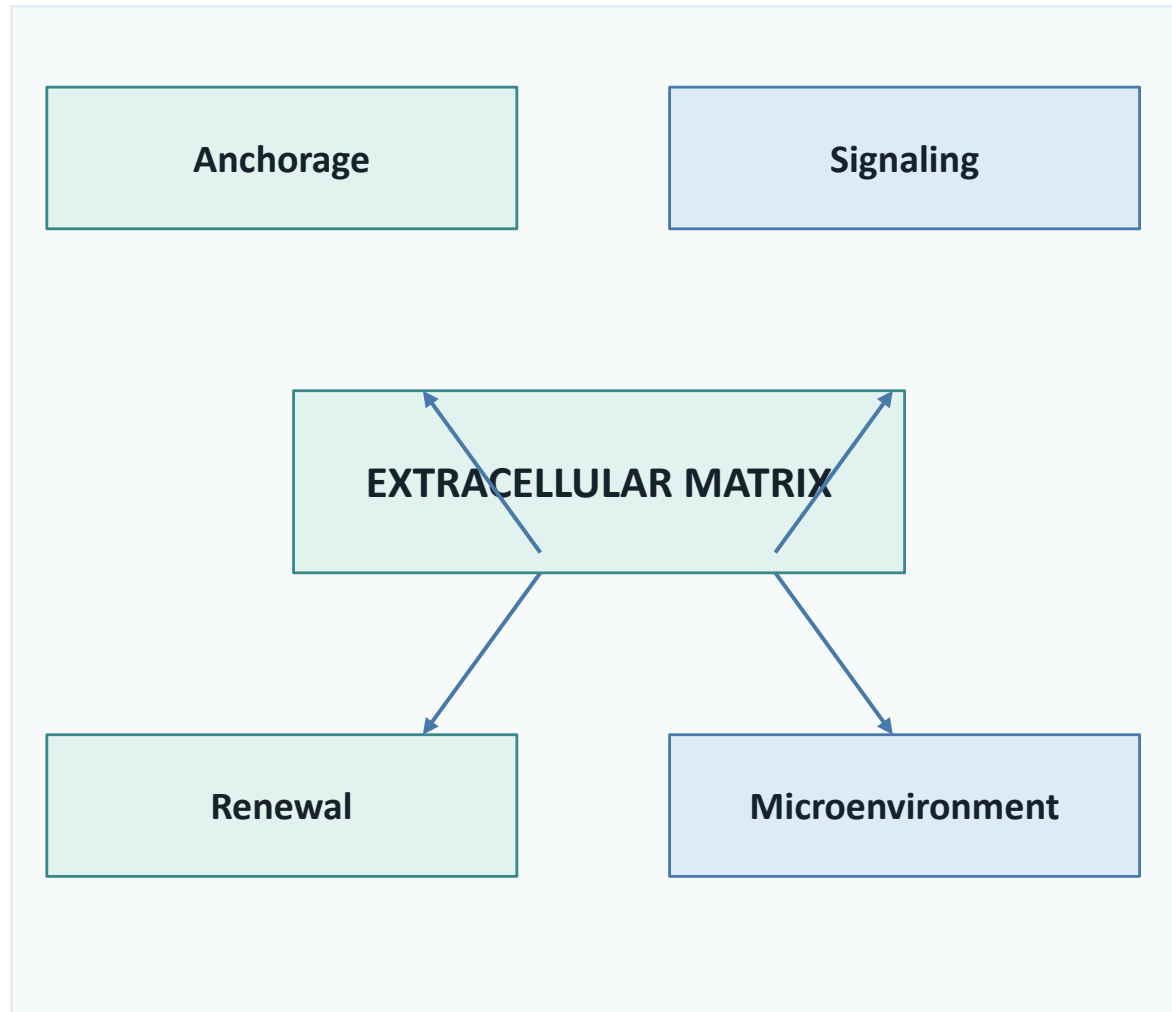
- The ECM is a protein-rich extracellular network contributing substantially to tissue organization.
- Its interactions with living cells determine architecture and functional responsiveness.
- ECM synthesis and breakdown continuously reshape the tissue environment.

ECM is not a passive tissue “filler”



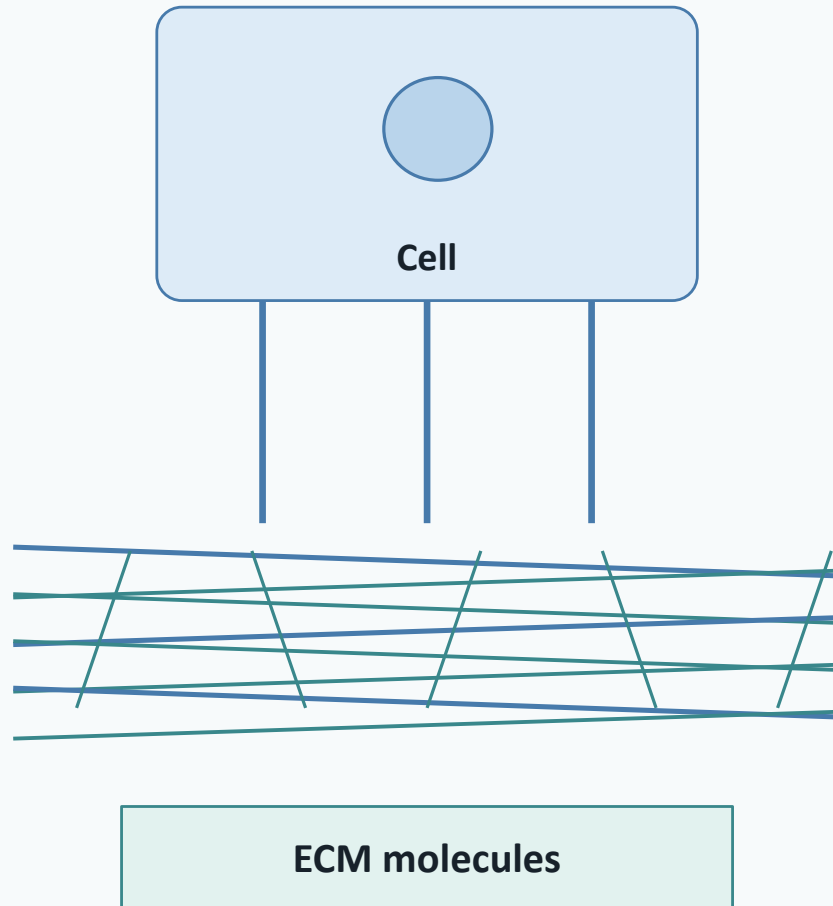
- Matrix molecules carry both mechanical loads and instructive signals.
- Cells sense their surroundings through matrix-binding receptors.
- Tissue outcome depends on reciprocal cell–matrix interaction.

Four core functions define ECM biology



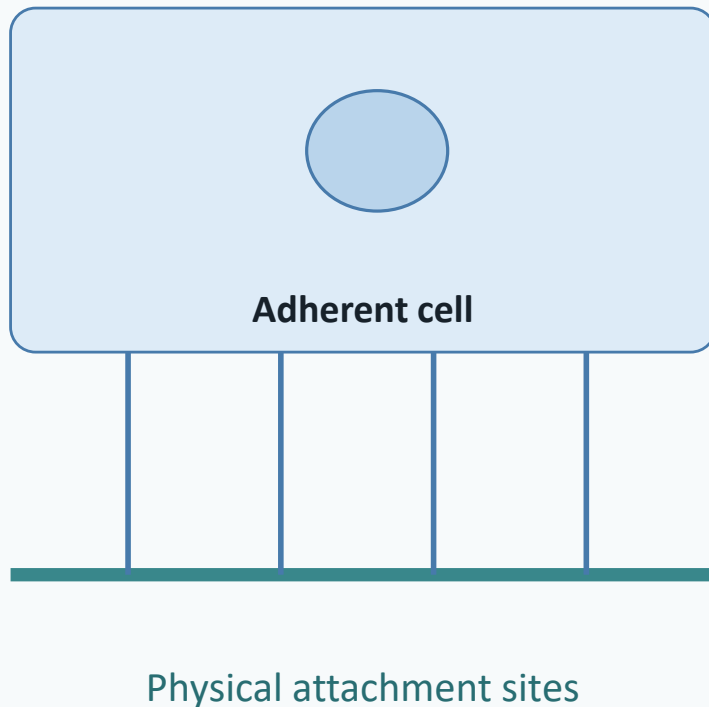
- Mechanical support: Anchorage, migration, and polarity.
- Signaling: Growth-factor display and integrin pathways.
- Organized renewal and formation of specialized tissue microenvironments.

Cellular architecture depends on extracellular cues



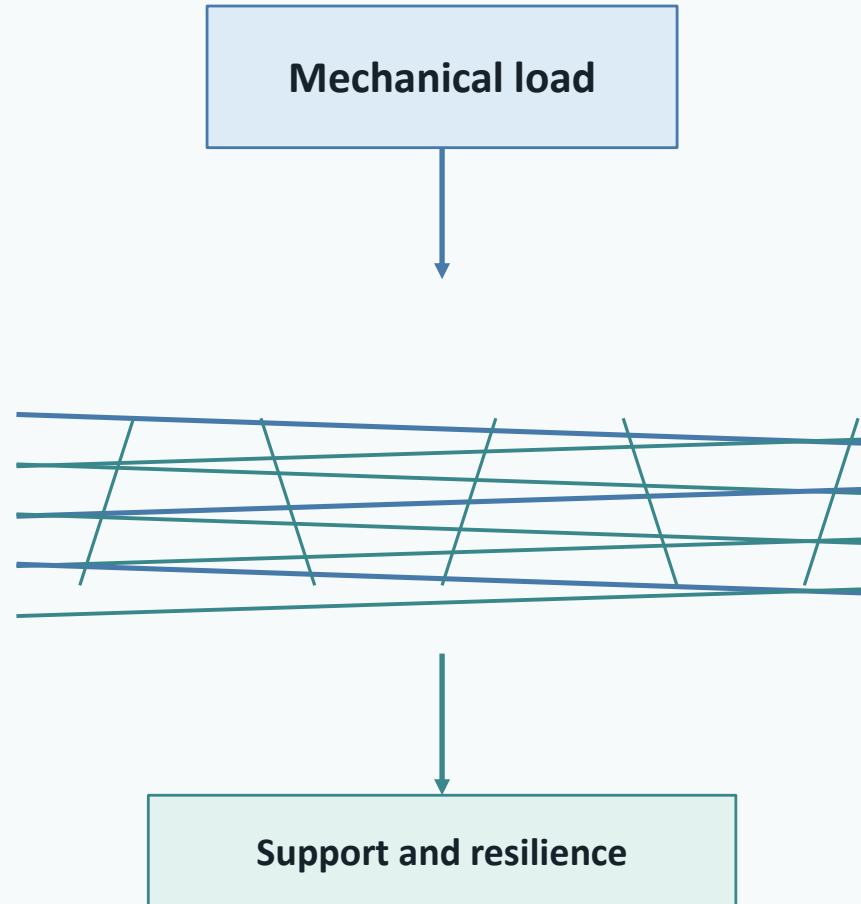
- Parenchymal cells lie within an organized matrix-containing microenvironment.
- Cell adhesion joins the external matrix to the intracellular cytoskeleton.
- Disruption of this interface affects tissue cohesion and geometry.

ECM provides a substrate for anchorage



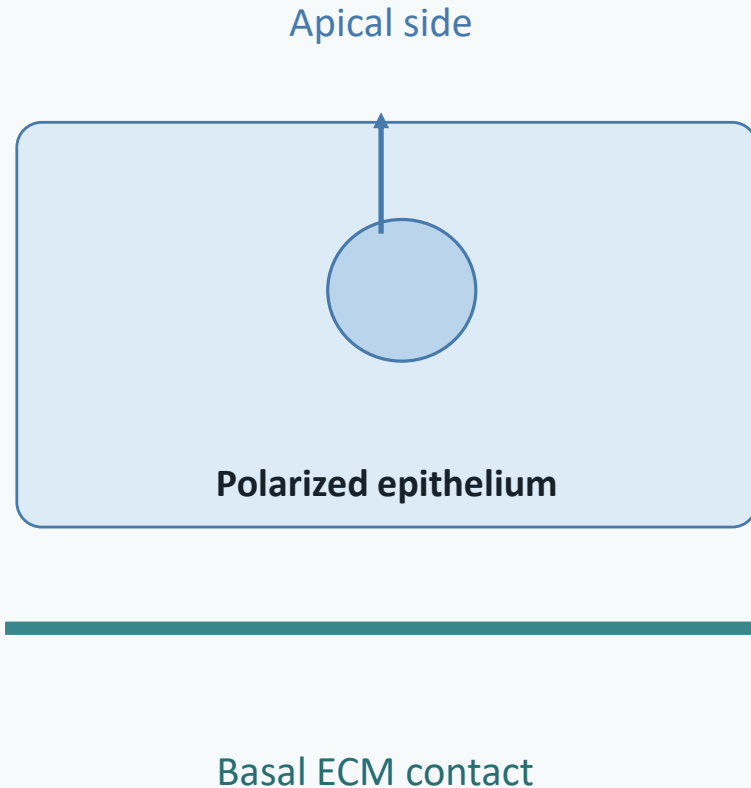
- Attachment depends on specific interactions between cellular receptors and matrix ligands.
- Anchorage positions cells relative to their neighbors and supporting tissues.
- Stability requires coordination of extracellular and cytoskeletal elements.

Mechanical support does not imply rigidity



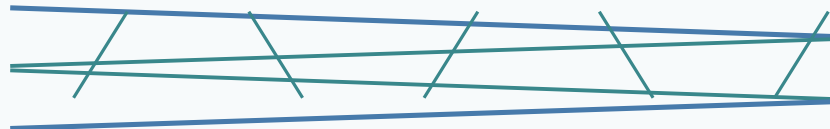
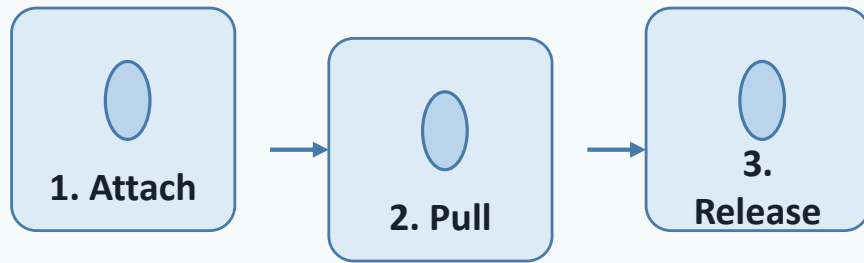
- The ECM can sustain tension and deform under physiological loading.
- Different tissue compartments use distinct matrix arrangements.
- A supportive matrix can also be hydrated and semifluid.

Matrix contacts help maintain cell polarity



- ECM adhesion provides orientation cues at basal cellular surfaces.
- Polarity permits spatial specialization within organized epithelia.
- When matrix organization is lost, tissue architecture can become disordered.

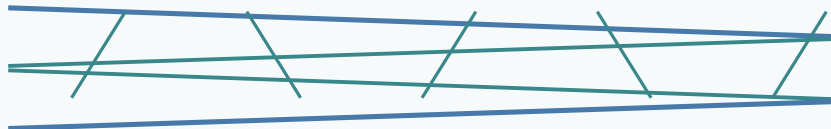
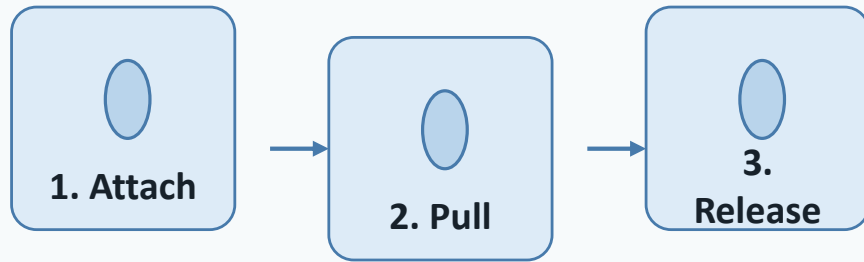
Migration occurs on a matrix substrate



Migration uses sequential matrix interactions

- Moving cells establish and release contacts with their extracellular environment.
- Traction is mechanically coupled to the actin cytoskeleton.
- Cell movement therefore depends on adhesion and cytoskeletal remodeling.

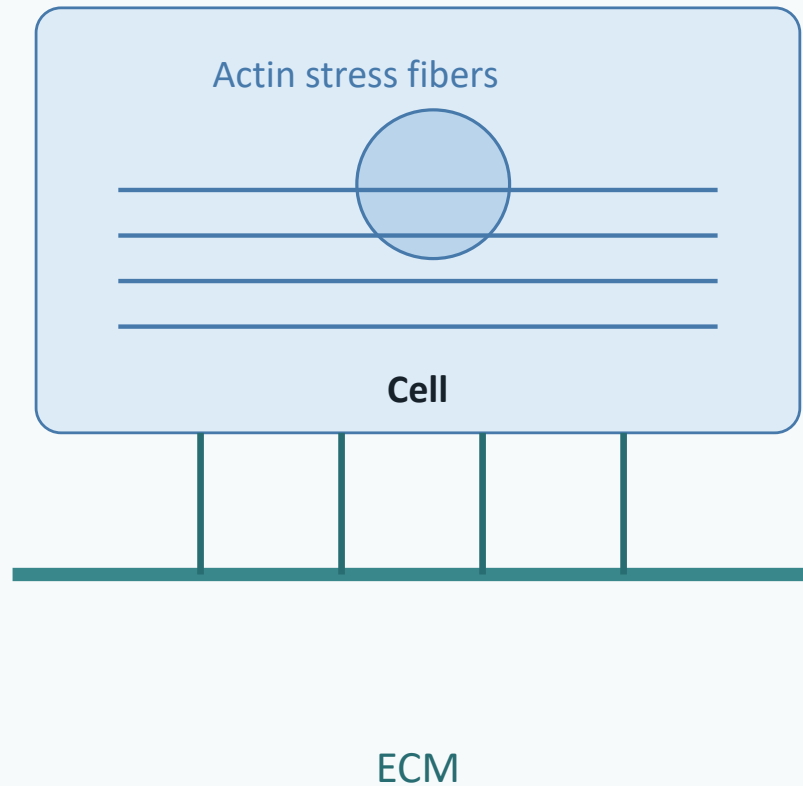
ECM supports both adhesion and motion



Migration uses sequential matrix interactions

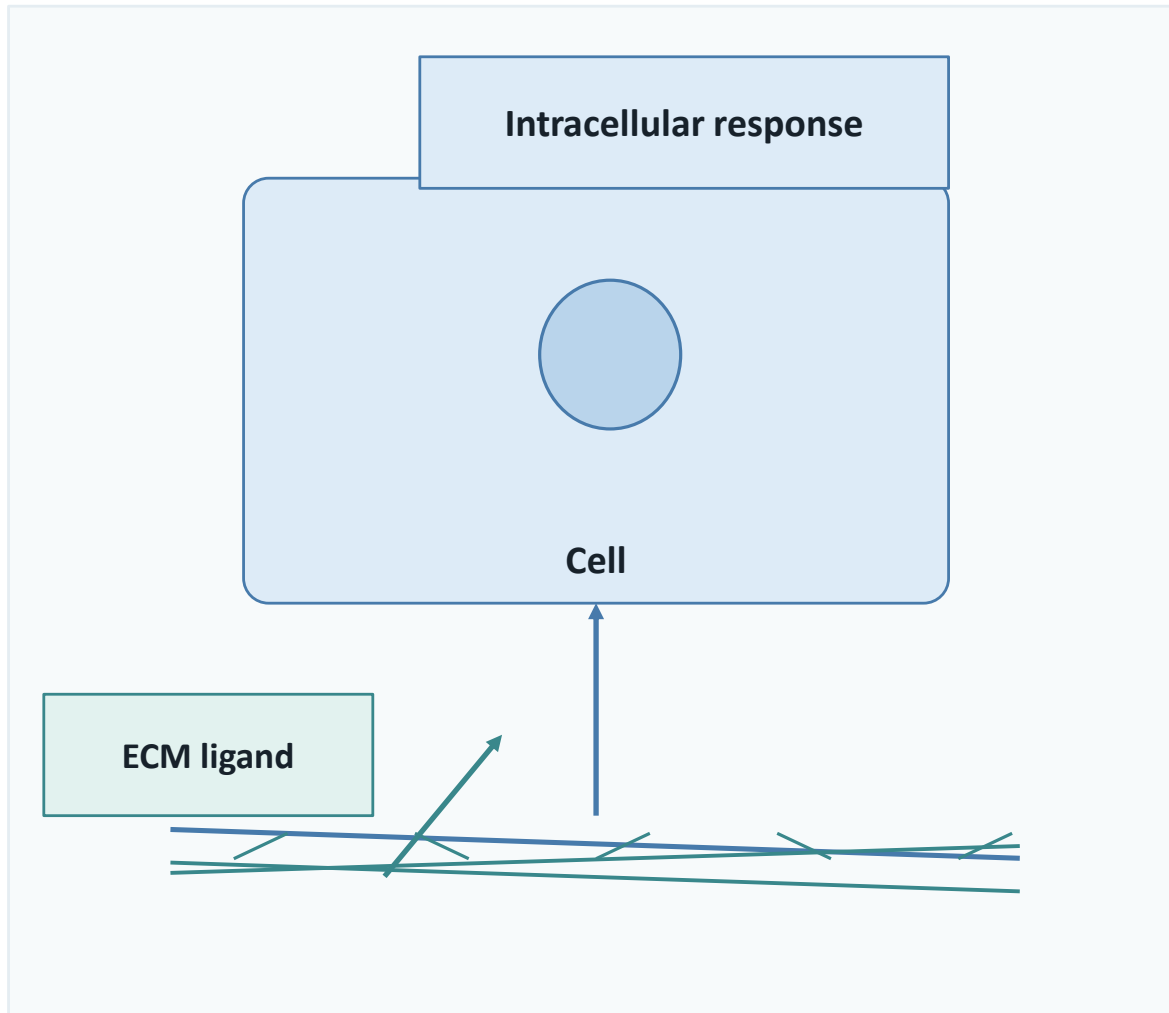
- Stable anchorage and motility are related but distinct cellular behaviors.
- Changing cell–matrix contact can permit movement without abolishing all attachment.
- The balance is important during development and tissue repair.

ECM transmits physical information



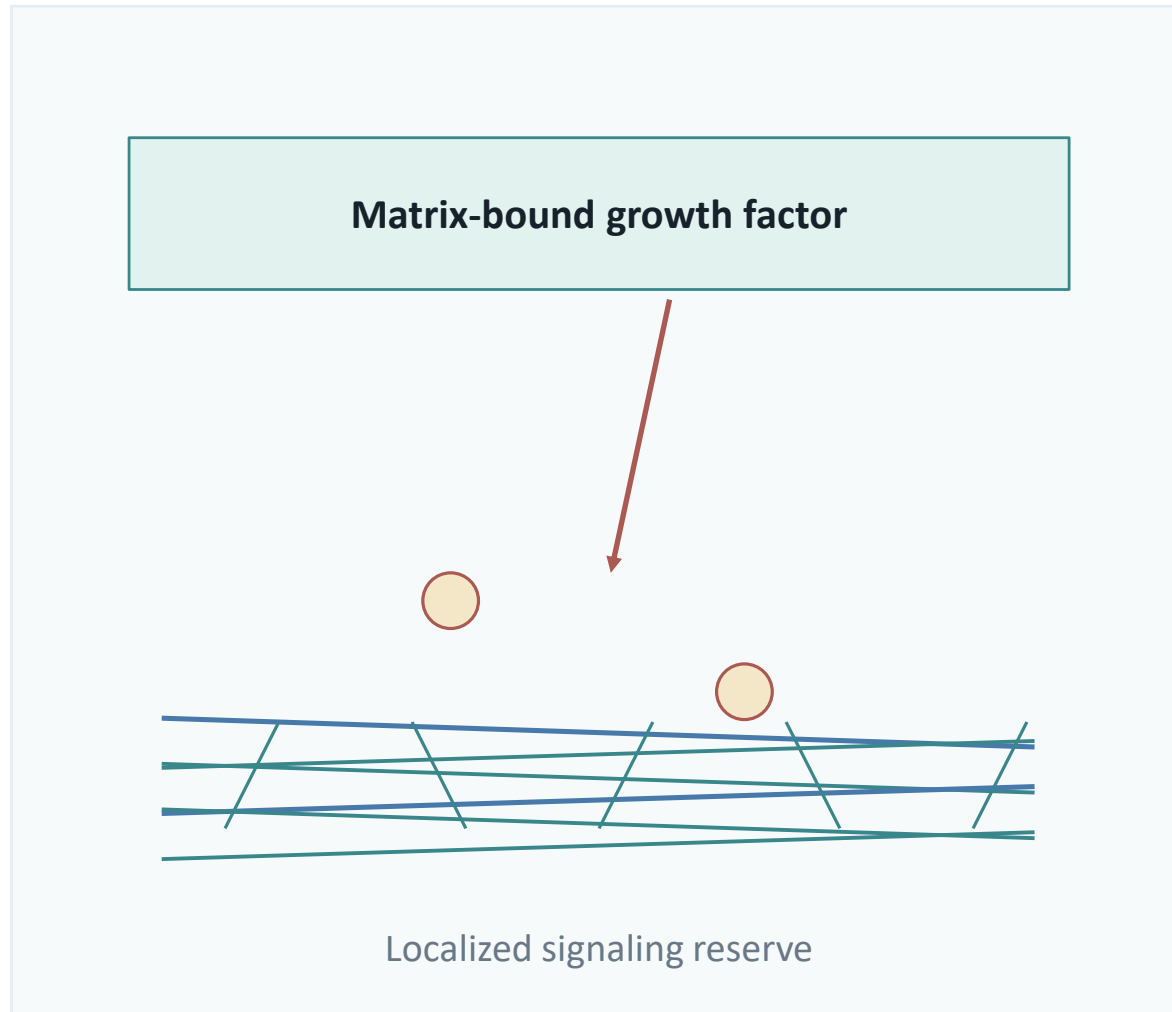
- Integrin-linked junctions couple extracellular structures to cell mechanics.
- Cytoskeletal changes can alter cell shape and movement.
- Mechanical and biochemical signaling are integrated rather than independent.

The ECM is also a signaling platform



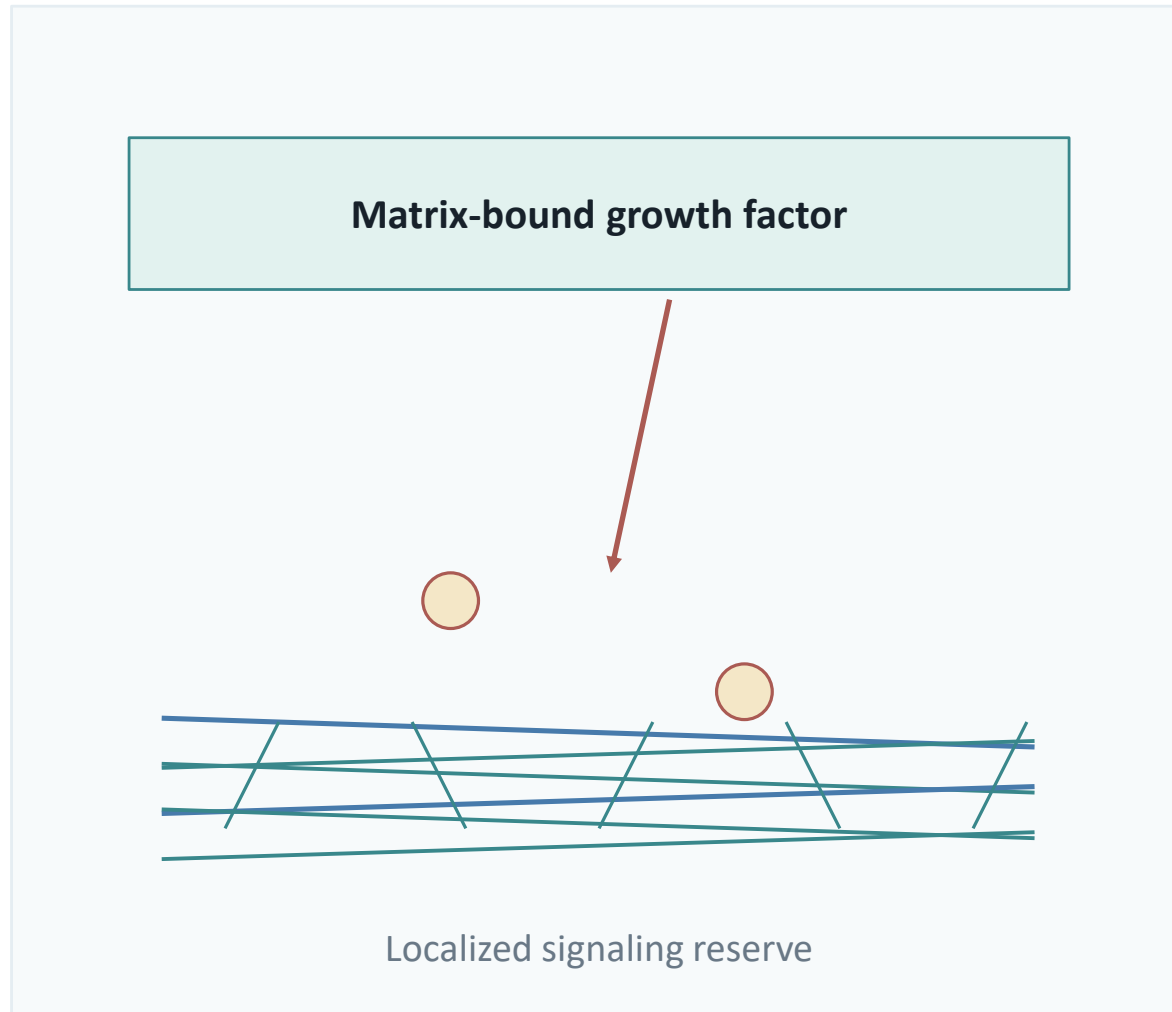
- Matrix ligands engage receptors that initiate intracellular signal transduction.
- This influences proliferation, differentiation, attachment, migration, and shape.
- The cellular response depends on concurrent growth-factor signals.

Growth factors can bind the matrix



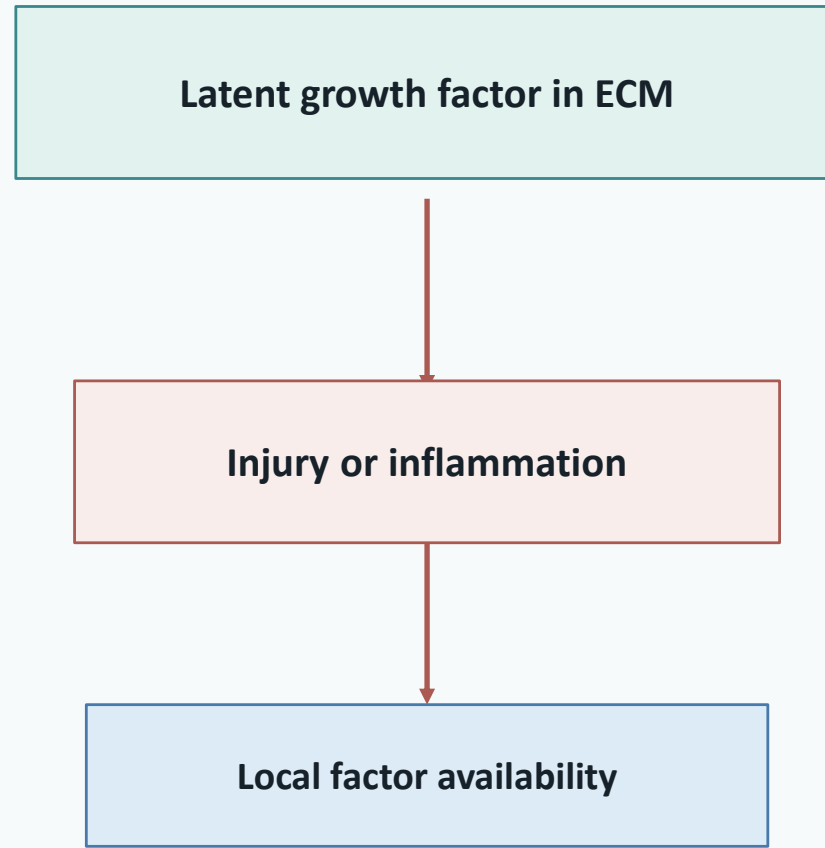
- The ECM can retain and present regulatory molecules near cells.
- Binding may localize growth factors within specific tissue compartments.
- Consequently, ECM organization influences signal availability.

Matrix acts as a growth-factor depot



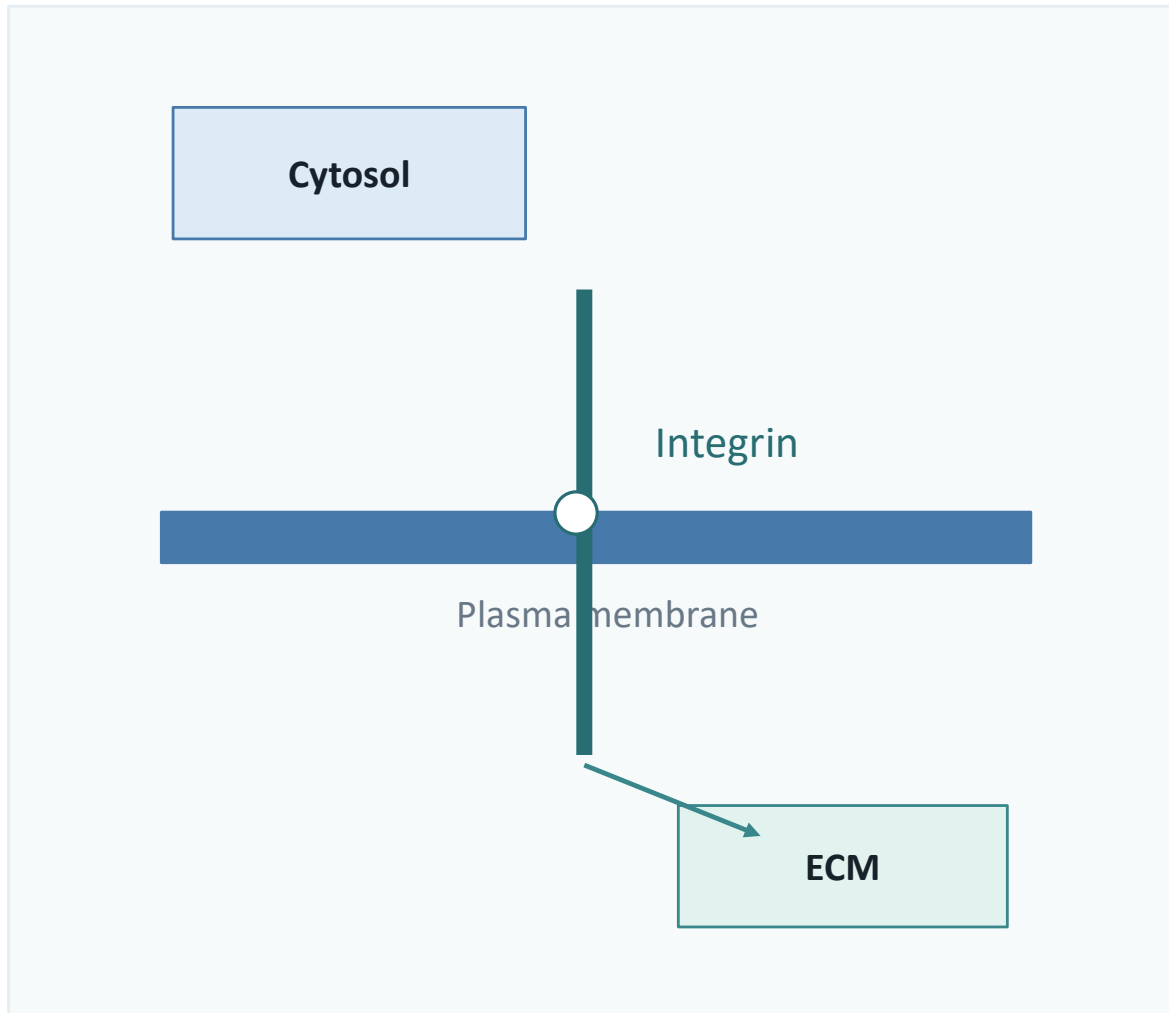
- Certain growth factors are stored in latent or matrix-bound forms.
- This reservoir can be mobilized when local tissue conditions change.
- The concept links structural injury to biochemical responses.

Injury can activate stored growth-factor signals



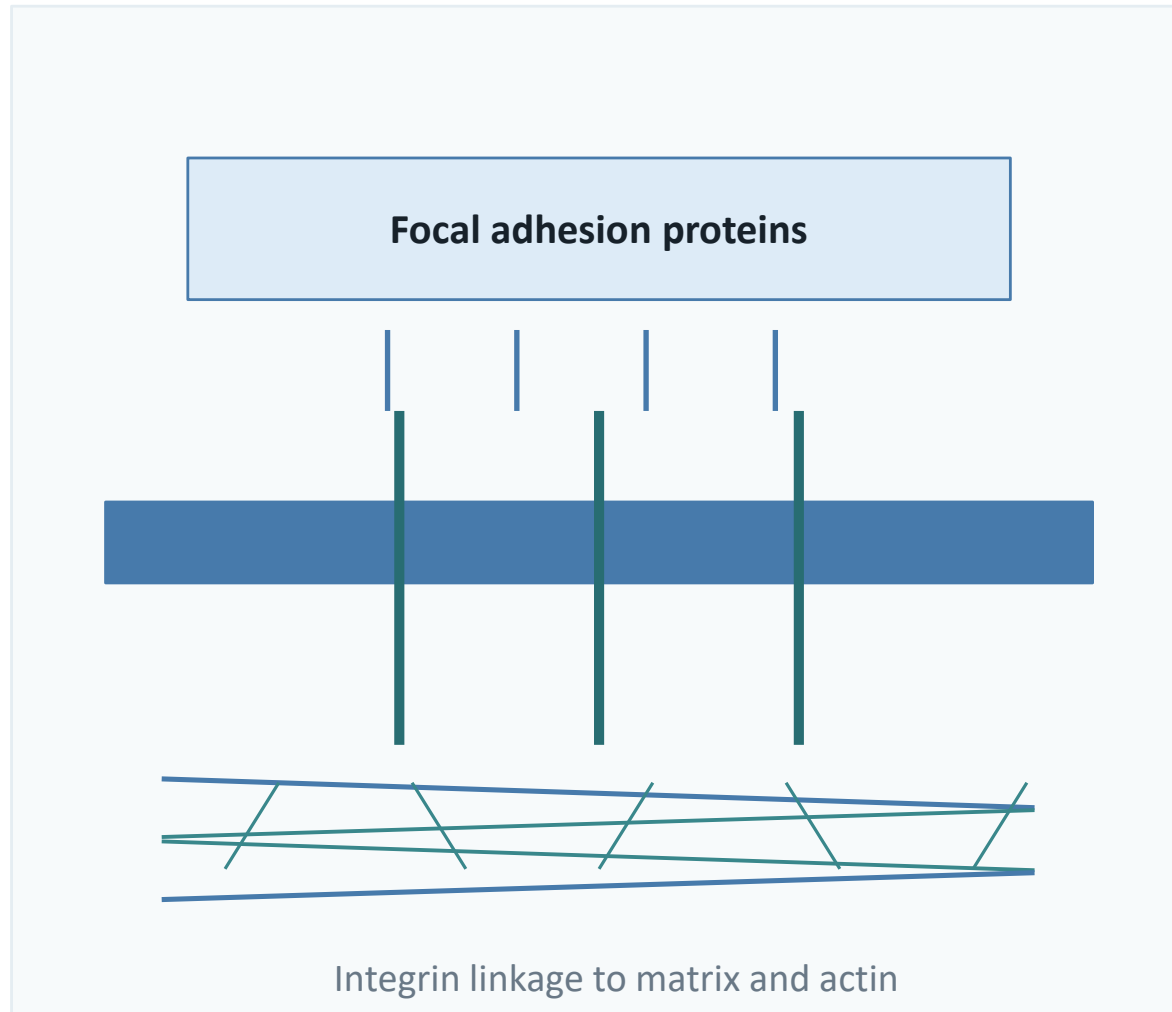
- Local injury and inflammation can activate growth factors held in the ECM.
- Signaling thus becomes spatially concentrated where remodeling is required.
- Anatomical matrix disruption changes both structure and regulatory signaling.

Integrins link ECM to the cell interior



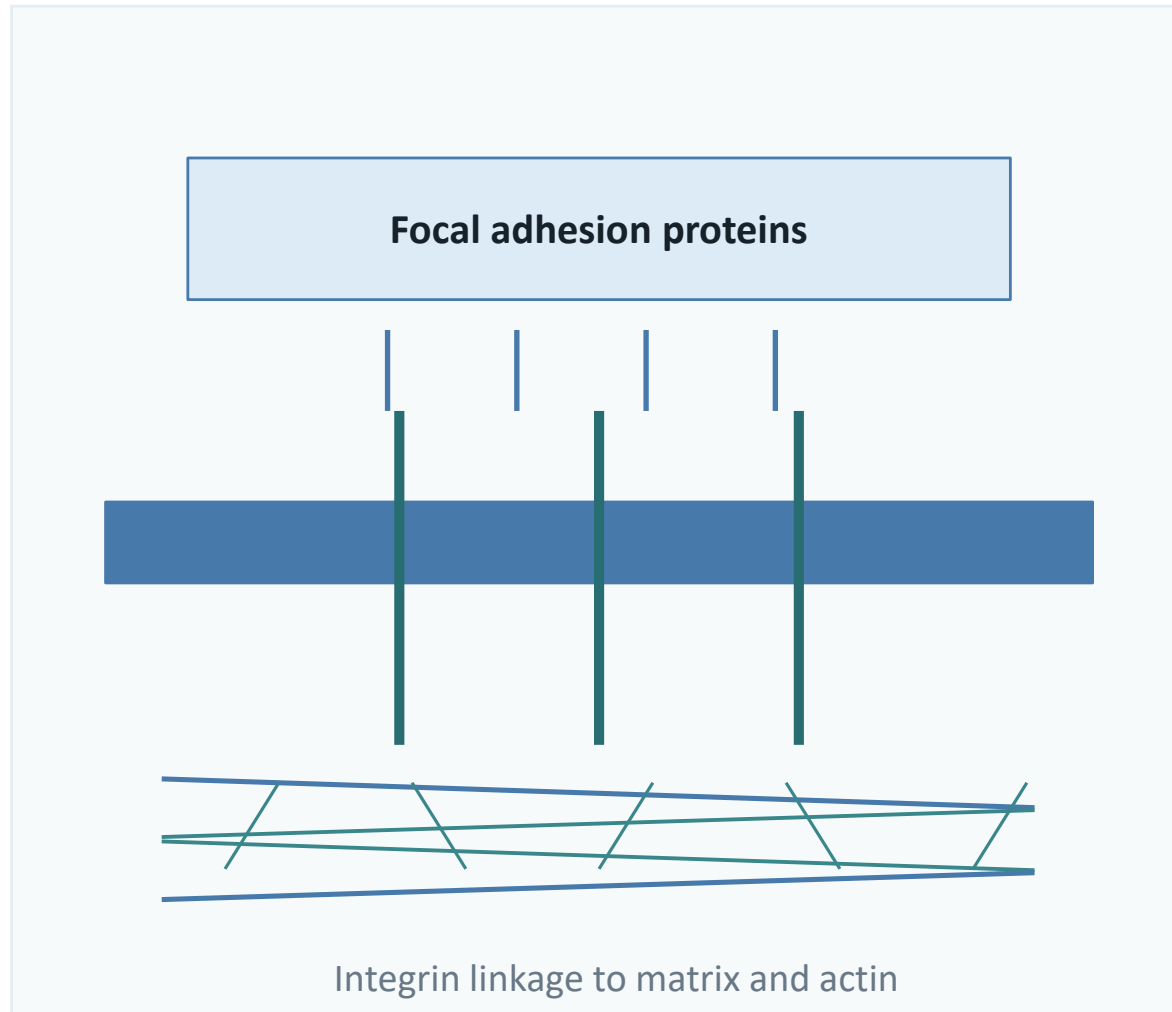
- Integrins are membrane-spanning receptors for extracellular matrix ligands.
- Their intracellular connections communicate with cytoskeletal components.
- Adhesion can therefore alter intracellular signaling, not merely attachment.

Focal adhesions couple receptors and cytoskeleton



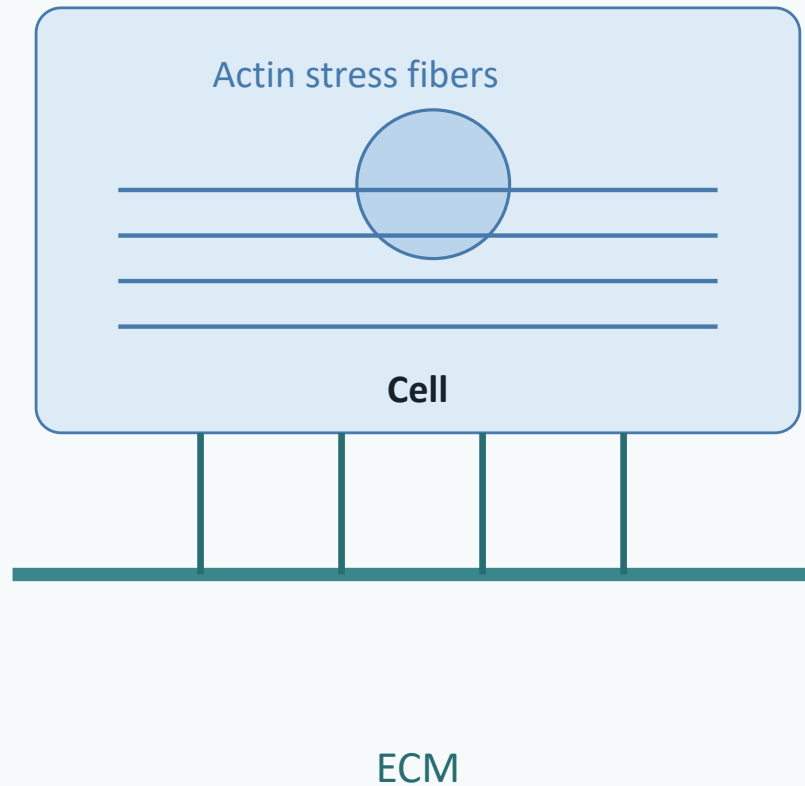
- Integrin-linked focal adhesions are multiprotein connection sites.
- They bridge ECM engagement with actin-based cytoskeletal structures.
- This arrangement supports both mechanical anchorage and signal transfer.

Focal adhesions contain adaptor proteins



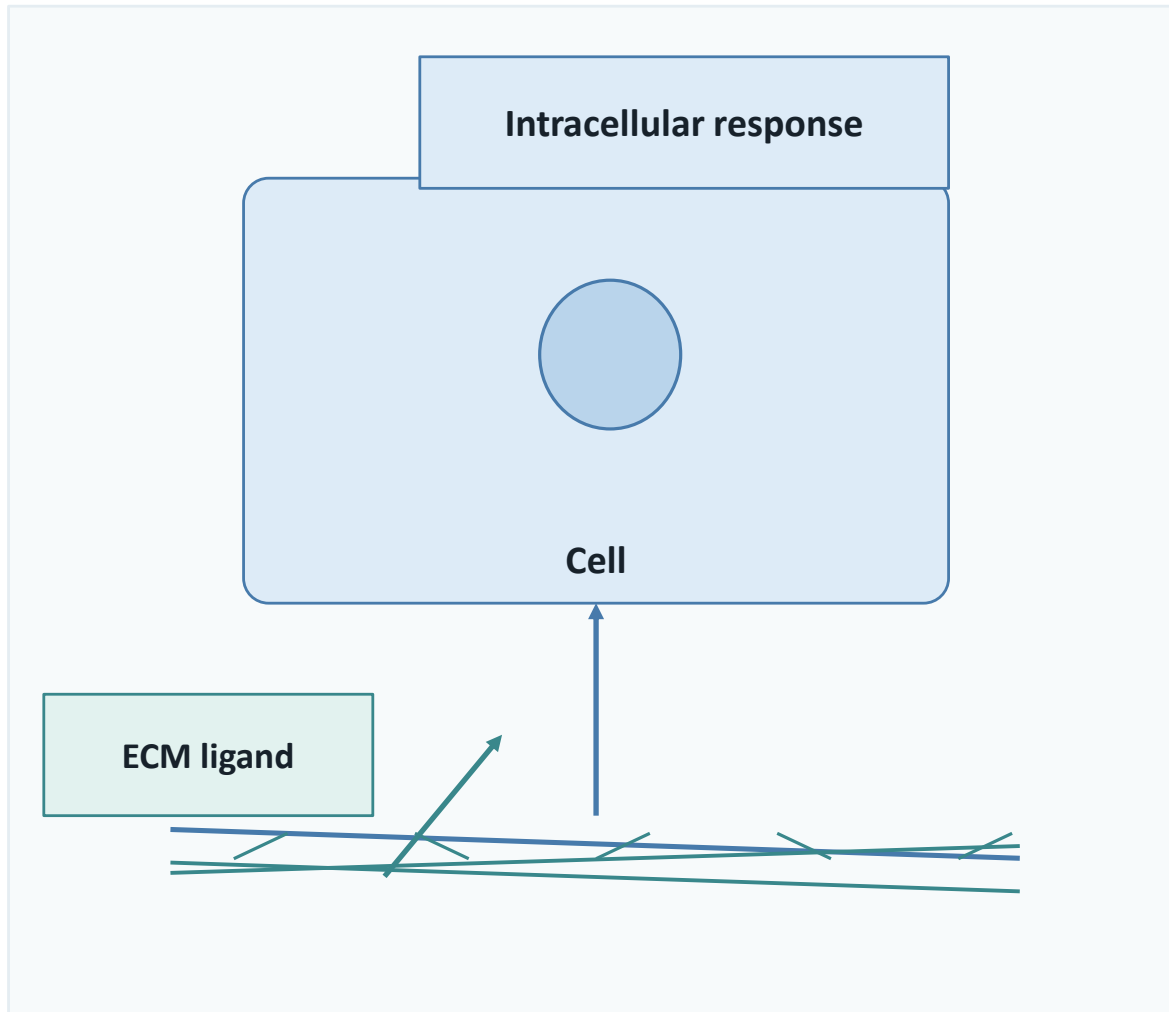
- Vinculin, α -actinin, and talin among focal adhesion components.
- Adaptor proteins help organize the connection between integrins and actin.
- Simplified diagrams represent functional relationships, not protein stoichiometry.

The actin cytoskeleton participates in ECM responses



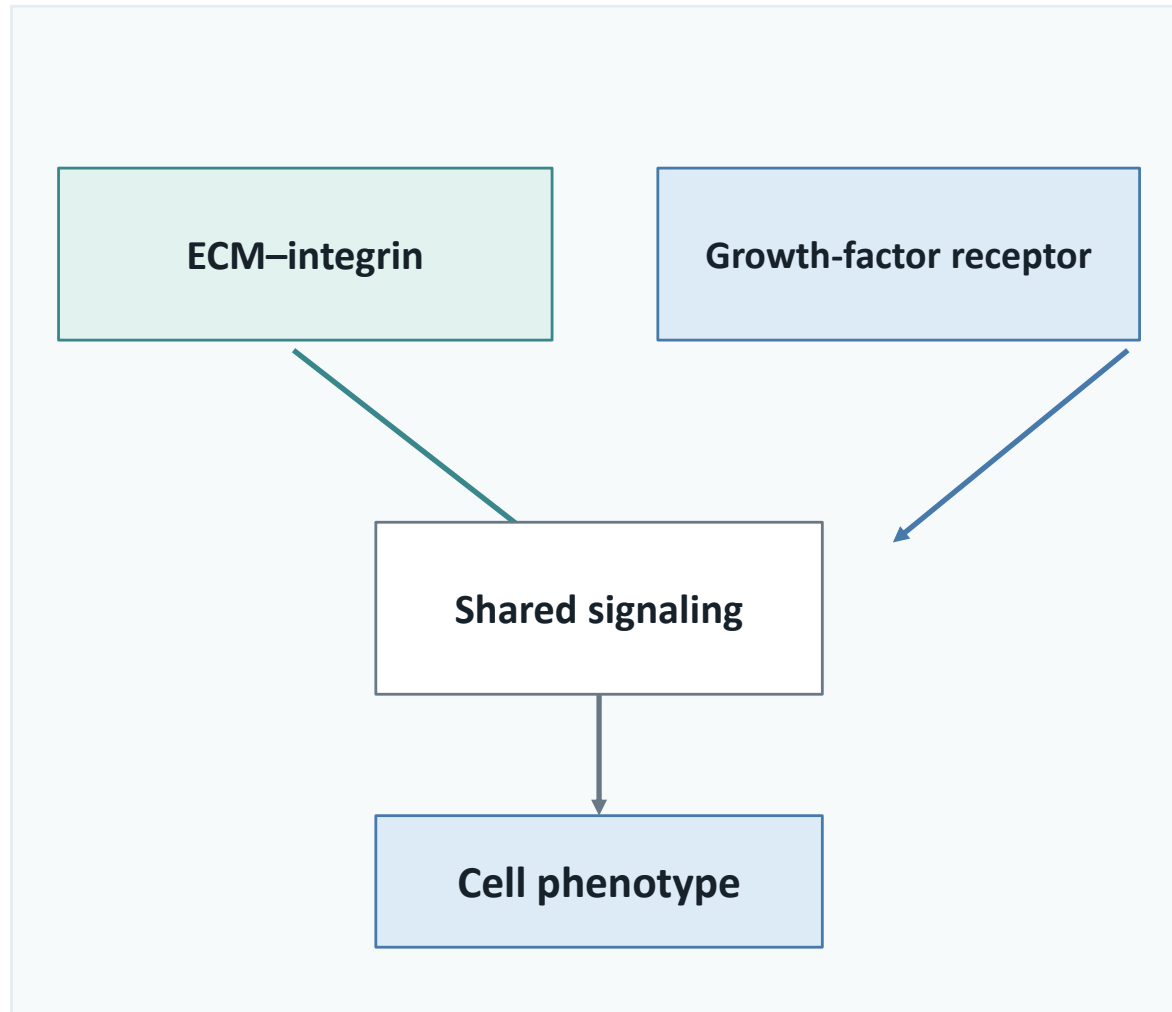
- ECM contacts alter cytoskeletal organization and cellular geometry.
- Actin-linked forces contribute to adhesion and directed movement.
- Changes at the cell surface can be propagated to intracellular pathways.

ECM receptor engagement produces intracellular signals



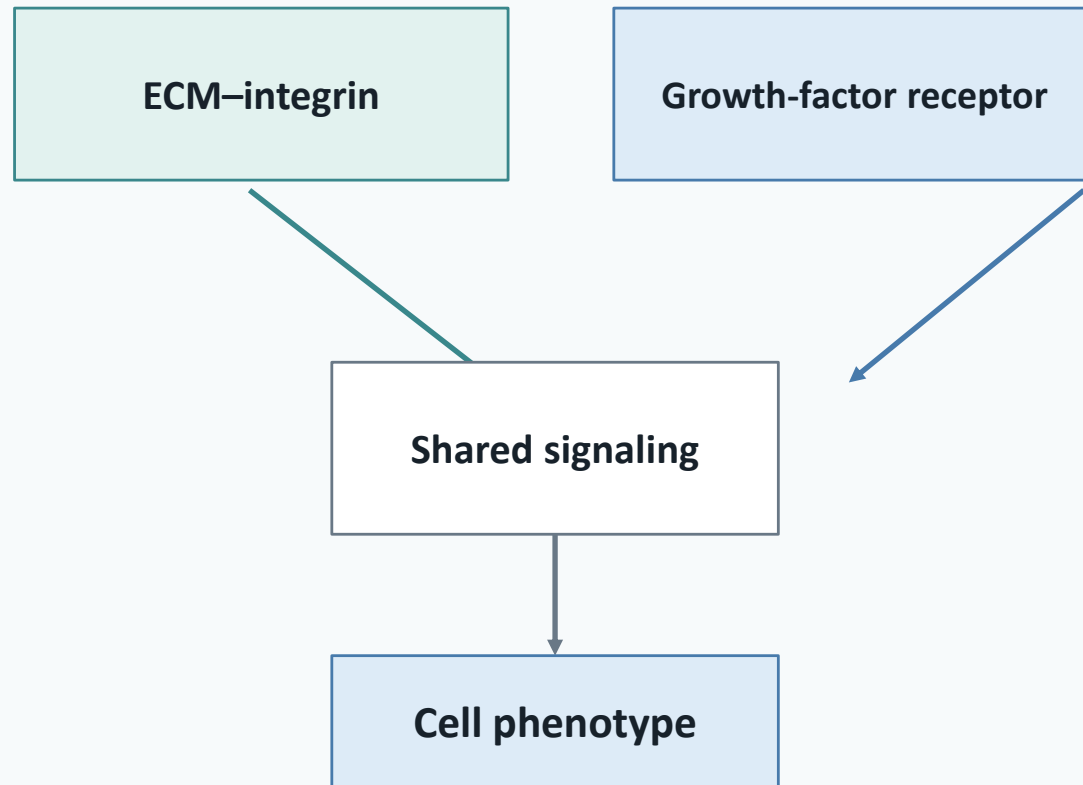
- Focal adhesion signaling generates intracellular messengers.
- Signals may influence cytoplasmic pathways or nuclear responses.
- The specific outcome depends on the cell and other activated receptors.

Growth-factor receptors provide a second input



- Cells also detect growth factors through their own membrane receptors.
- Growth-factor receptor signaling can overlap with integrin pathways.
- Neither pathway should be interpreted as operating in isolation.

ECM and growth-factor pathways converge



- Both matrix adhesion and soluble signals are integrated inside cells.
- Shared signaling routes can coordinate multiple phenotypic responses.
- An extracellular cue should be interpreted within its cellular context.

Integrated signals shape the cell phenotype

Integrated cellular signals

Possible cellular responses

Proliferation

Differentiation

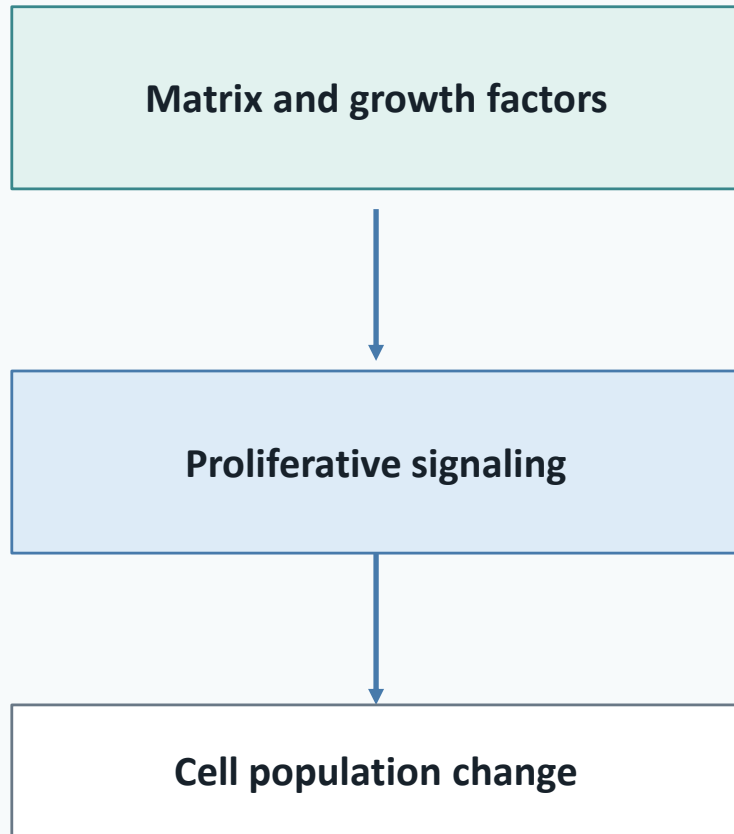
Migration

Protein synthesis

Shape and attachment

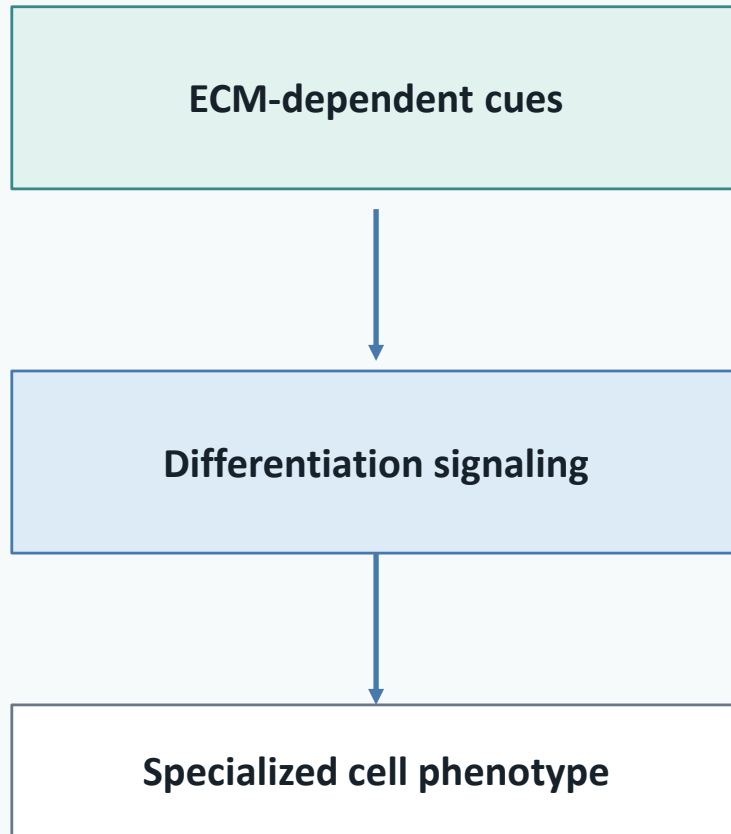
- Proliferation, differentiation, protein synthesis, attachment, migration, and shape change.
- These are distinct outputs, not obligatorily simultaneous responses.
- The ECM influences the decision space within which cells respond.

Proliferation is sensitive to matrix context



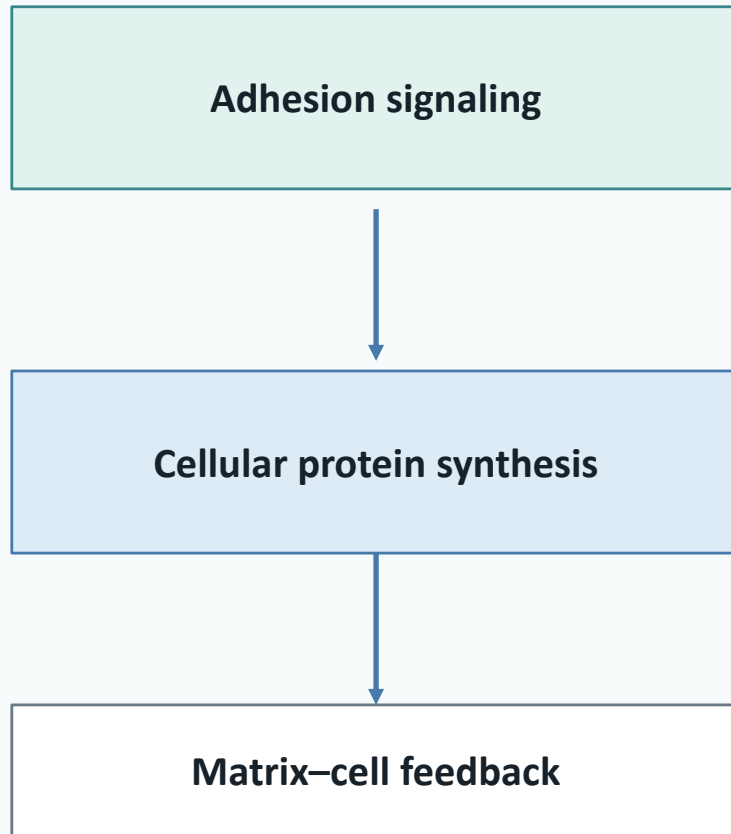
- Matrix engagement contributes to regulation of proliferative signaling.
- Growth-factor presentation and integrin input are complementary.
- Cell proliferation is thus partly constrained by tissue microenvironment.

Differentiation reflects contextual signaling



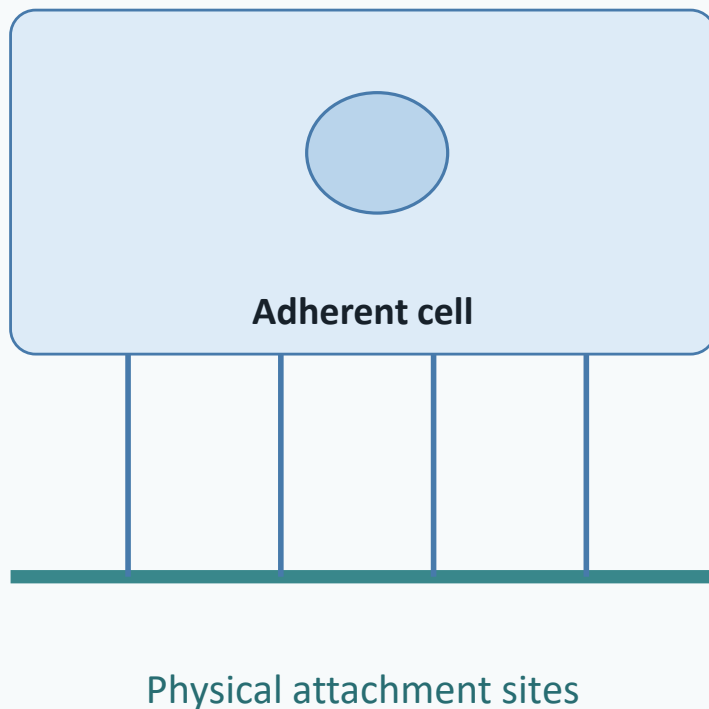
- ECM contacts can modulate pathways involved in cell differentiation.
- Cell fate responses depend on the combined extracellular cue profile.
- The same matrix principle applies during development and renewal.

Protein synthesis can respond to ECM cues



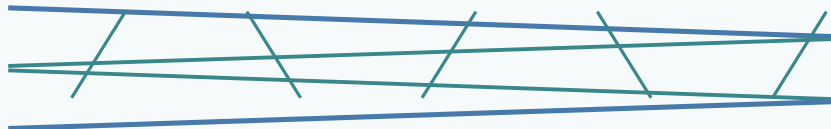
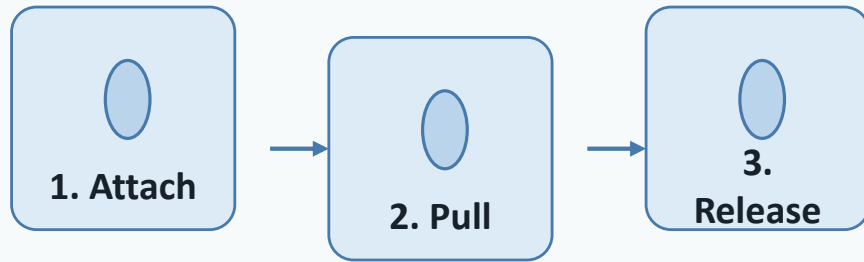
- Signal transduction initiated at cell–matrix interfaces can alter biosynthetic behavior.
- Cellular responses include changes in protein synthesis.
- ECM is therefore involved in feedback between cells and their environment.

Attachment and cell shape are regulated outputs



- Cell shape depends on the physical arrangement of matrix contacts.
- Cytoskeletal signaling couples substrate attachment to geometry.
- Changes in adhesion can affect morphology without changing cell identity.

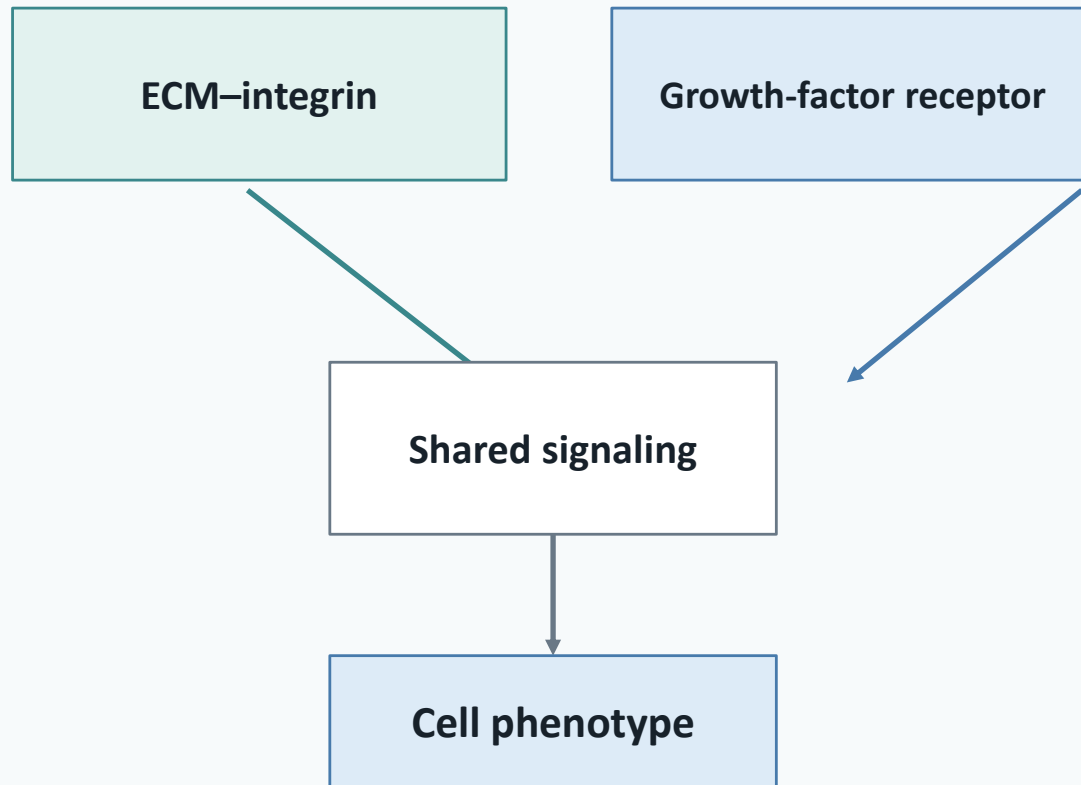
Locomotion integrates adhesion and signaling



Migration uses sequential matrix interactions

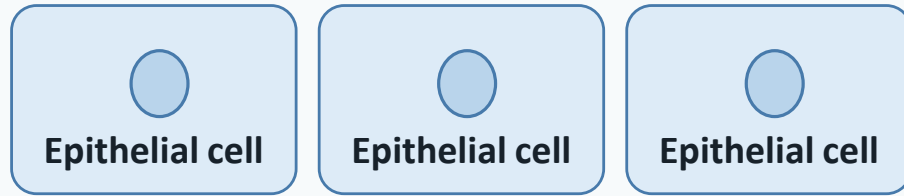
- Migration requires matrix interaction and coordinated internal movement.
- Cell-surface receptors transduce environmental signals during locomotion.
- This underlies controlled repositioning during normal tissue dynamics.

Mechanism exercise: Two converging inputs

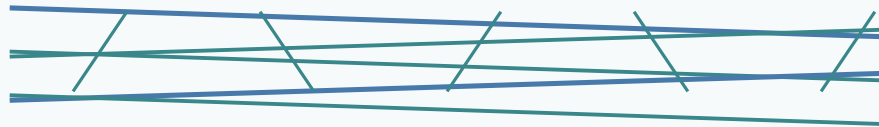


- A cell receives ECM signals through integrins and growth-factor signals through their receptors.
- The pathways overlap before generating a context-dependent response.
- Predicting phenotype from only one input can be misleading.

ECM is a scaffold for tissue renewal



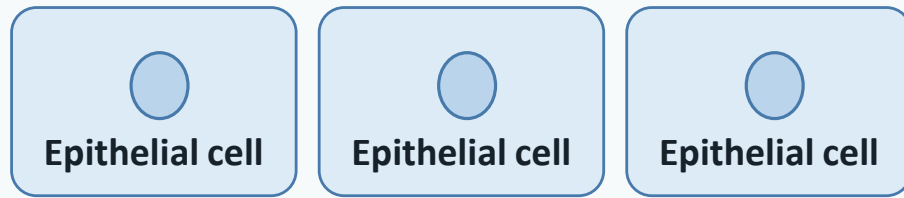
Continuous basement membrane



Maintained spatial template for growth

- Organized regeneration requires an existing basement membrane or stromal framework.
- The scaffold helps maintain the geometry of parenchymal cell replacement.
- Architectural integrity is therefore a determinant of effective repair.

Basement membrane preservation favors order

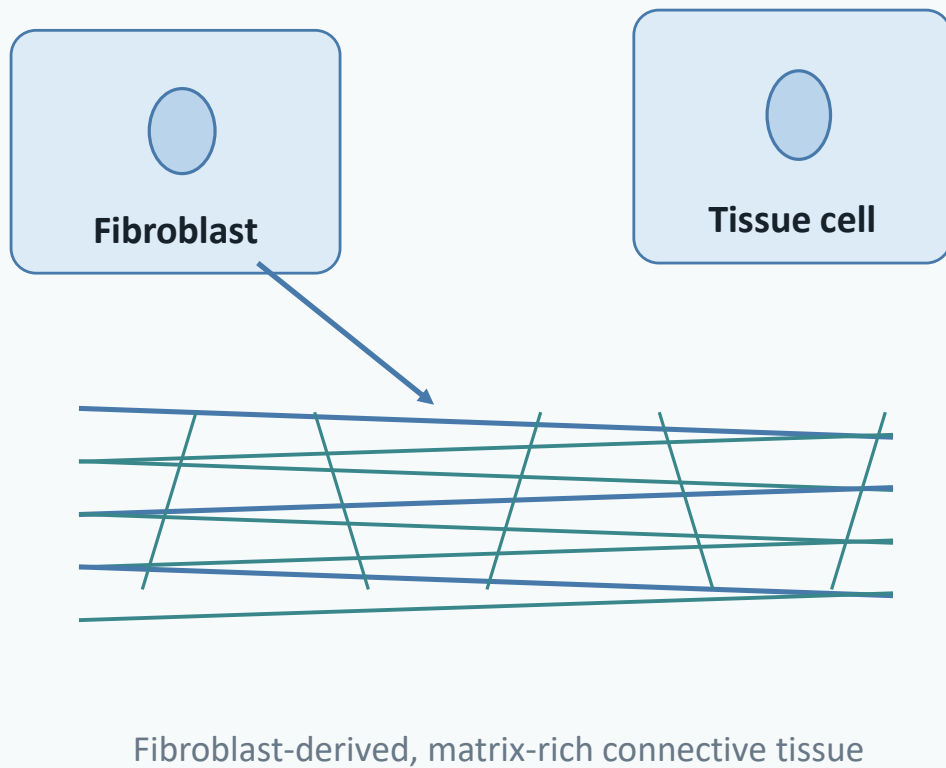


Continuous basement membrane

Maintained spatial template for growth

- An intact cellular supporting plane provides spatial guidance.
- Preserved boundaries help renewing cells reconstruct original relationships.
- Its importance is architectural as well as biochemical.

Stromal scaffolds also direct regeneration

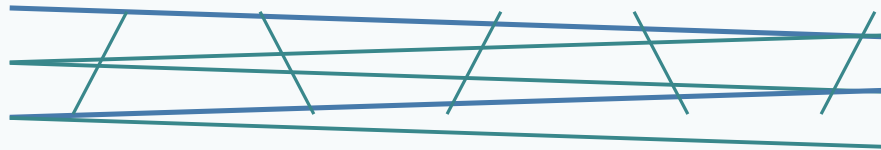


- Matrix networks between supporting cells preserve organ-scale arrangement.
- Regenerated cells need a coherent extracellular setting.
- Loss of stromal organization impairs reconstruction of normal tissue.

Matrix disruption can impair regeneration



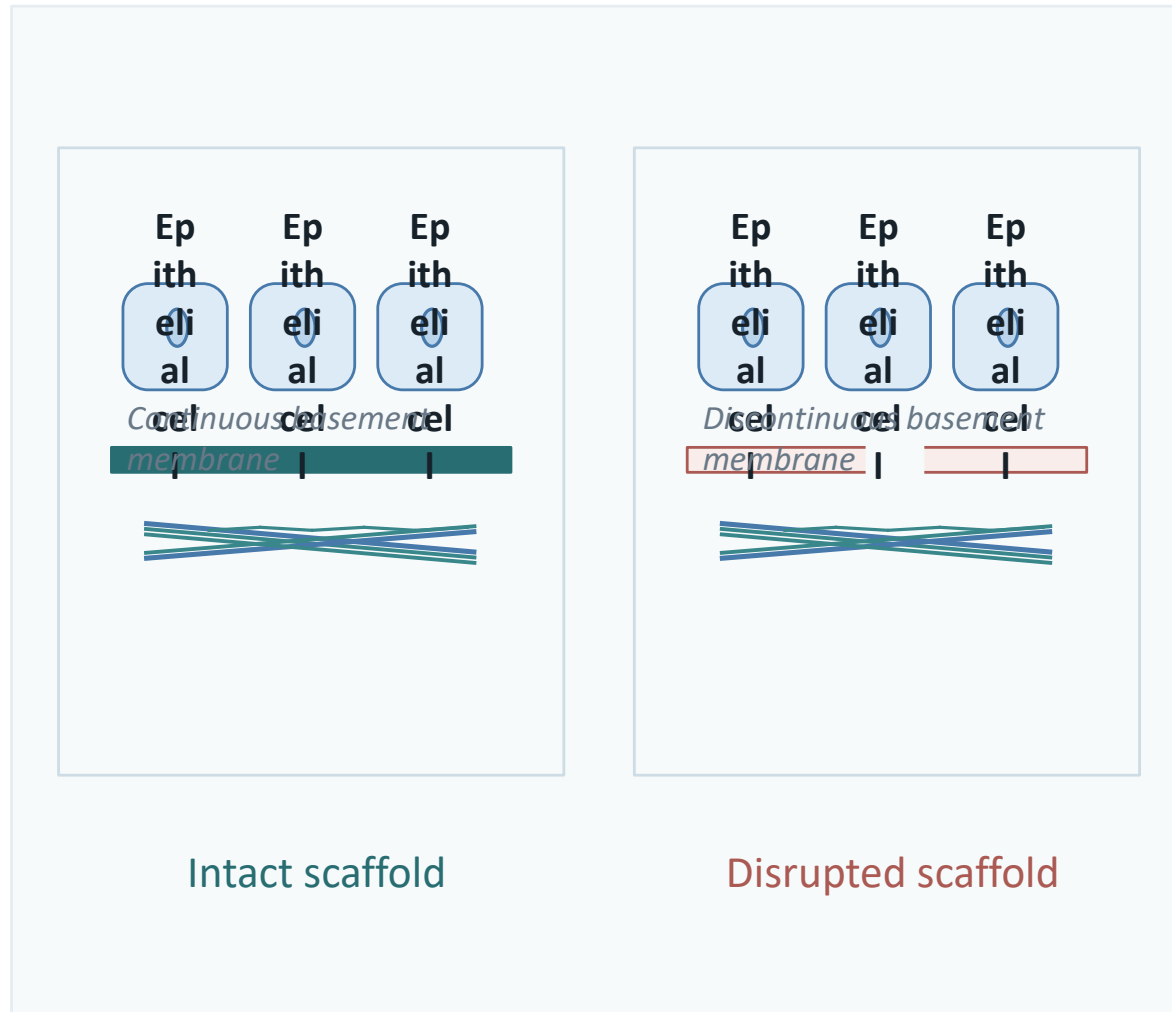
Discontinuous basement membrane



Loss of matrix continuity

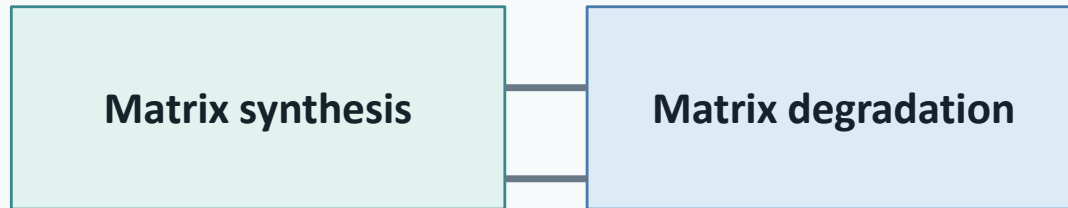
- If the scaffold is destroyed, proliferating cells may not reconstruct normal architecture.
- Tissue repair can restore continuity without fully restoring prior organization.
- Anatomical integrity and cellular survival are separate questions.

Intact versus disrupted matrix: Repair trajectory



- Preserved basement/stromal structure offers a template for organized cell replacement.
- Disrupted scaffolding weakens spatial cues during tissue renewal.
- This helps explain why injury severity includes damage to the matrix.

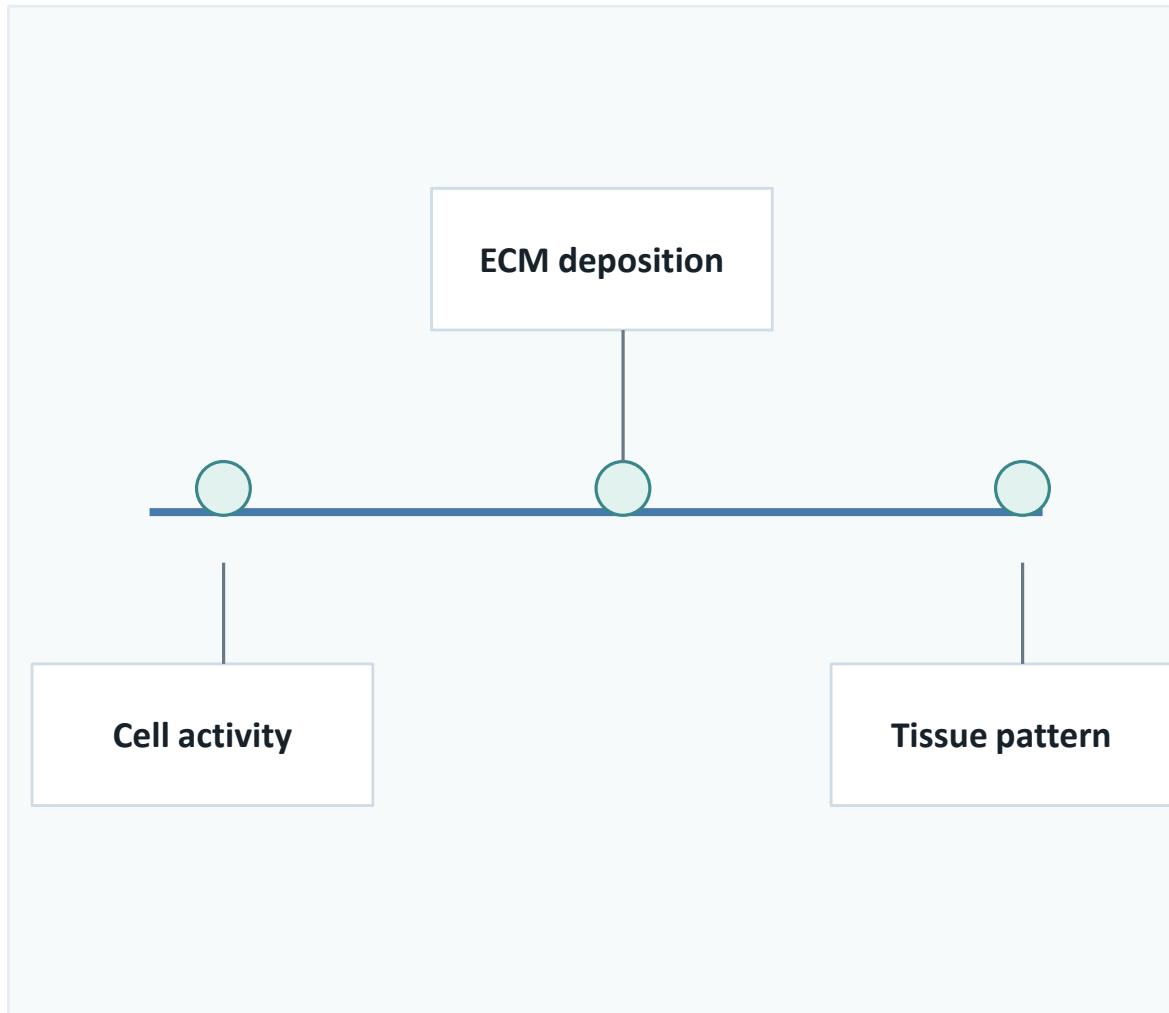
Matrix remodeling is a balance of processes



Dynamic tissue architecture

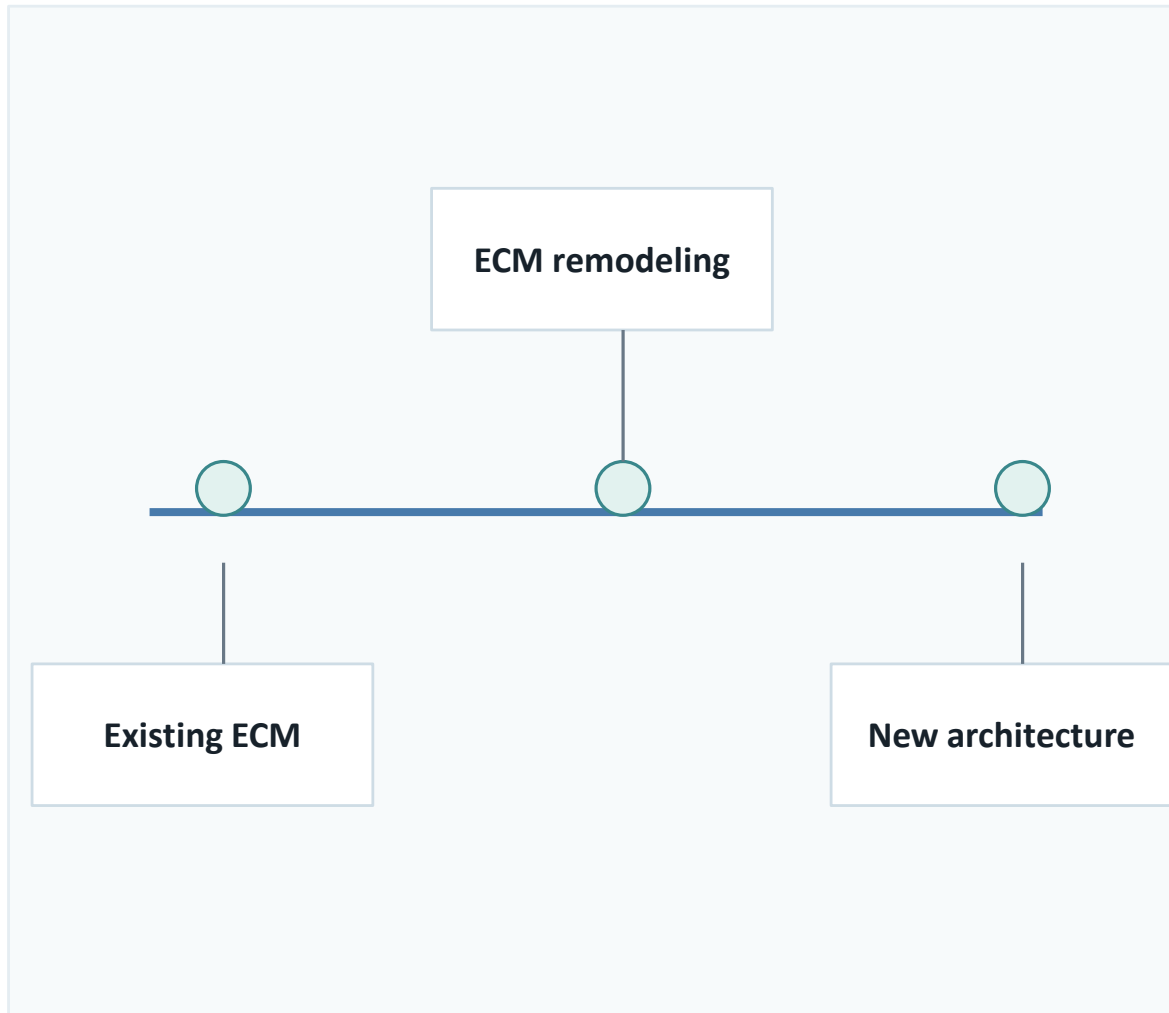
- ECM is continuously formed and broken down.
- Synthesis and degradation accompany normal and pathological tissue change.
- Net matrix abundance alone does not describe its organization or function.

ECM synthesis changes tissue architecture



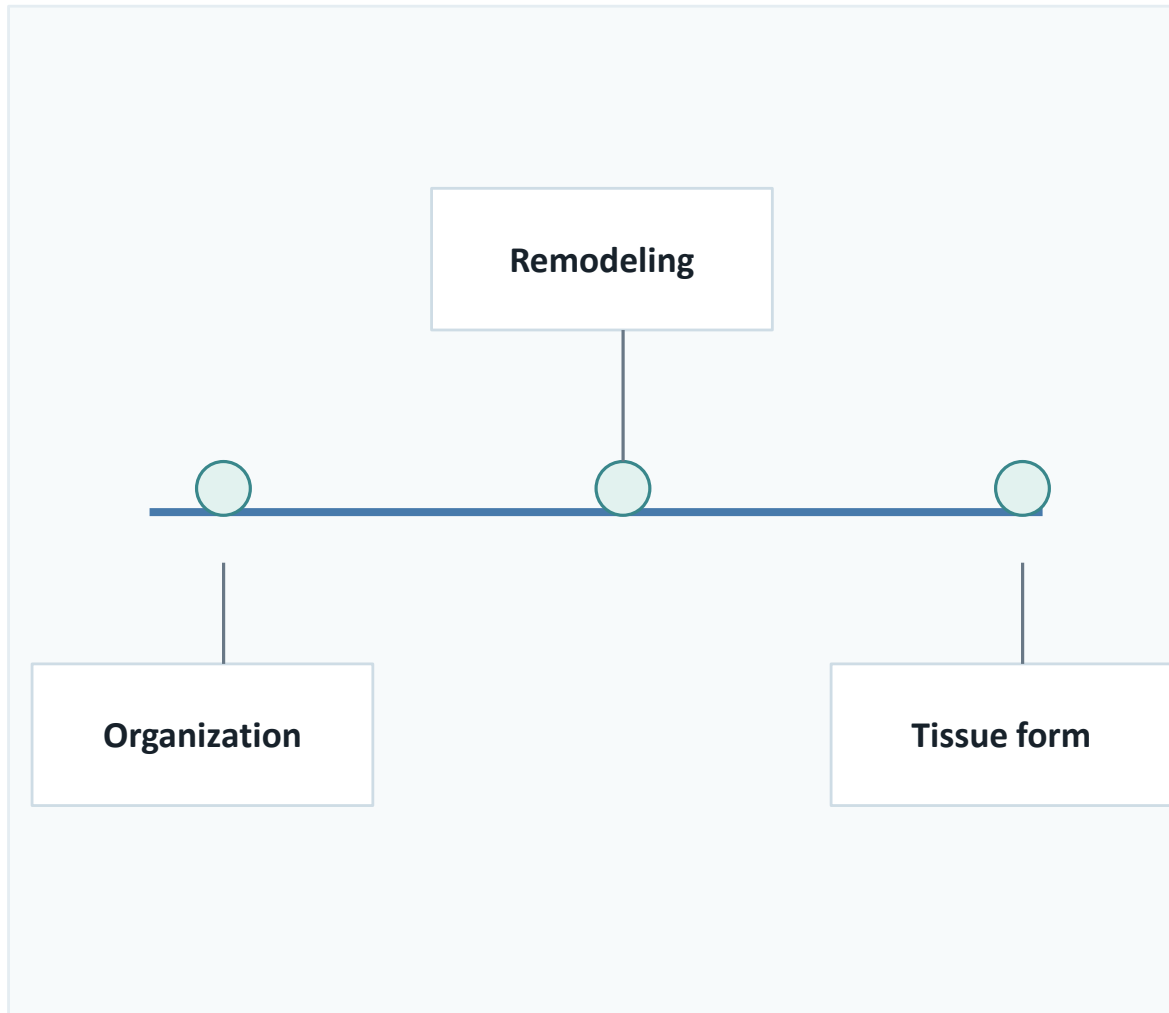
- Matrix-producing cells deposit extracellular constituents into defined compartments.
- New deposition contributes to tissue growth and rebuilding.
- Its functional value depends on appropriate composition and spatial arrangement.

ECM degradation can permit reorganization



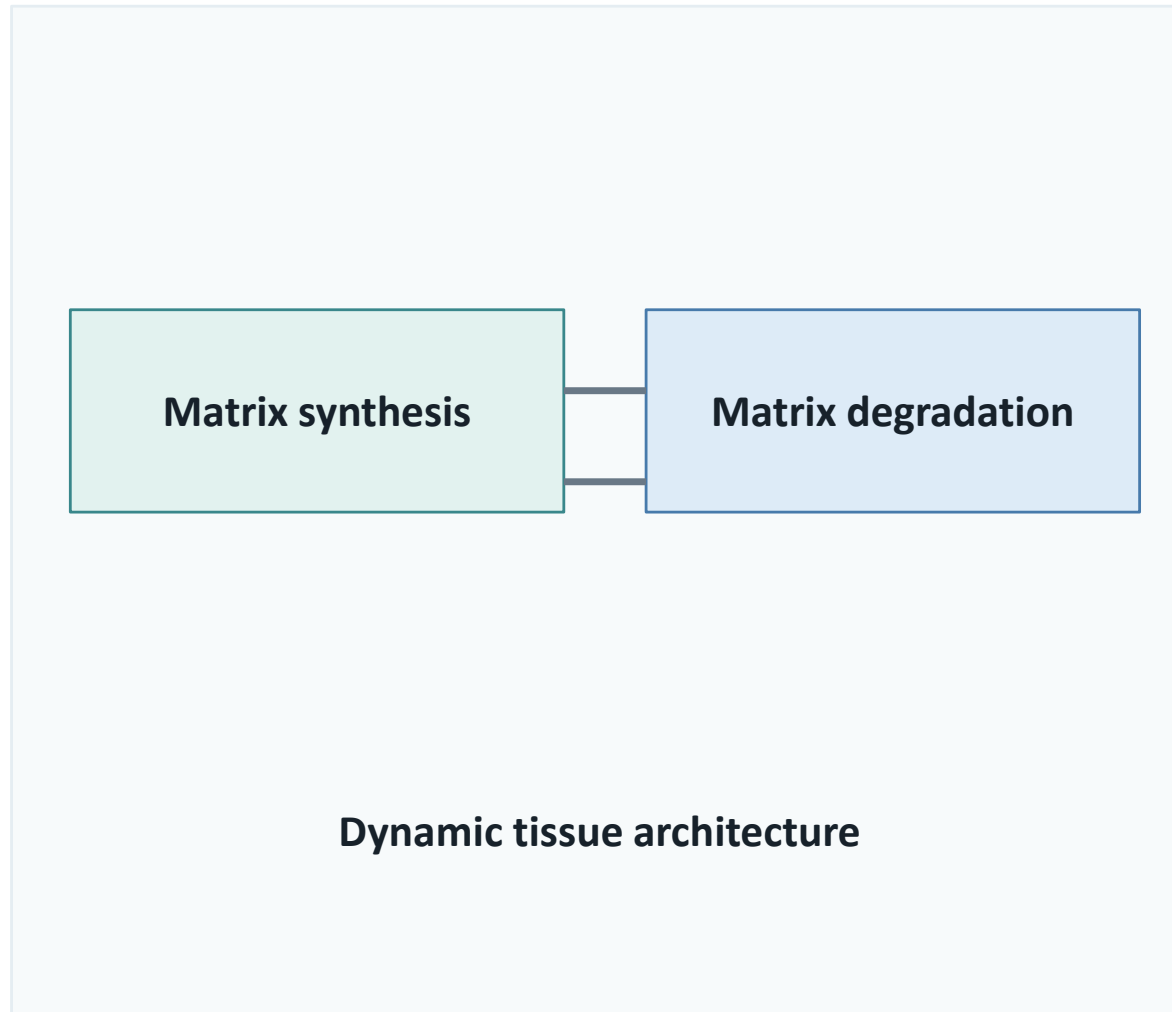
- Matrix turnover removes or changes pre-existing extracellular structures.
- Reorganization creates opportunities for cell movement and tissue restructuring.
- Unbalanced degradation may compromise scaffold integrity.

Morphogenesis requires matrix remodeling



- Development entails coordinated cell movement and changing extracellular architecture.
- The ECM supplies both a substrate and signals for these processes.
- Synthesis and degradation accompany the formation of tissue structures.

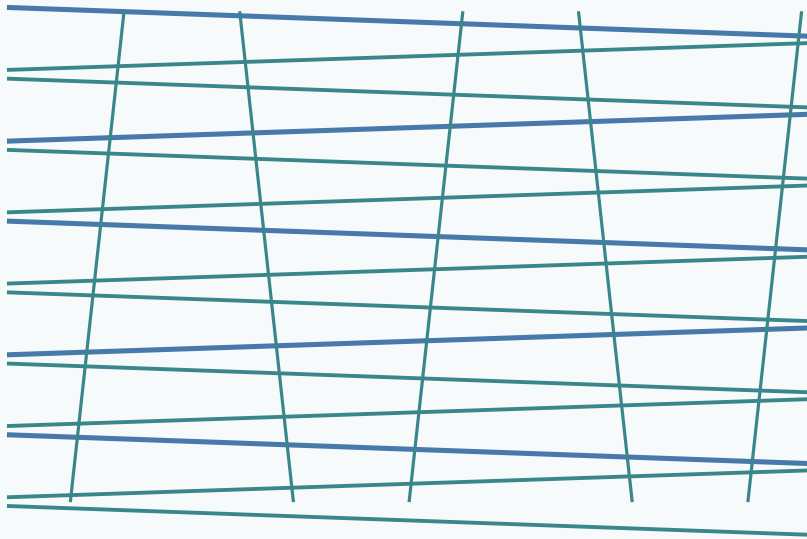
Repair involves dynamic changes in the ECM



- Following injury, matrix composition and organization evolve over time.
- Regeneration benefits from preserved supporting structures.
- Excess or disordered remodeling may alter final tissue form.

Persistent ECM accumulation is relevant to fibrosis

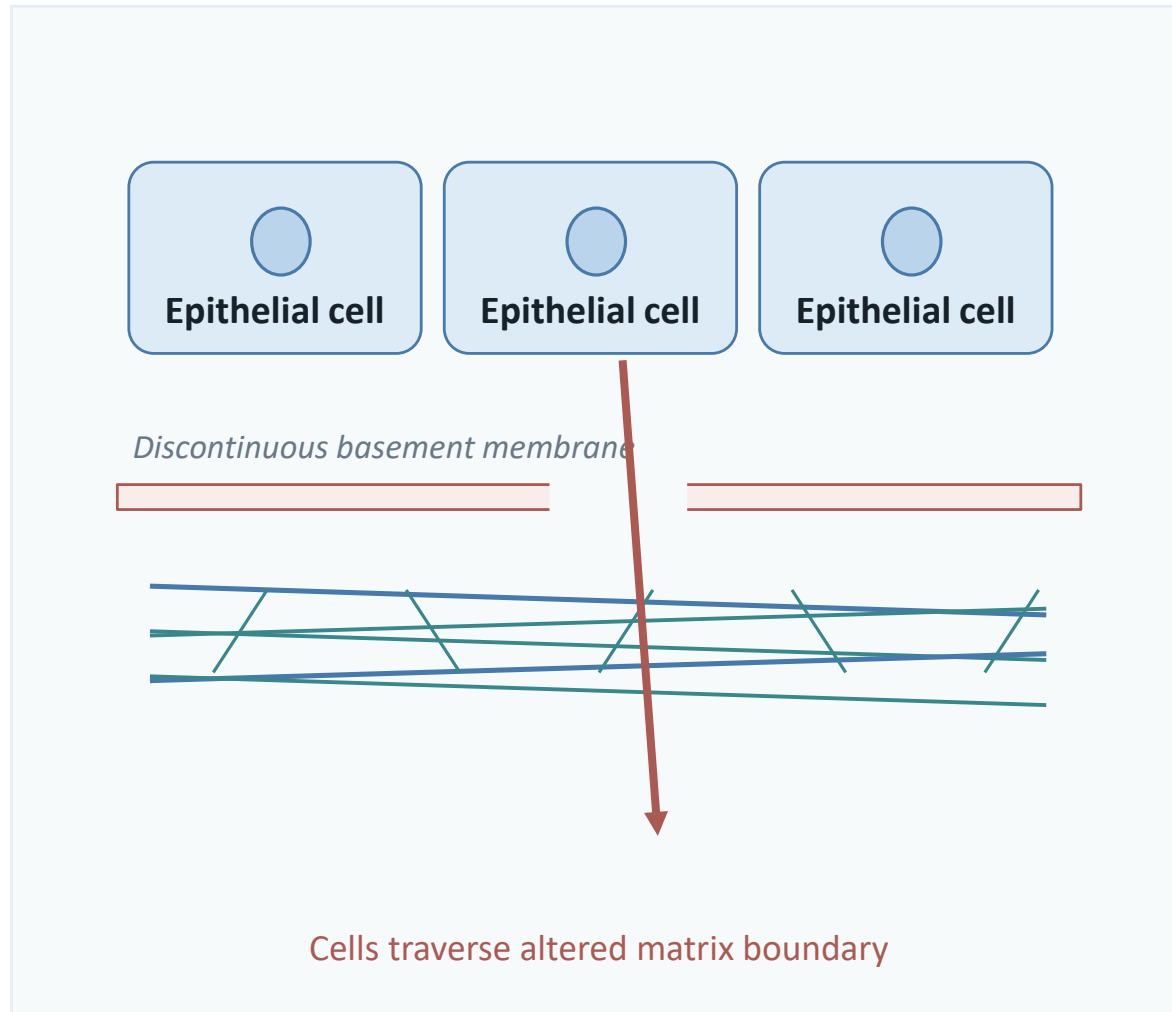
Excess matrix accumulation



Altered tissue architecture

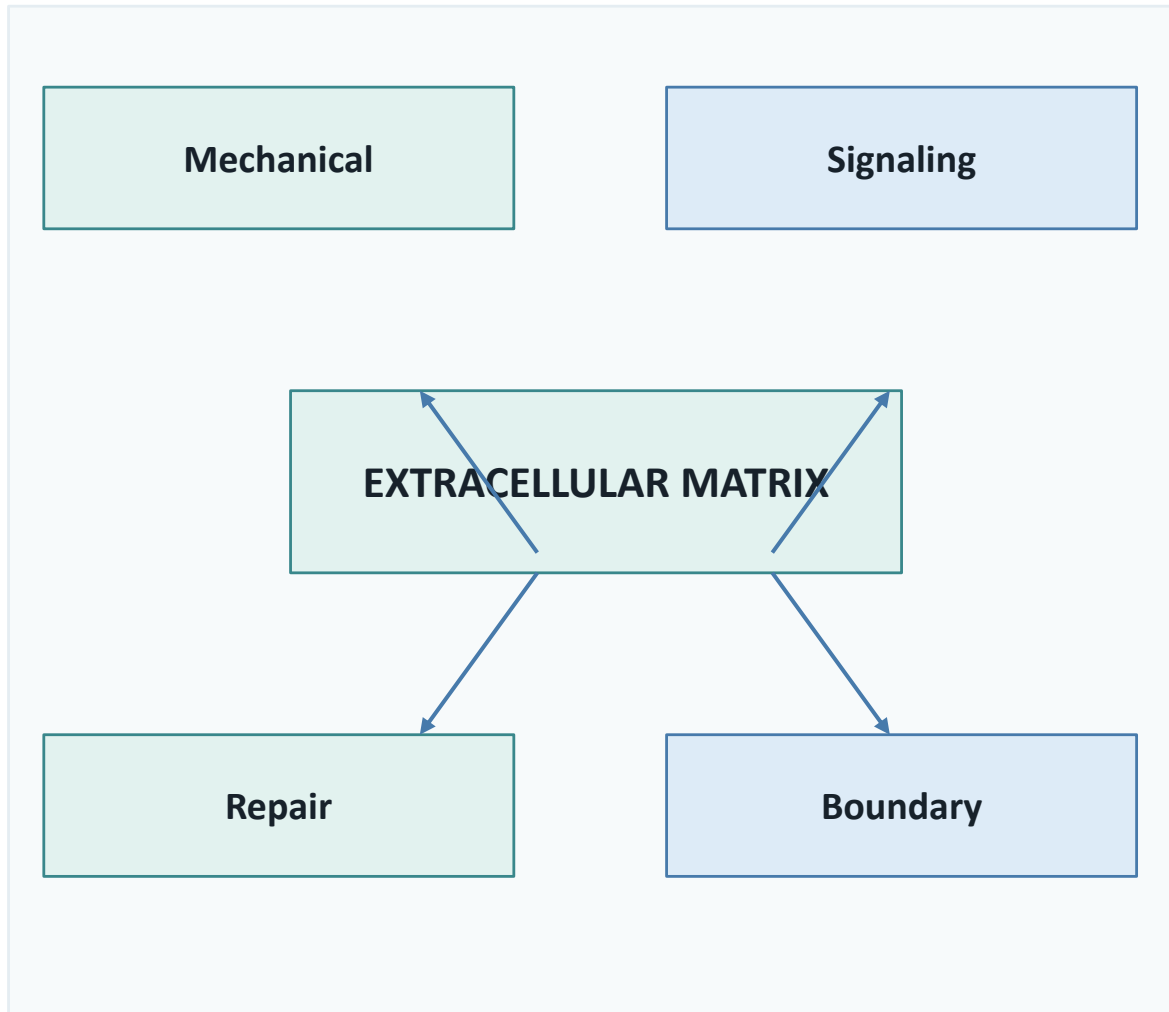
- Chronic fibrosis is associated with abnormal matrix remodeling and deposition.
- Accumulated ECM can alter the relationships between parenchymal and stromal cells.
- Fibrosis illustrates how a necessary repair mechanism can become pathological.

ECM remodeling also participates in tumor invasion



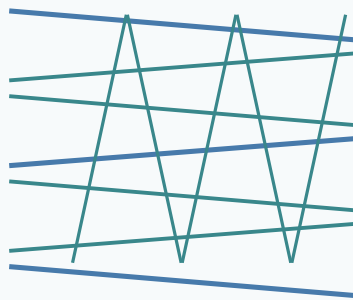
- Tumor invasion requires interactions with the extracellular environment.
- Matrix organization and degradation are relevant to movement across tissue boundaries.
- The source links ECM remodeling with invasion and metastasis.

A change in ECM can have several consequences

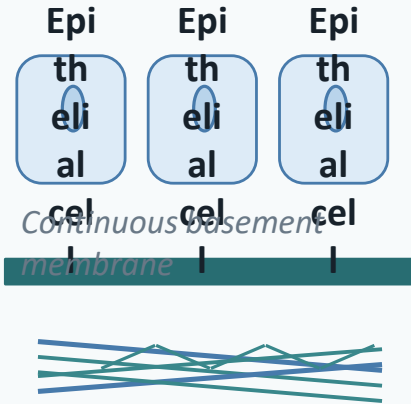


- Mechanical behavior, receptor signaling, and renewal capacity may change together.
- Interpret injury as a cell–matrix system rather than a cellular event alone.
- Identical cell damage may have different outcomes when the scaffold differs.

The ECM has two major anatomical forms



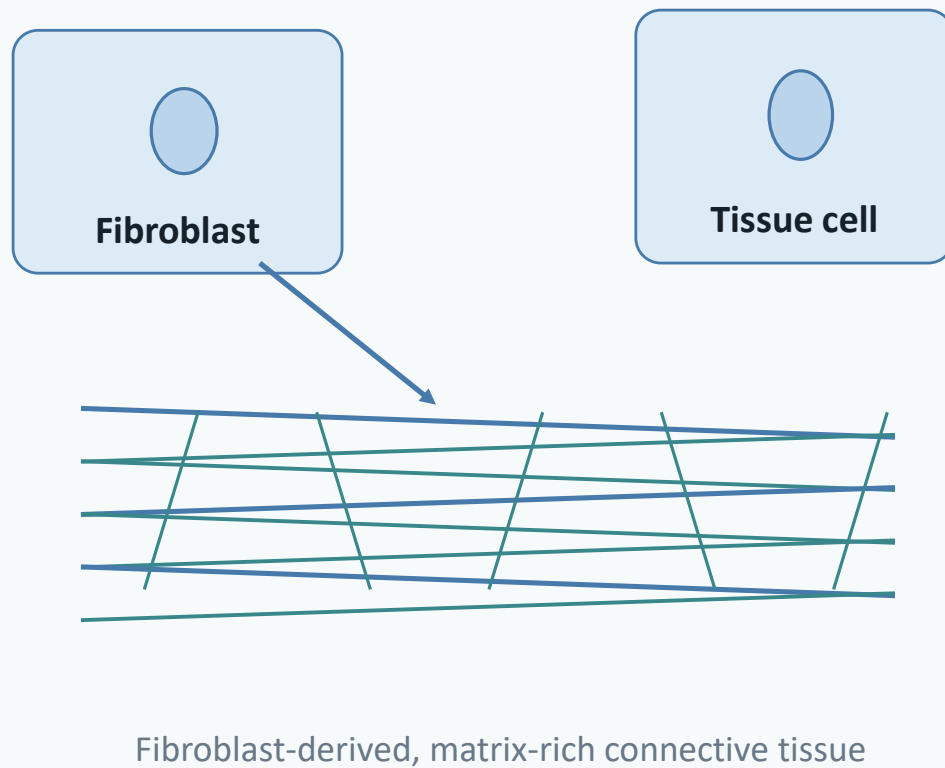
Interstitial matrix



Basement membrane

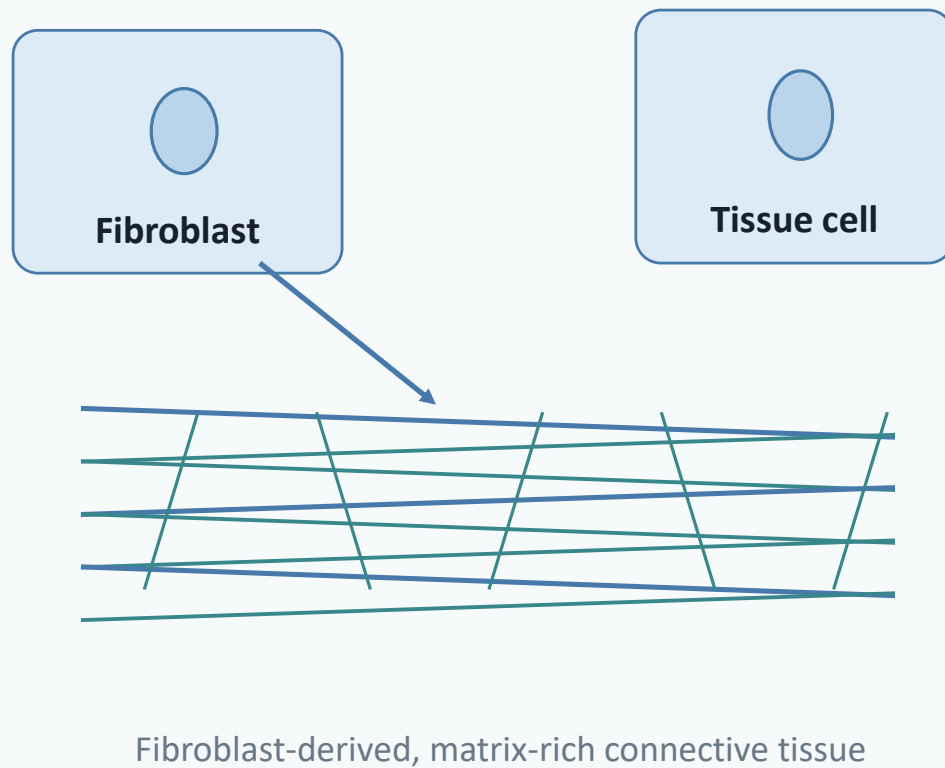
- Interstitial matrix occupies connective-tissue spaces.
- Basement membrane is a specialized matrix layer associated with certain cell surfaces.
- Their architecture and general composition differ despite overlapping components.

Interstitial matrix occupies tissue spaces



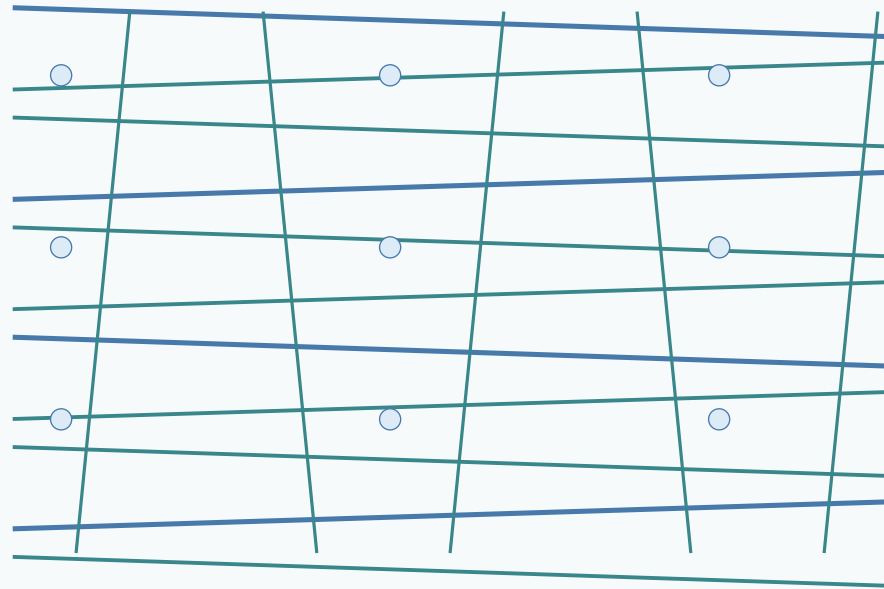
- It lies between stromal cells and among parenchymal and supporting structures.
- Examples include connective tissues adjacent to vascular and smooth-muscle elements.
- Its position allows a distributed three-dimensional support system.

Mesenchymal cells make interstitial matrix



- Fibroblasts are a principal example of matrix-synthesizing mesenchymal cells.
- The extracellular products form a network around cells rather than inside them.
- Production is coordinated with tissue maintenance and repair.

Interstitial matrix is a semifluid three-dimensional gel

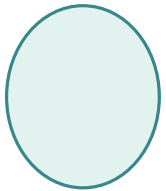


Hydrated three-dimensional matrix

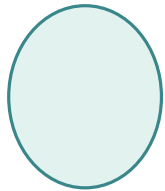
- An amorphous three-dimensional, semifluid matrix.
- Water-rich regions coexist with a structural macromolecular network.
- This architecture can absorb deformation while supporting tissue.

Fluid-rich interstitial matrix cushions compression

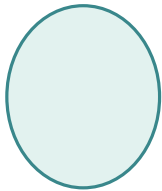
Fluid-rich matrix buffers deformation



GI tract



Bladder

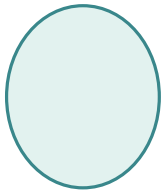


Arteries

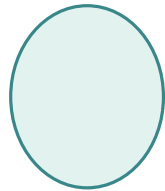
- Interstitial fluid contributes to tissue response under compressive force.
- The source highlights gastrointestinal, bladder, and periarterial locations.
- These examples show that ECM mechanics are organ-context dependent.

Different organs experience different deformation

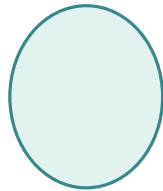
Fluid-rich matrix buffers deformation



Peristalsis



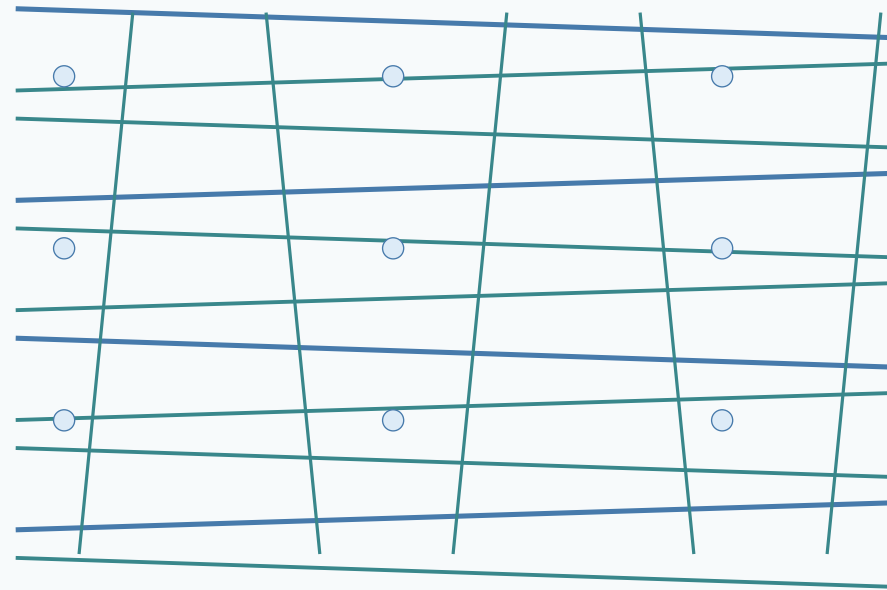
Urination



Pulsation

- Gastrointestinal tissues accommodate peristaltic movement.
- Urinary bladder tissues accommodate changes during filling and voiding.
- Periarterial soft tissues respond to pulsatile vascular motion.

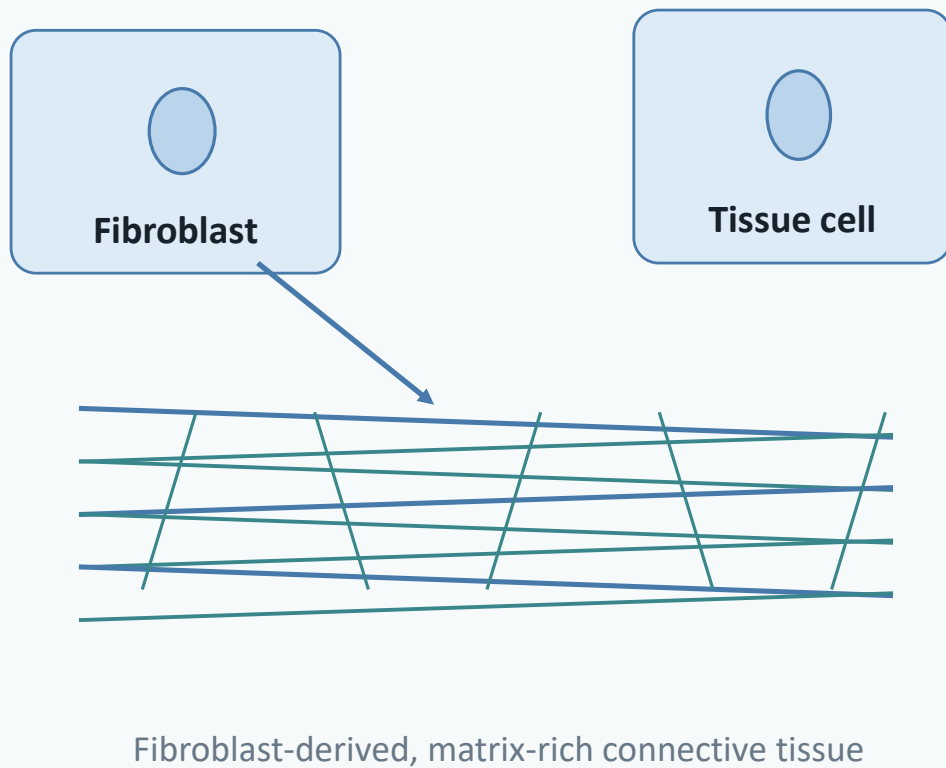
Interstitial ECM contains diverse macromolecules



Hydrated three-dimensional matrix

- Listed constituents include fibrillar and nonfibrillar collagens.
- Fibronectin, elastin, proteoglycans, and hyaluronate are also present.
- This deck emphasizes organization; Molecular chemistry is treated separately in Topic 13.

Interstitial architecture connects cells and stroma

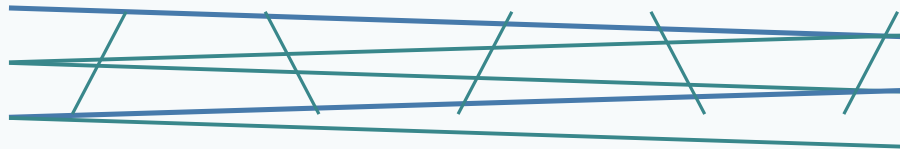


- Matrix fibers and hydrated components occupy intercellular spaces.
- Mesenchymal cells synthesize much of the matrix framework.
- Its continuous distribution permits mechanical and signaling connections.

Basement membrane forms a specialized matrix surface



Continuous basement membrane



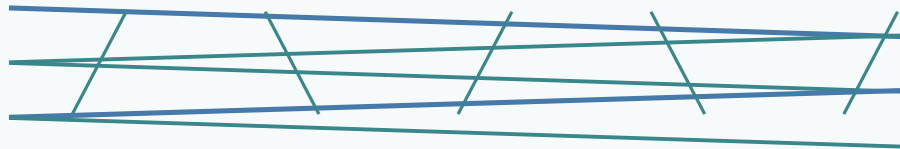
Thin planar supporting matrix

- Basement membranes occur adjacent to epithelial, endothelial, and smooth-muscle cells.
- They are organized as relatively flat lamellar meshes.
- This anatomy is distinct from the diffuse three-dimensional interstitial gel.

Basement membranes organize cell-associated spaces



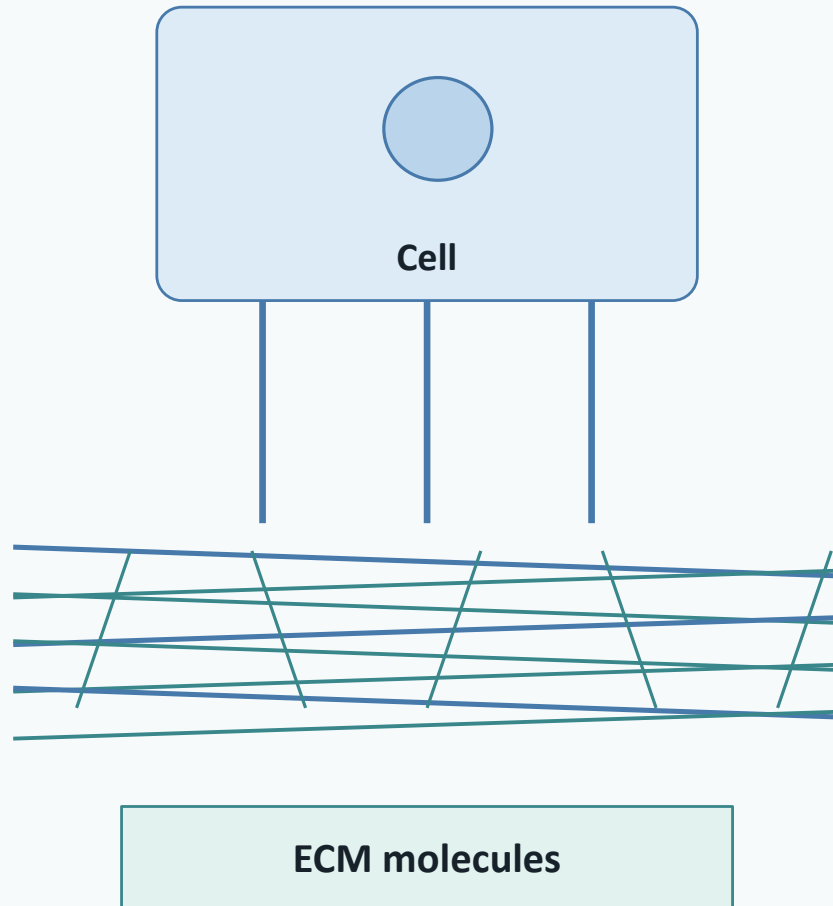
Continuous basement membrane



Thin planar supporting matrix

- Epithelial basement membrane separates epithelium from connective tissue.
- Endothelial and smooth-muscle basement membranes define other specialized surfaces.
- The same organizational principle applies in different anatomical sites.

Basement membrane has dual cellular origins

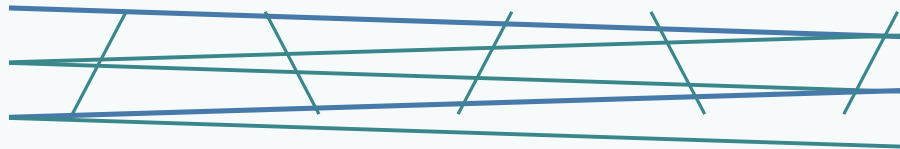


- Components are synthesized by overlying cells and underlying mesenchymal cells.
- Its architecture reflects contributions from adjacent tissue compartments.
- It is a shared cell–matrix interface rather than an isolated coating.

Type IV collagen and laminin are key constituents



Continuous basement membrane



Thin planar supporting matrix

- The source identifies nonfibrillar type IV collagen and laminin as major components.
- They contribute to the structural framework of the basement membrane.
- The individual molecular properties are addressed in the adjacent component topic.

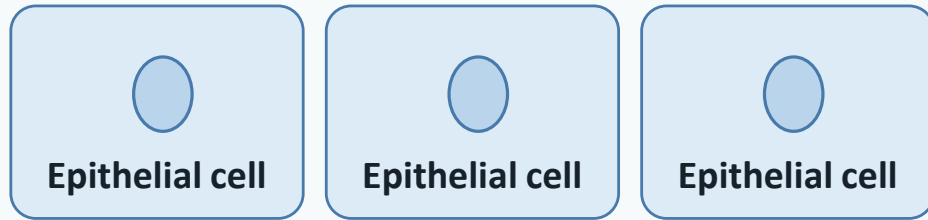
A basement “membrane” is not a sealed sheet

Porous mesh: Spaces exist between matrix elements

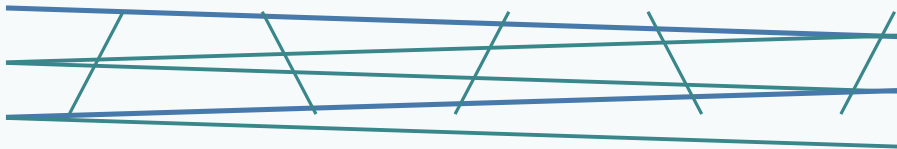


- Despite its name, basement membrane is a porous extracellular mesh.
- It creates an organized interface rather than an impermeable partition.
- Specialized functions depend on its local molecular organization.

Basement membrane separates tissue compartments



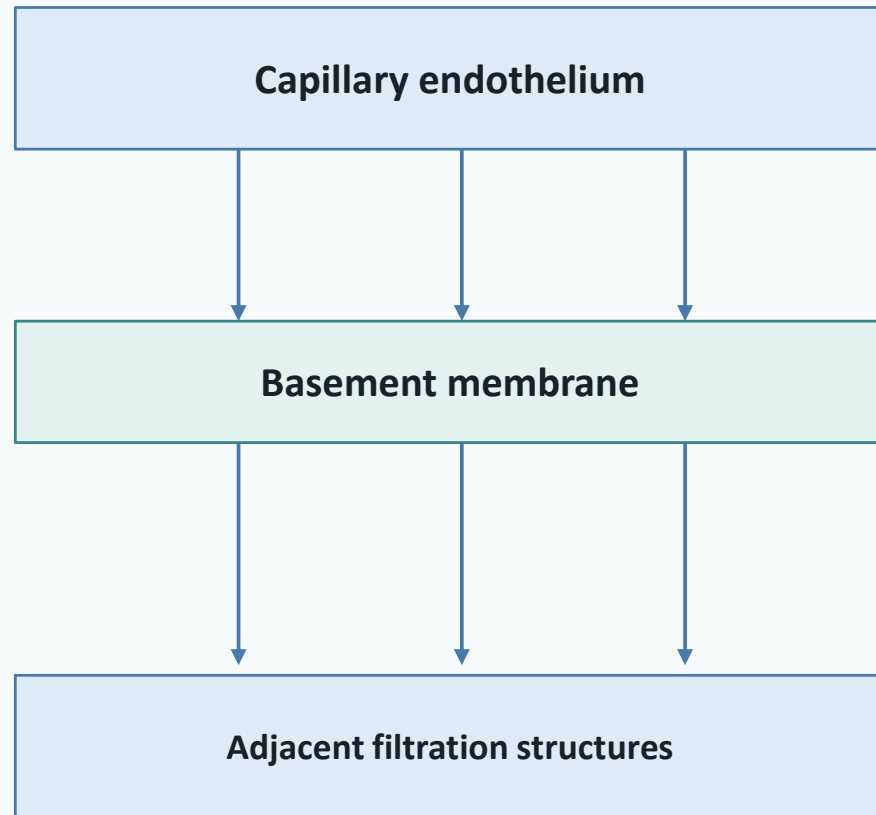
Continuous basement membrane



Thin planar supporting matrix

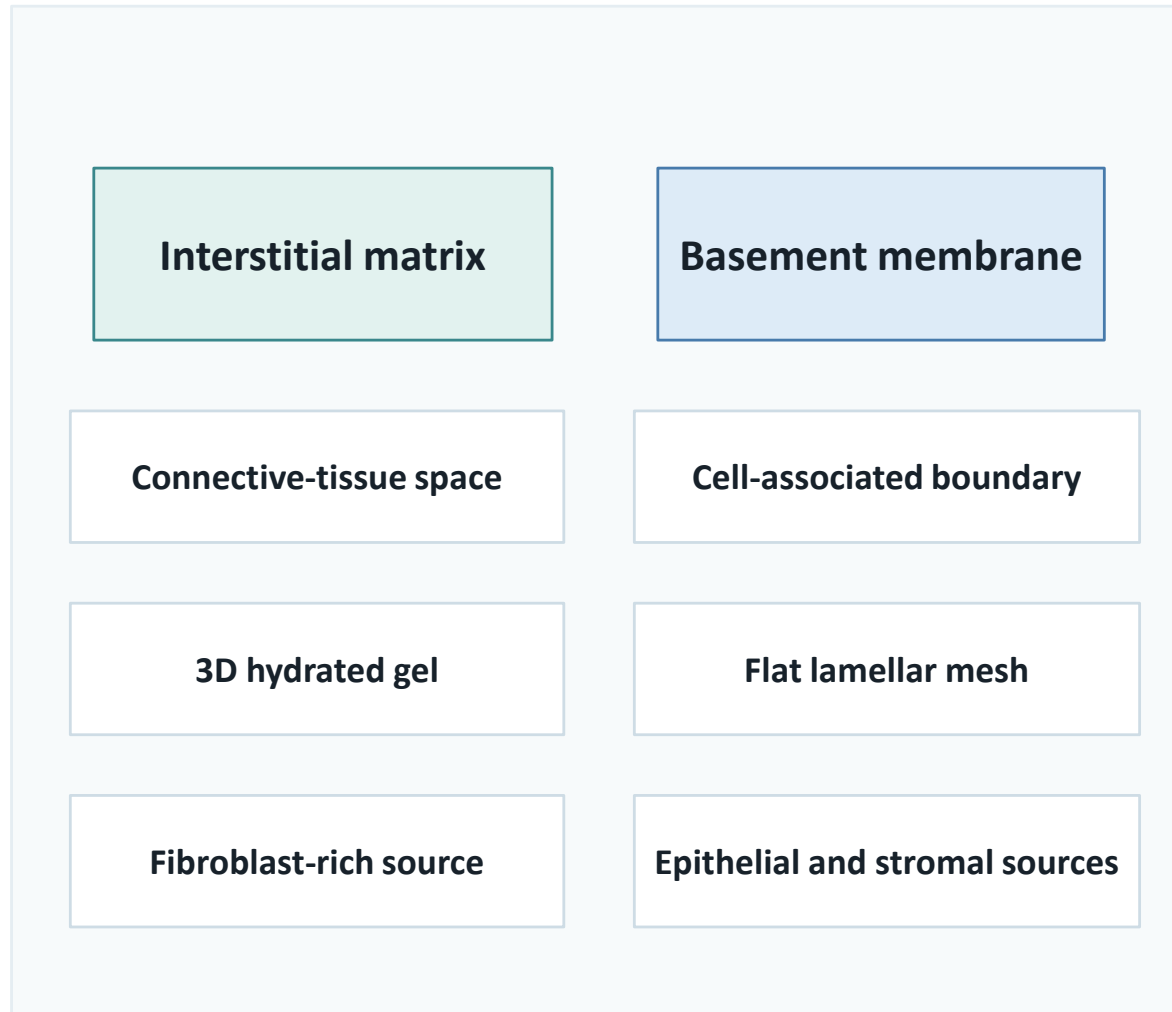
- It establishes a boundary between epithelium and subjacent connective tissue.
- Boundaries maintain spatial relationships during normal homeostasis.
- Compartment architecture can be altered by tissue injury or invasion.

Renal basement membrane contributes to filtration



- In the kidney, basement membrane participates in the filtration apparatus.
- This illustrates a specialized physiological task beyond mechanical support.
- Filtration depends on additional cellular and structural elements, not ECM alone.

Interstitial and basement matrix: Key contrast



- Interstitial ECM: Distributed connective-tissue network and hydrated three-dimensional gel.
- Basement membrane: Planar, cell-associated matrix mesh.
- Both support tissues and regulate cellular responses, but in different geometries.

Clinical reasoning: A preserved matrix template

Observed feature

Cells remain near an intact basal matrix



ECM question

Can organized regeneration occur?

- Conceptual example: Cells survive an injury while their basal ECM architecture remains intact.
- Prediction: Residual scaffolding can guide spatially organized replacement.
- The key distinction is restoration of structure versus cell proliferation alone.

Clinical reasoning: A damaged filtration interface

Observed feature

Renal matrix architecture is altered

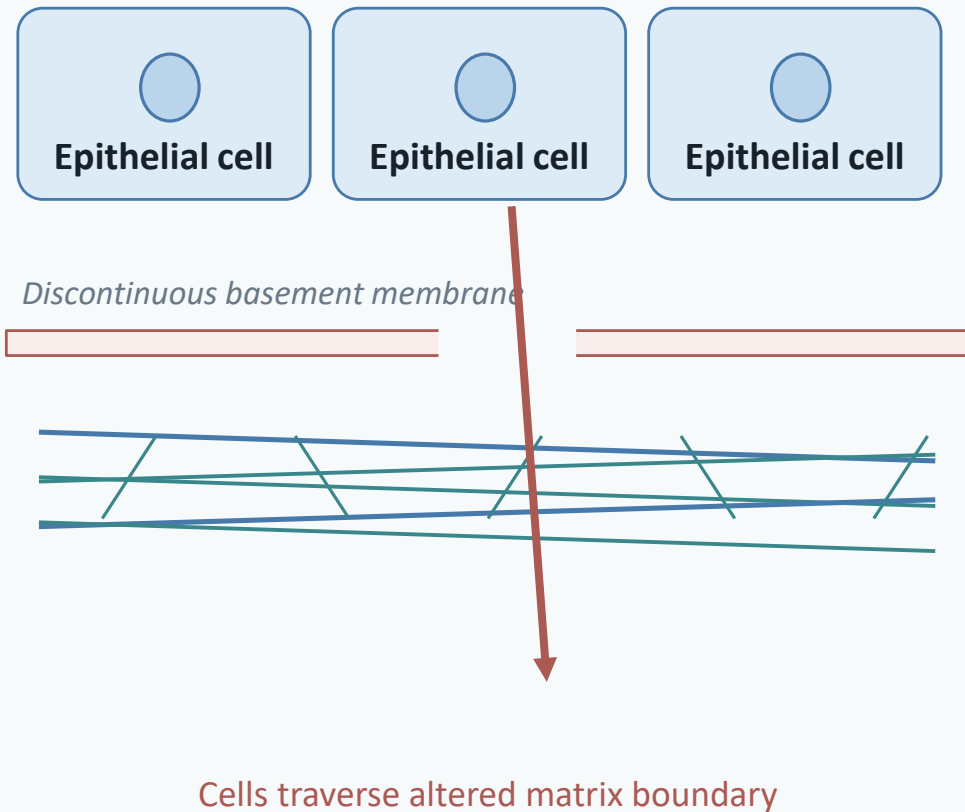


ECM question

Which tissue-specific function is at risk?

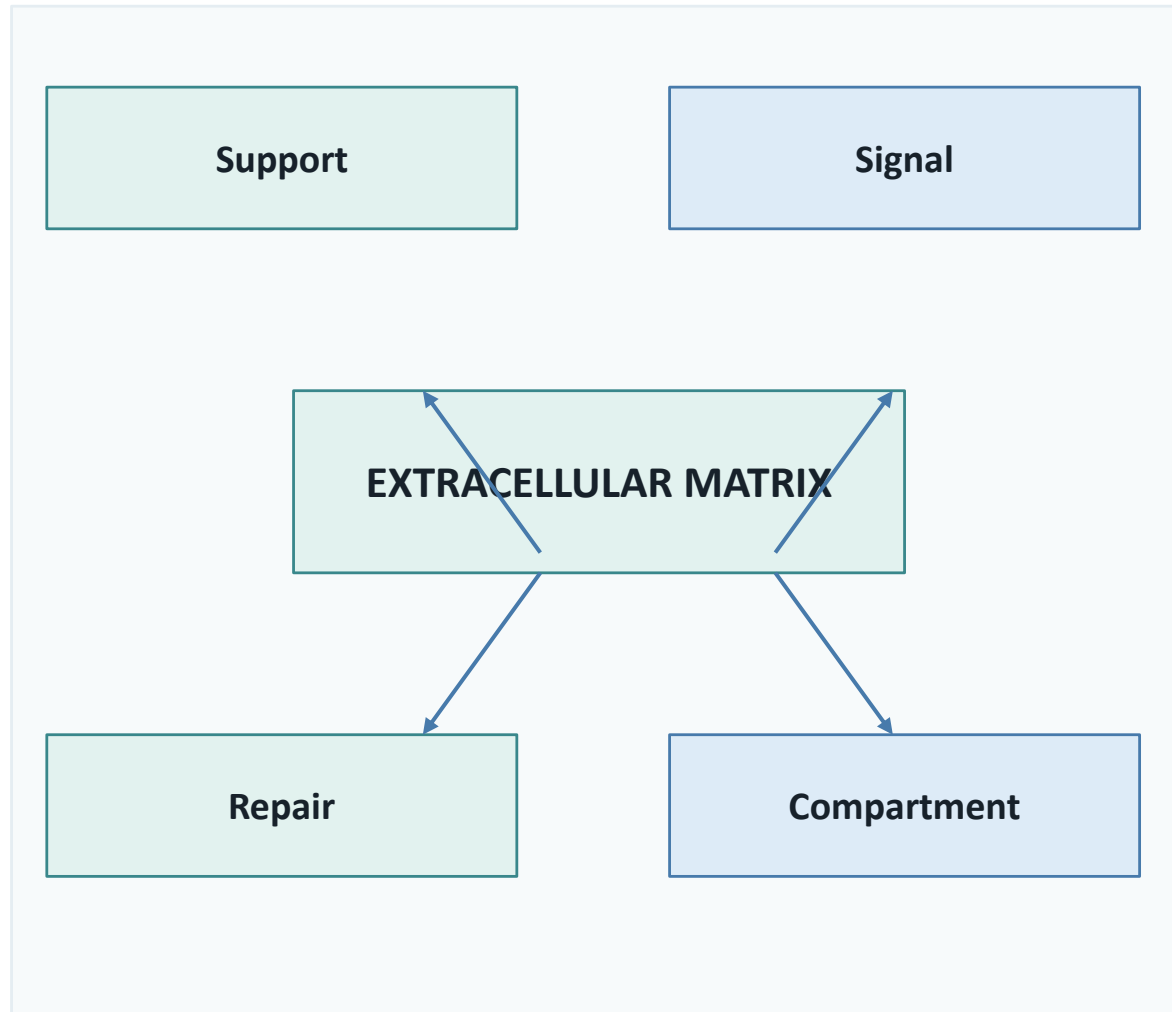
- Conceptual example: The renal basement-membrane mesh is structurally abnormal.
- The potential consequence concerns filtration, not only tissue strength.
- ECM organization should be considered alongside associated filtration cells.

Clinical reasoning: Invasive tissue behavior



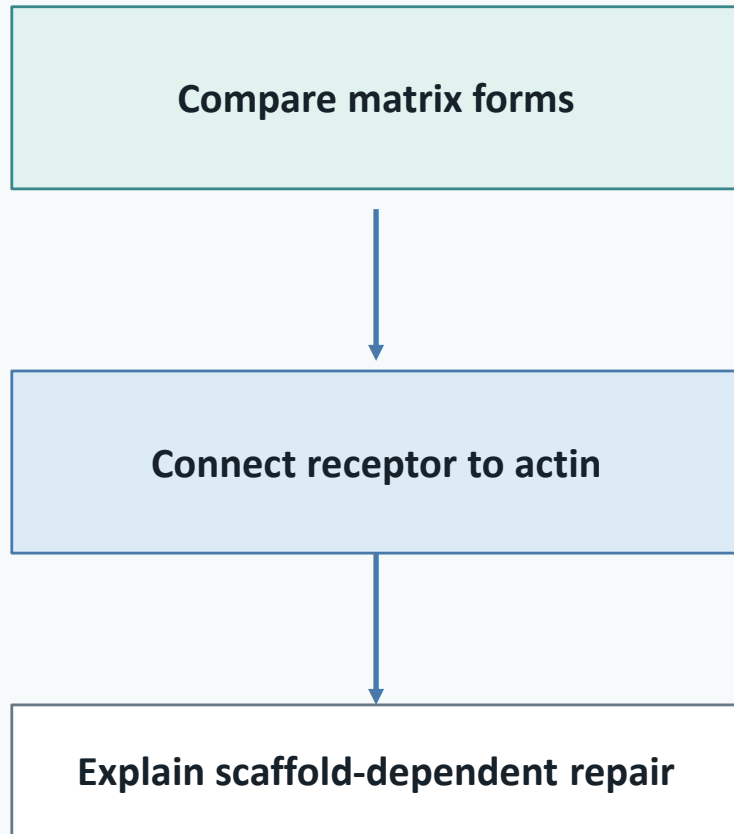
- Conceptual example: Epithelial cells cross an altered basement-membrane boundary.
- Cell movement must be considered together with matrix interaction and remodeling.
- Boundary crossing is an anatomical concept; This schematic is not diagnostic evidence.

Integrative summary: ECM function determines tissue behavior



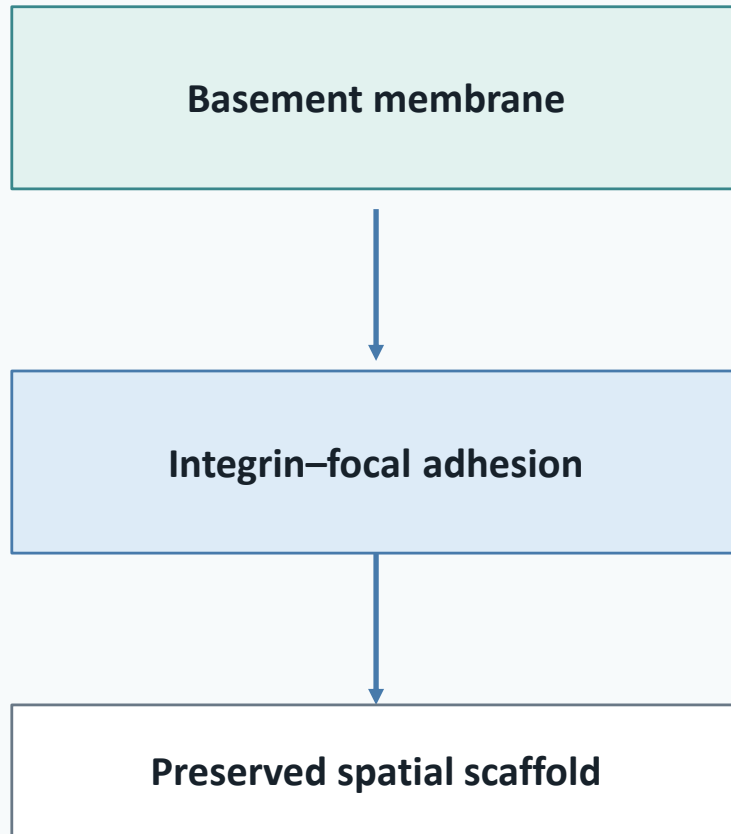
- Mechanical support, biochemical signaling, and architectural scaffolding are interconnected.
- Interstitial matrix and basement membrane differ by geometry and location.
- Balanced turnover enables renewal; Disordered remodeling contributes to pathology.

Self-assessment: Identify the ECM principle



- Which matrix form is a flat, cell-associated, porous mesh?
- What receptor family links matrix binding with focal adhesion signaling?
- Why may cell proliferation alone fail to restore an injured tissue?

Self-assessment: Worked answers



- Basement membrane is the planar, cell-associated matrix compartment.
- Integrins connect ECM engagement to focal adhesion and cytoskeletal signaling.
- Architectural regeneration requires a suitable basement or stromal scaffold.

Source and study boundary

Core reference

Robbins, Cotran & Kumar: Pathologic Basis of Disease, 11th edition (2026).

Chapter 1, “The Cell as a Unit of Health and Disease” — “Extracellular Matrix,” pp. 20–21.

Scope

This deck teaches ECM functions and anatomical organization. Detailed properties of individual matrix macromolecules belong to the adjacent “Components of the Extracellular Matrix” topic.