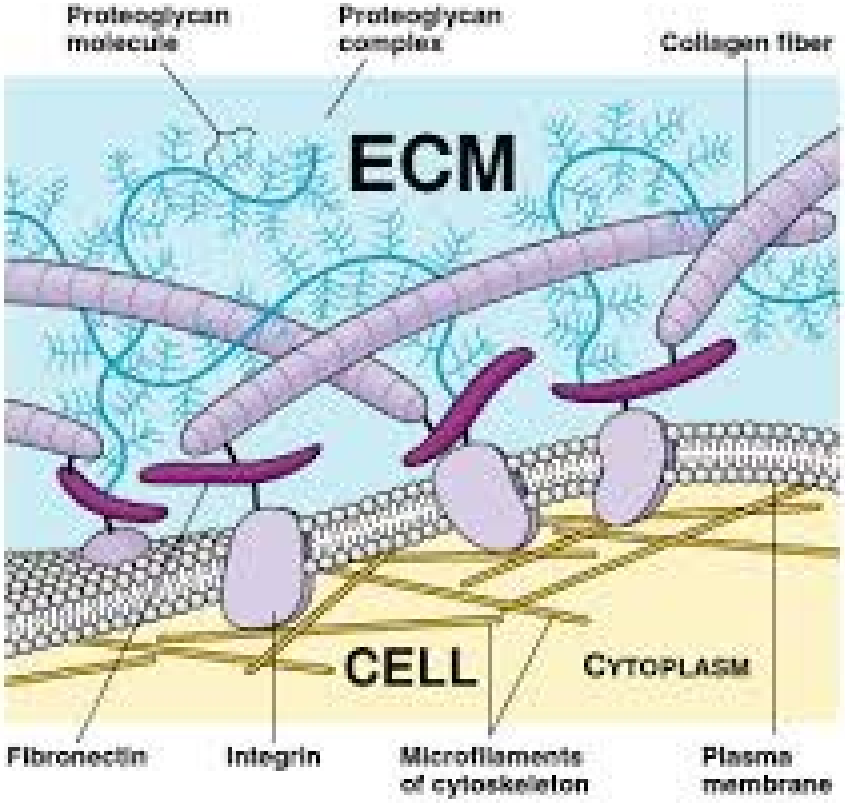
TeachEngineering

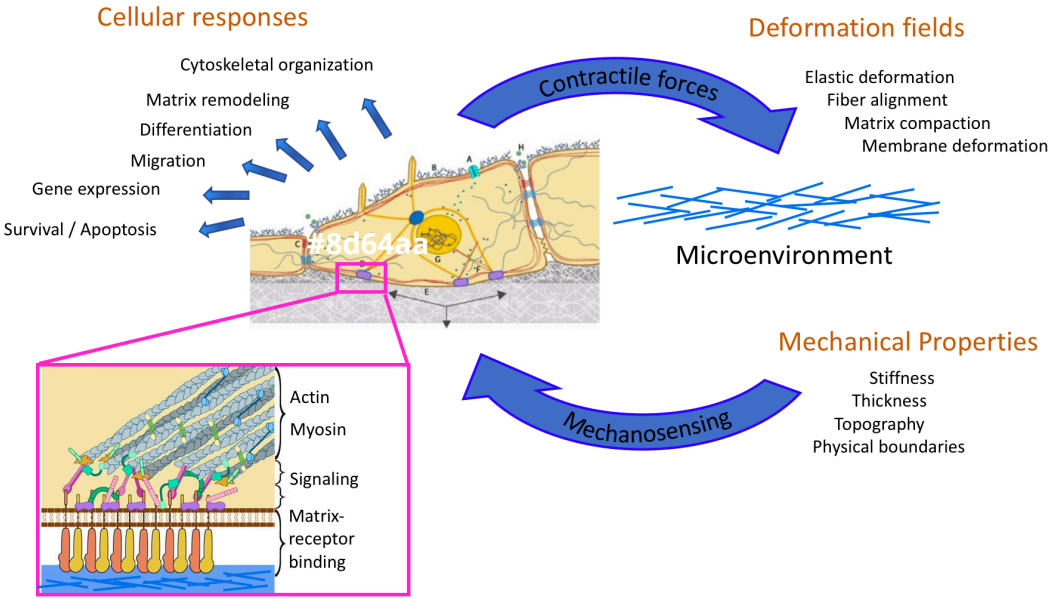
STEM Curriculum for K-12

The Extracellular Matrix and Molecular Biomechanics

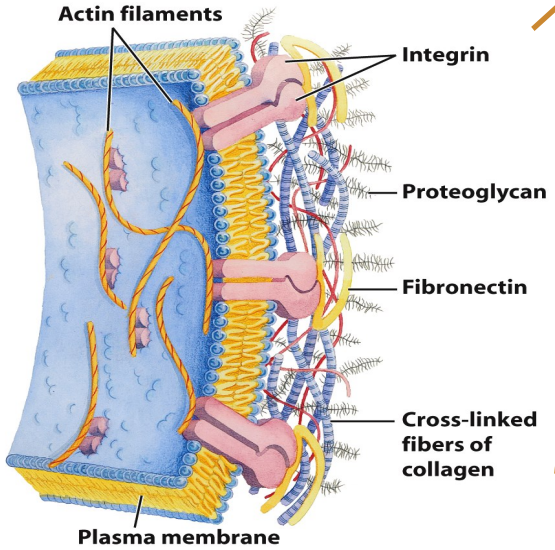


Center for Engineering MechanoBiology

An integrated research and education program for understanding, manipulating, and engineering function of molecules, cells, and tissues in plants and animals.



Extracellular Matrix



Forms Diverse Structures

- Bone
- Ligament
- Tendon
- Vessel
- Connective Tissue
- Skin

Biological Processes

- Adhesion
- Mechanical Support
- Migration
- Proliferation
- Signaling

Diseases

- Arthritis
- Atherosclerosis
- Cancer
- Asthma

Introduction to the ECM

Extracellular macromolecules

- Collagen, enzymes, and glycoproteins
- Provide structure and biochemical support

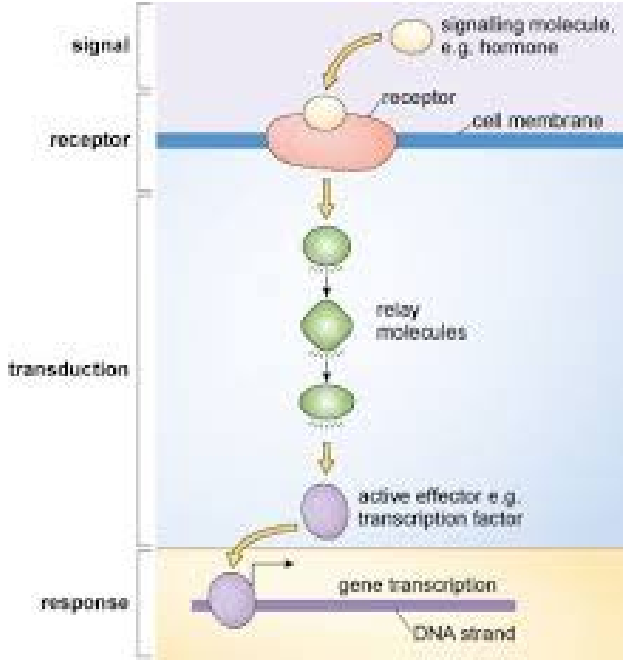
The extracellular matrix is a dense network of proteins that:

- Lies between cells
- Is made by the cells within the network

Composition varies between cell types

Functions- common to all cells

- Cell adhesion
- Cell to cell communication
- Cell differentiation



Introduction to the ECM

Animal cells

- Basement membrane (sheet-like deposit of ECM for epithelial cell to rest on)
- Interstitial matrix
- Connective tissue (varies in type by cell)

Plant cells

- Includes cell wall

Structure/Components

Secreted via exocytosis by the cell

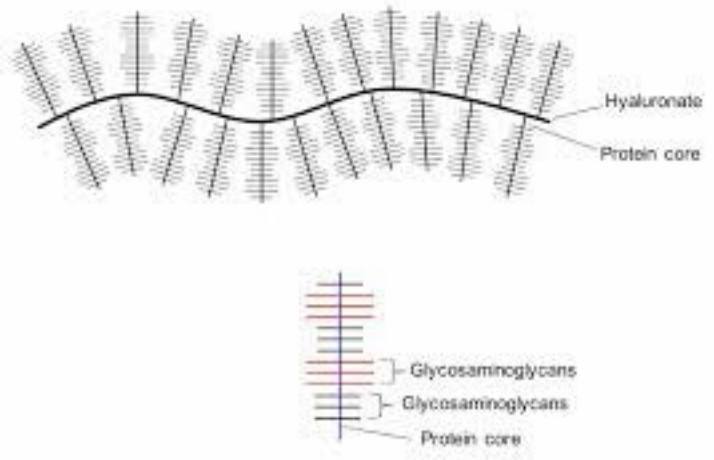
Mesh of proteins and glycosaminoglycans (GAGs)

1. Proteoglycans

- **Carbohydrates with net negative charge**
- **Attract Na^+ ions**
- **Regulate osmolarity of cells surrounding**

2. Heparin

- **Polysaccharides**
- **Related to development, blood coagulation, and tumor metastasis**



Structure/Components

Secreted via exocytosis by the cell
Mesh of proteins and GAGs

3. Chondroitin

Cartilage, tendons, ligaments and walls of aorta

4. Keratin

Cornea, bones, hair and horns of animals

5. Hyaluronic Acid

Polysaccharide with acid group attached
Resists compression, provides turgor
Absorbs H_20

Structure/Components

Secreted via exocytosis by the cell

Mesh of proteins and GAGs

6. Collagen

- **Provides structural support to tissues**
- **Family of >20 different proteins in the ECM**
- **Most abundant proteins in animals**
- **Secreted from cells and assembled in the extracellular space**

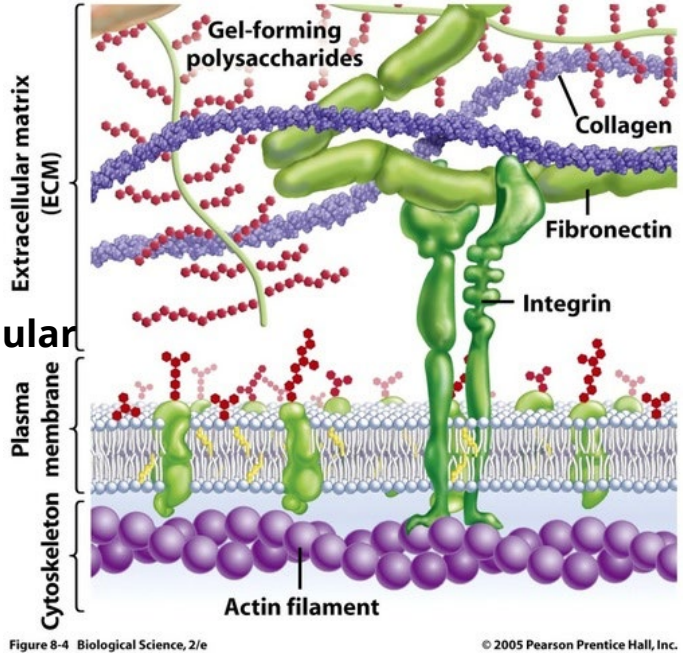


Figure 8-4 Biological Science, 2/e

Structure/Components

Secreted via exocytosis by the cell

Mesh of proteins and GAGs

7. Elastic fibers

Imparts elasticity to tissues

Elastin monomers (i.e., tropoelastin subunits) are organized into fibers

The fibers are so strong and stable they can last a lifetime

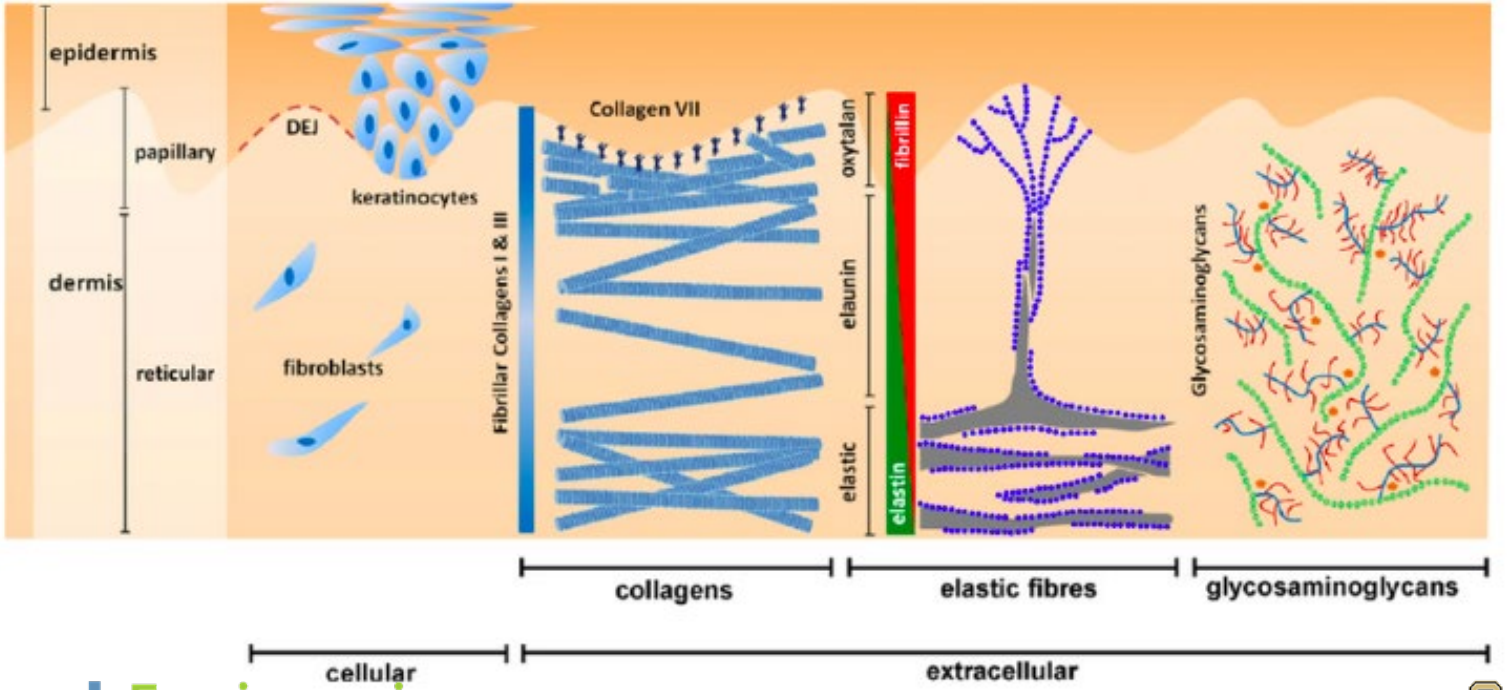
Strength of elastic fibers arises from covalent crosslinks

Elasticity of elastic fibers arises from the hydrophobic regions

Structure/Components

Secreted via exocytosis by the cell

Mesh of proteins and GAGs



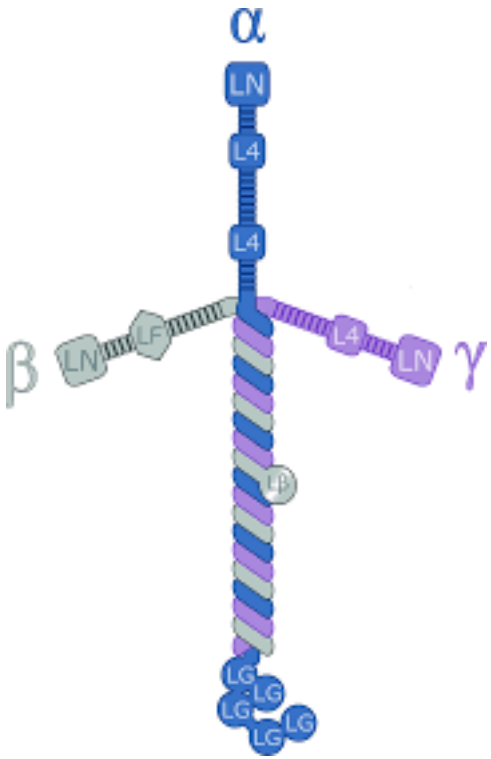
Structure/Components

Secreted via exocytosis by the cell

Mesh of proteins and GAGs

8. Laminins

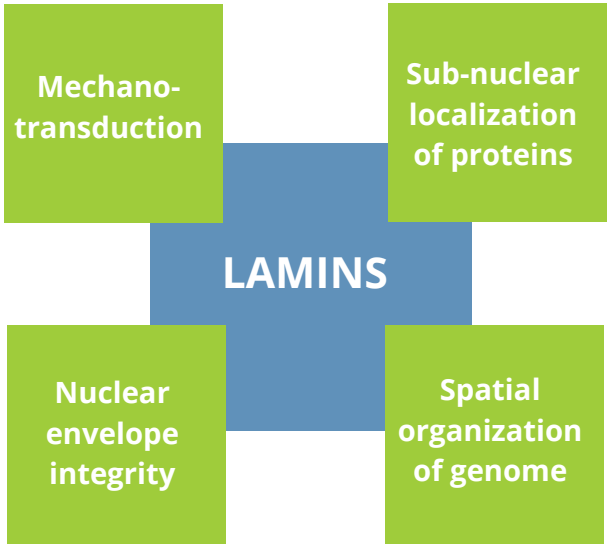
- **Family of ECM proteins**
- **Found in virtually all tissues of all animals**
- **Provide an adhesive substrate for cells**
- **Resist tensile forces in tissues**



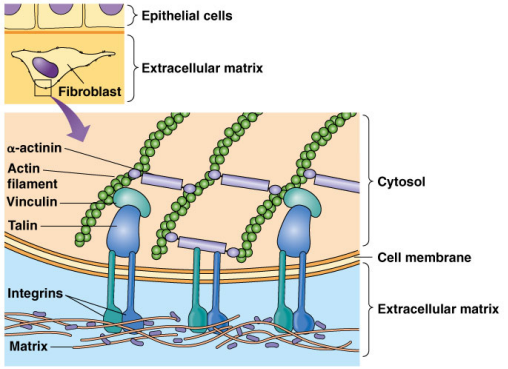
Structure/Components

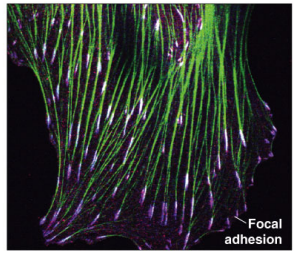
Secreted via exocytosis by the cell

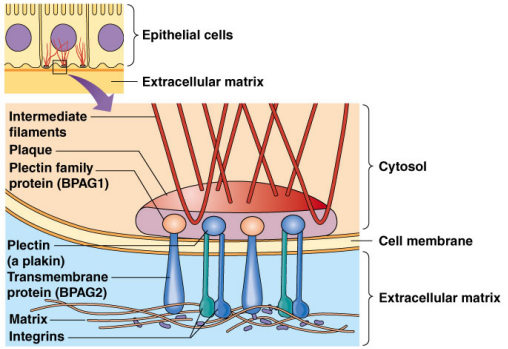
Mesh of proteins and GAGs

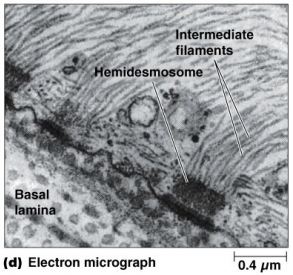


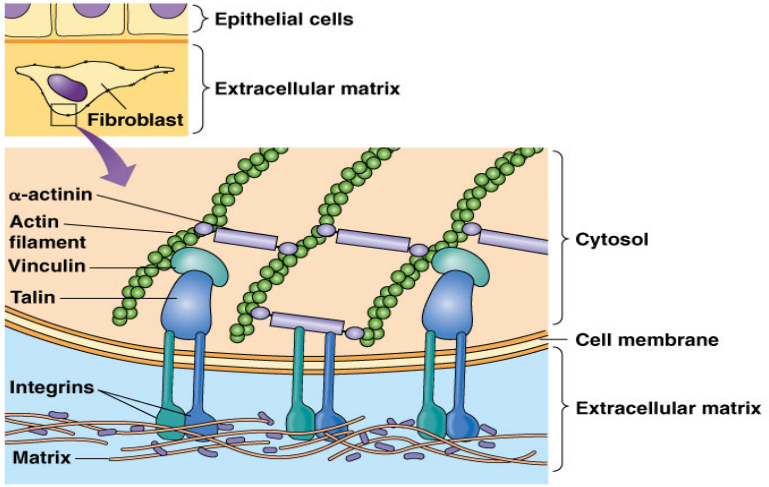
- Chromatin organization
- DNA damage response
- Telomere length homeostasis
- Nucleocytoplasmic transport
- Antioxidant response
- DNA replication
- Gene regulation



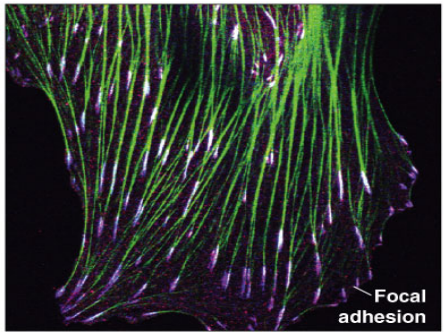






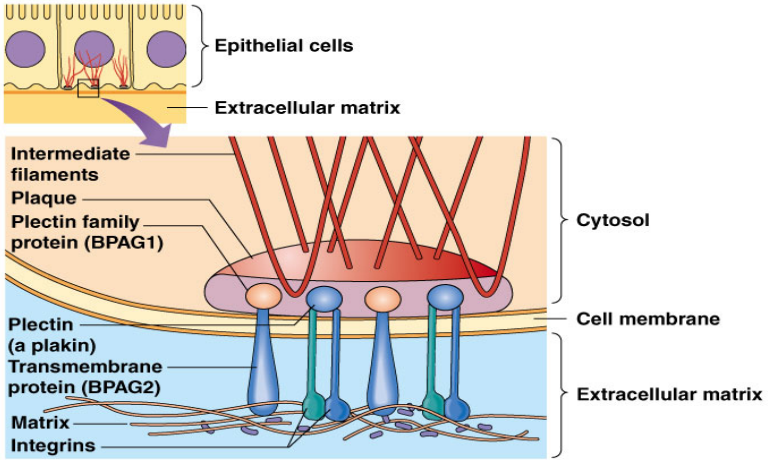


(a) Focal adhesion

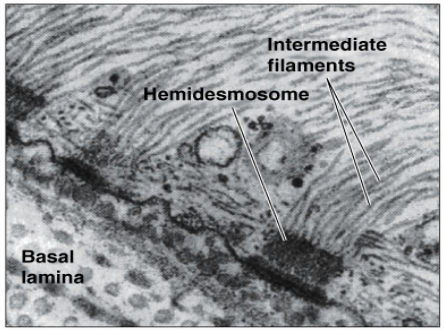


(b) Immuoflourescence

20 μm



(c) Hemidesmosome

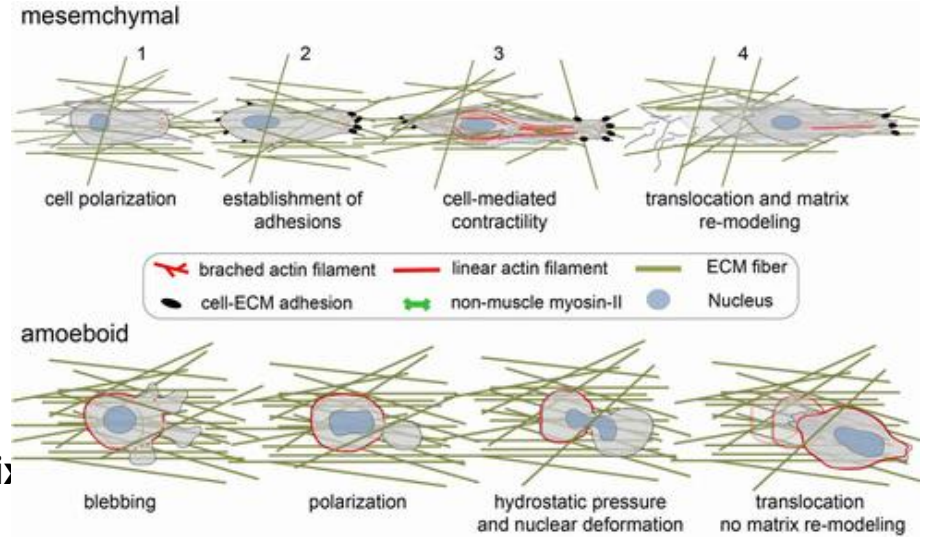


(d) Electron micrograph

0.4 μm

Structure/Components

The Basal Laminas

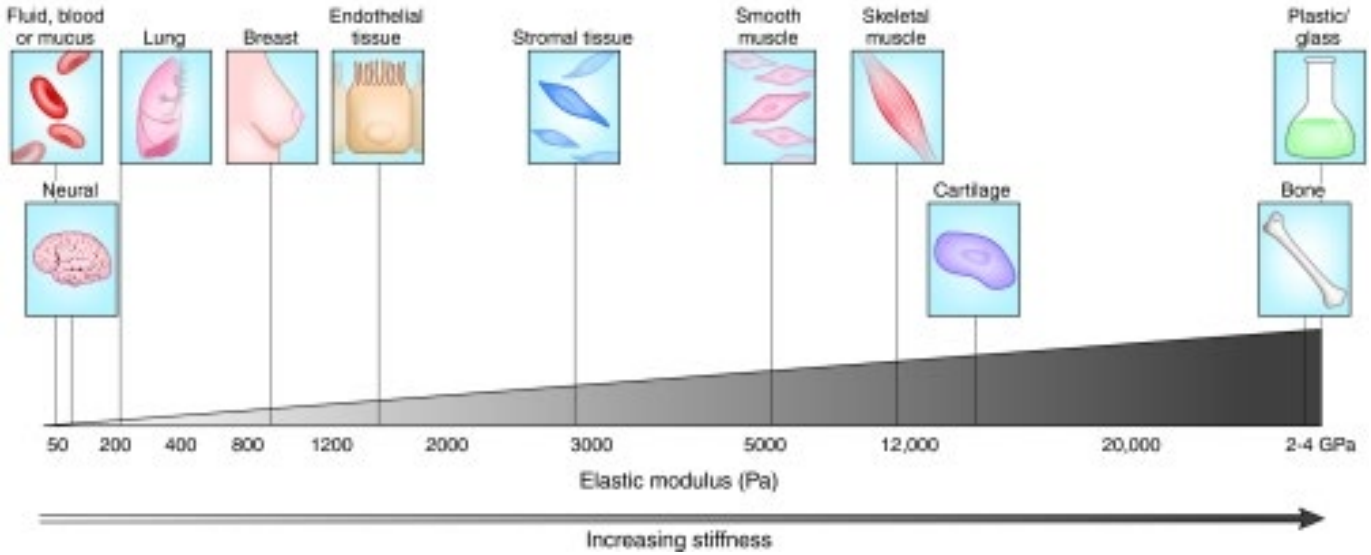


Structure and Function

- Specialized sheets of extracellular matri
- Composed of at least 2 distinct layers
- Found at the basal surface of epithelial sheets, neuromuscular junctions, and in the nucleus
- Is a supportive network to maintain epithelial tissues
- Diffusion barrier
- Collection site for soluble proteins, e.g., growth factors
- Guidance signal for migrating neurons
- Can sense mechanical properties in environment
- Regulates cell migration, proliferation, differentiation and apoptosis

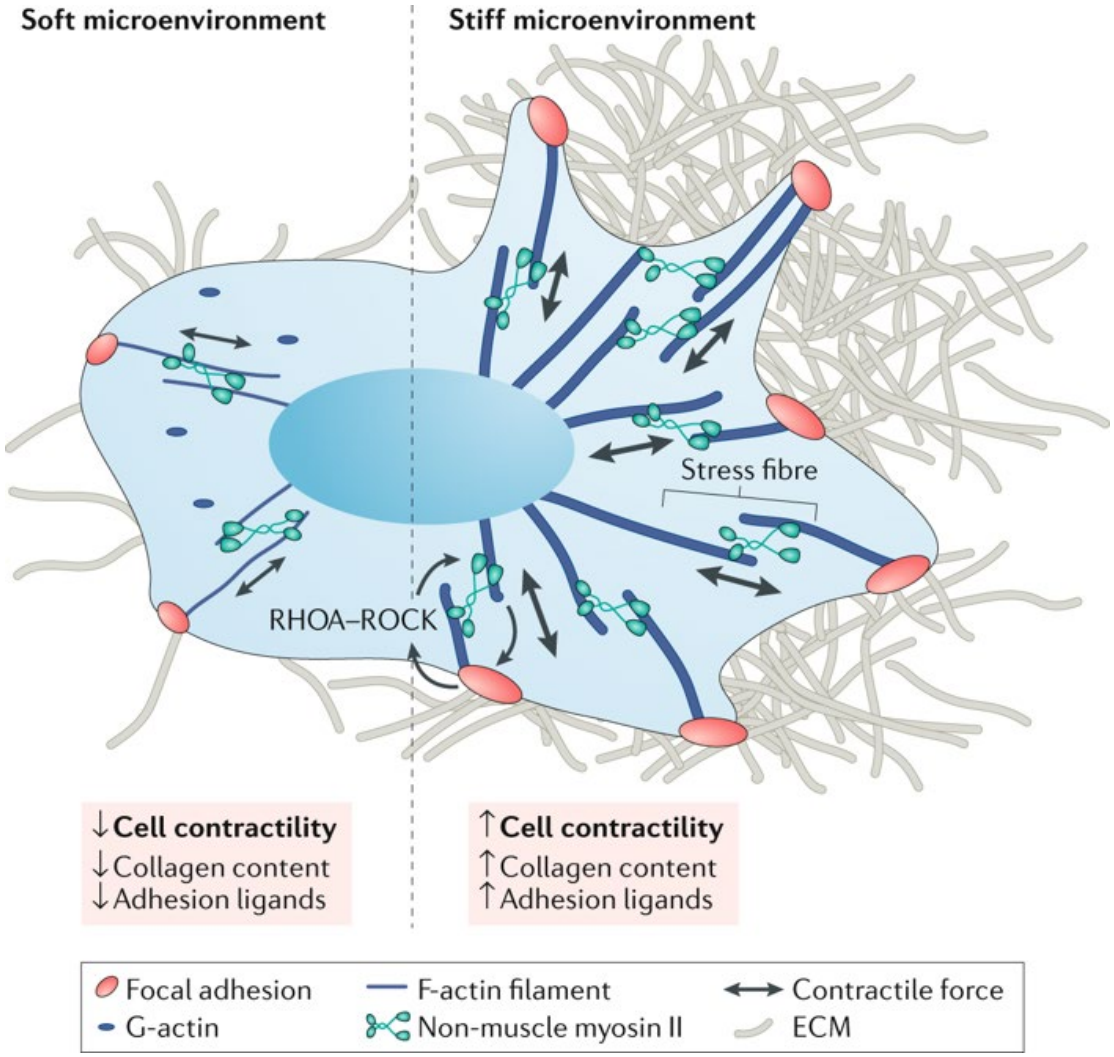
Structure/Components

The Basal Laminas



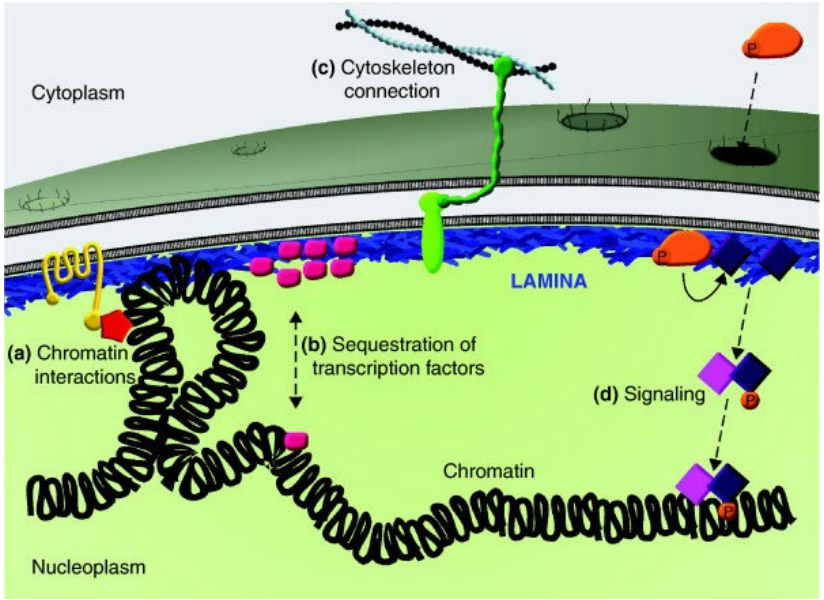
Structure

- **Can vary in stiffness and elasticity**
- **Dependent on collagen versus elastin concentration**


Soft microenvironment
Stiff microenvironment
Stress fibre
RHOA–ROCK
↓Cell contractility
↓Collagen content
↓Adhesion ligands
↑Cell contractility
↑Collagen content
↑Adhesion ligands
Focal adhesion
G-actin
F-actin filament
Non-muscle myosin II
Contractile force
ECM

Structure/Components

Lamin A



Nuclear Lamin

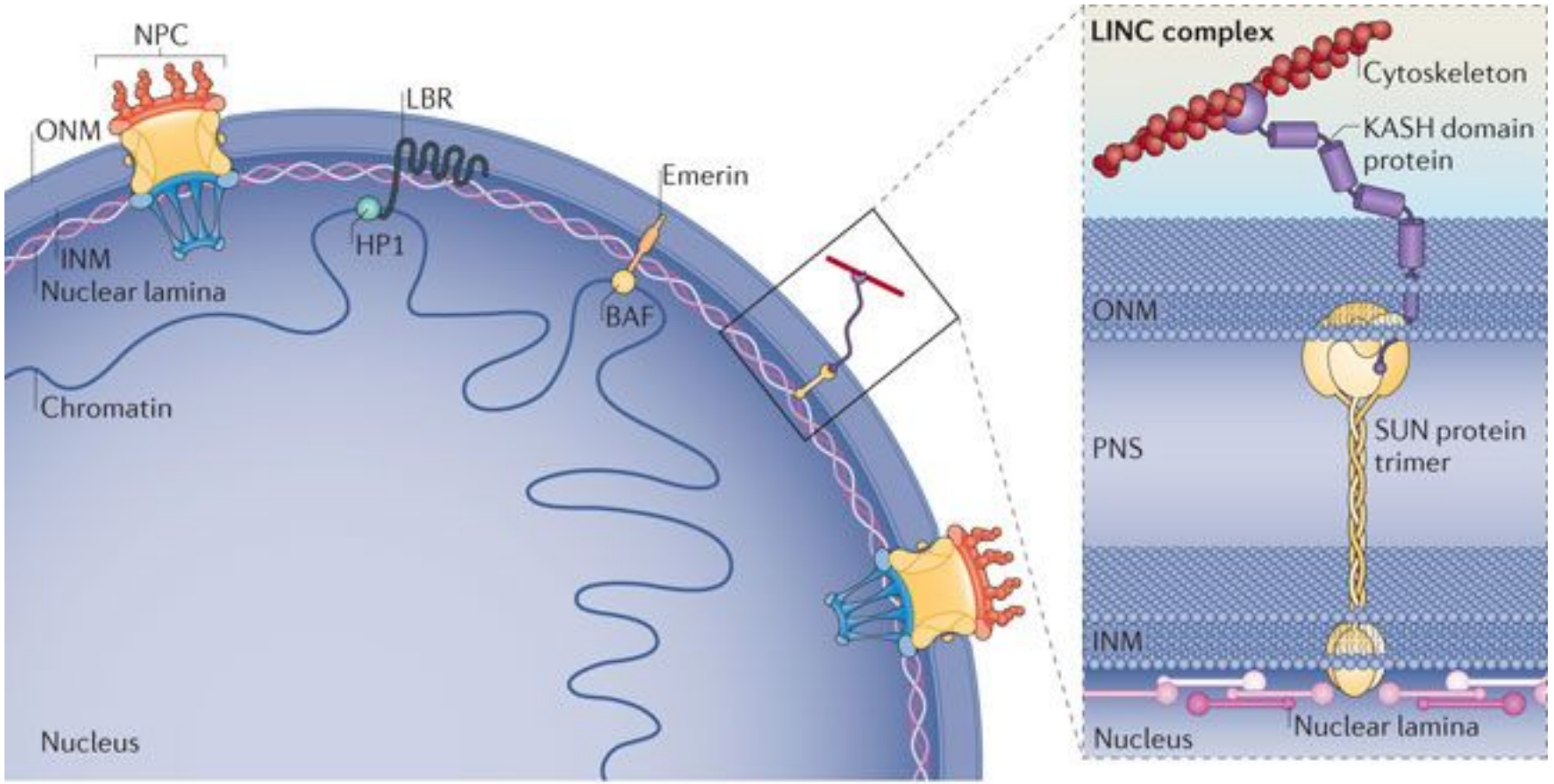
Occurs around the nuclear membrane

Determines flexibility of membrane

Protects DNA

Low amounts= more flexibility, more likely to migrate

High amounts= more stiff, less likely to migrate


NPC
ONM
LBR
Emerin
HP1
INM
Nuclear lamina
BAF
Chromatin
Nucleus
LINC complex
Cytoskeleton
KASH domain protein
ONM
PNS
SUN protein trimer
INM
Nucleus
Nuclear lamina

Structure/Components

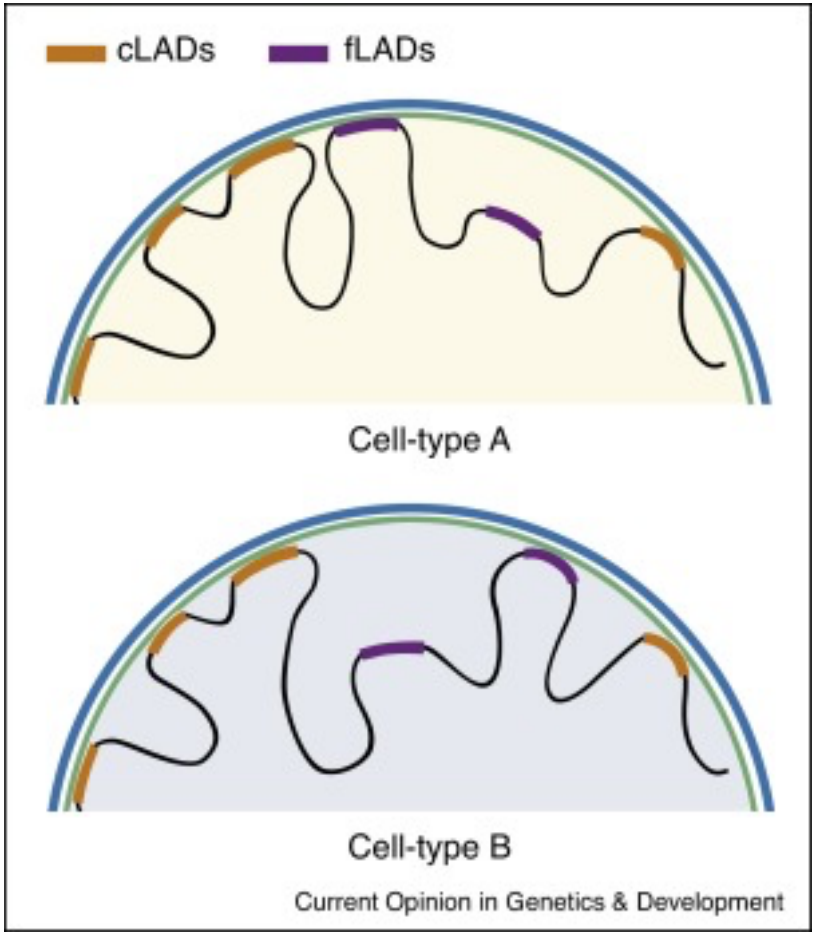
Lamin A

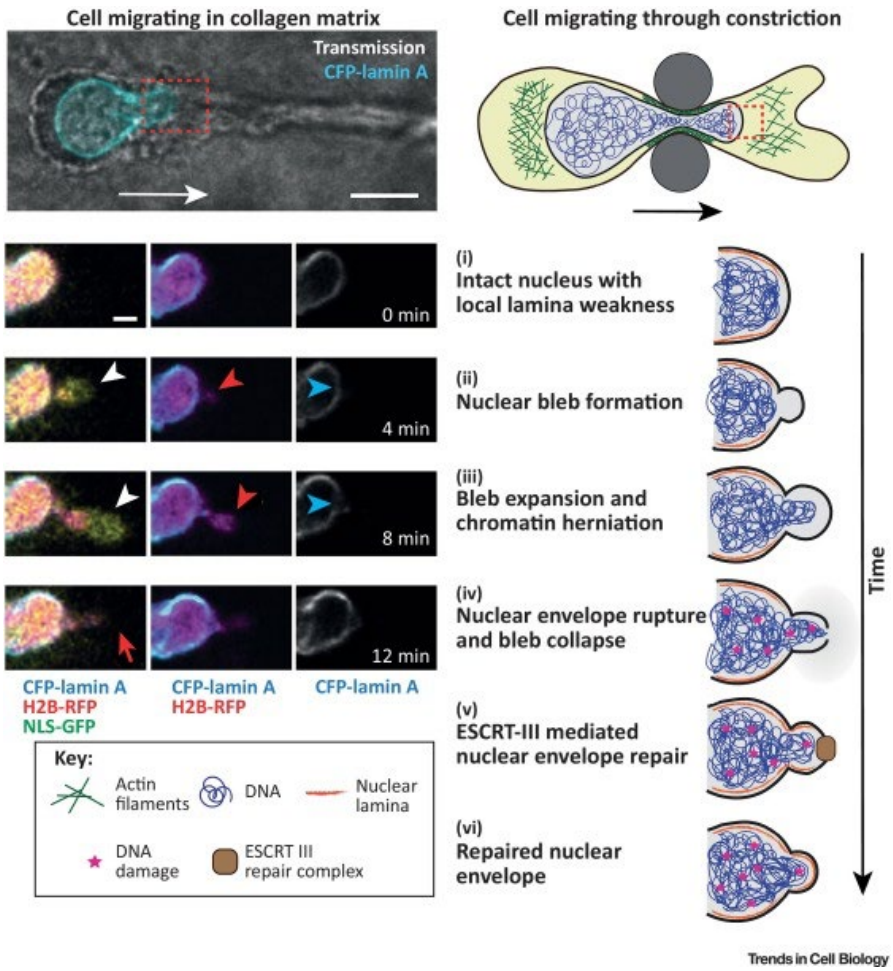
Nuclear Lamin

Effects on gene expression

Adhesion complexes and the actin-myosin cytoskeleton

Contractile forces are transmitted through transcellular structures




Cell migrating in collagen matrix
Transmission
CFP-lamin A
Cell migrating through constriction
0 min
4 min
8 min
12 min
CFP-lamin A
H2B-RFP
NLS-GFP
CFP-lamin A
H2B-RFP
CFP-lamin A
Key:
Actin filaments
DNA
Nuclear lamina
DNA damage
ESCRT III repair complex
(i)
Intact nucleus with local lamina weakness
(ii)
Nuclear bleb formation
(iii)
Bleb expansion and chromatin herniation
(iv)
Nuclear envelope rupture and bleb collapse
(v)
ESCRT-III mediated nuclear envelope repair
(vi)
Repaired nuclear envelope
Time
Trends in Cell Biology