

Tissue stem cells

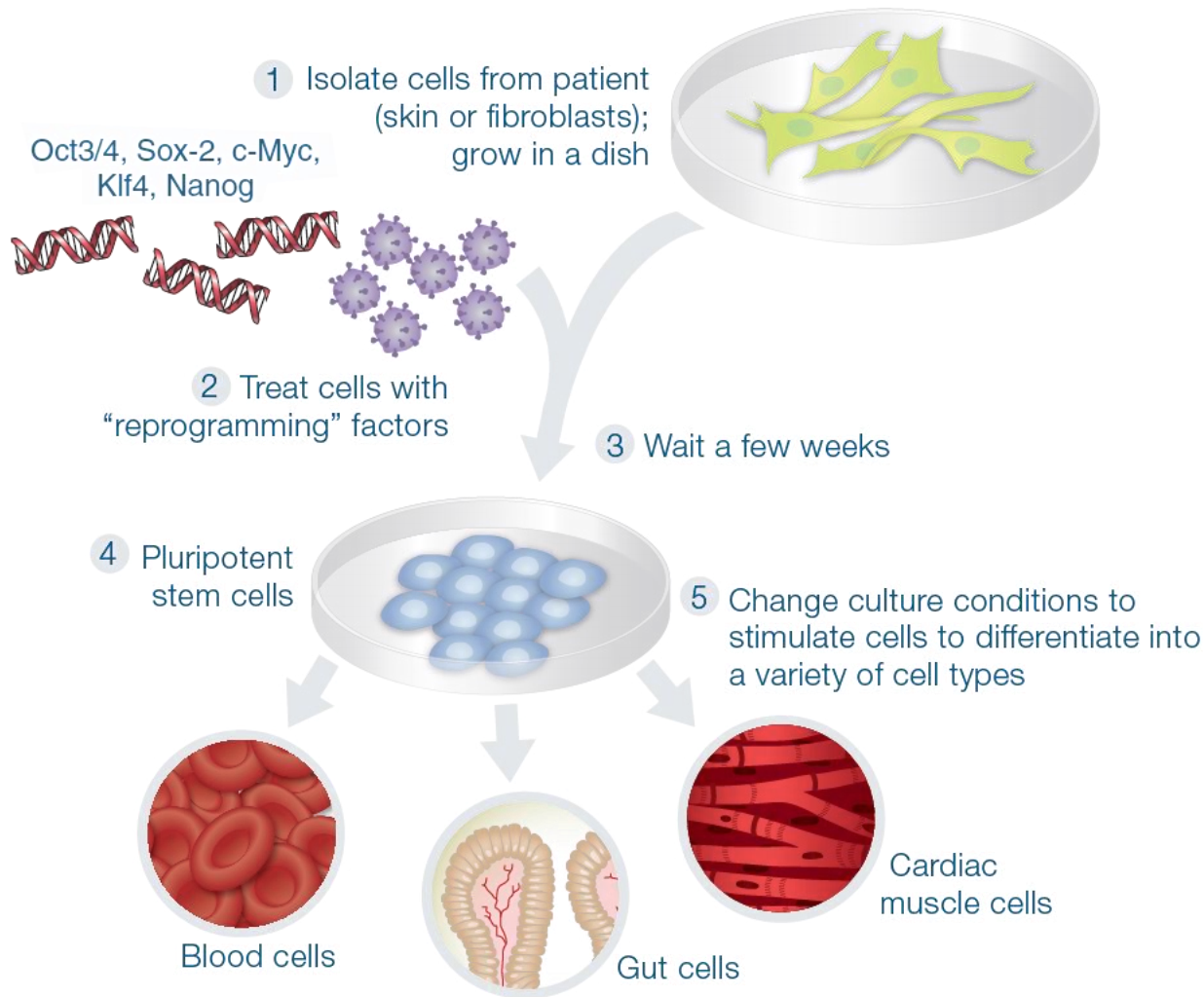
Therapeutic potential
without graft rejection

Rare and very difficult to
isolate to purity

Bone marrow
hematopoietic stem cells
although rare can be
purified and are used in
certain leukemias,
lymphomas

Bone marrow mesenchymal
stem cells differentiate into
chondroblasts, osteoblasts,
and myoblasts

Creating **iPS** cells



Regenerative medicine

Reprogramming factors = genes critical for “stem-cell-ness”

No graft rejection

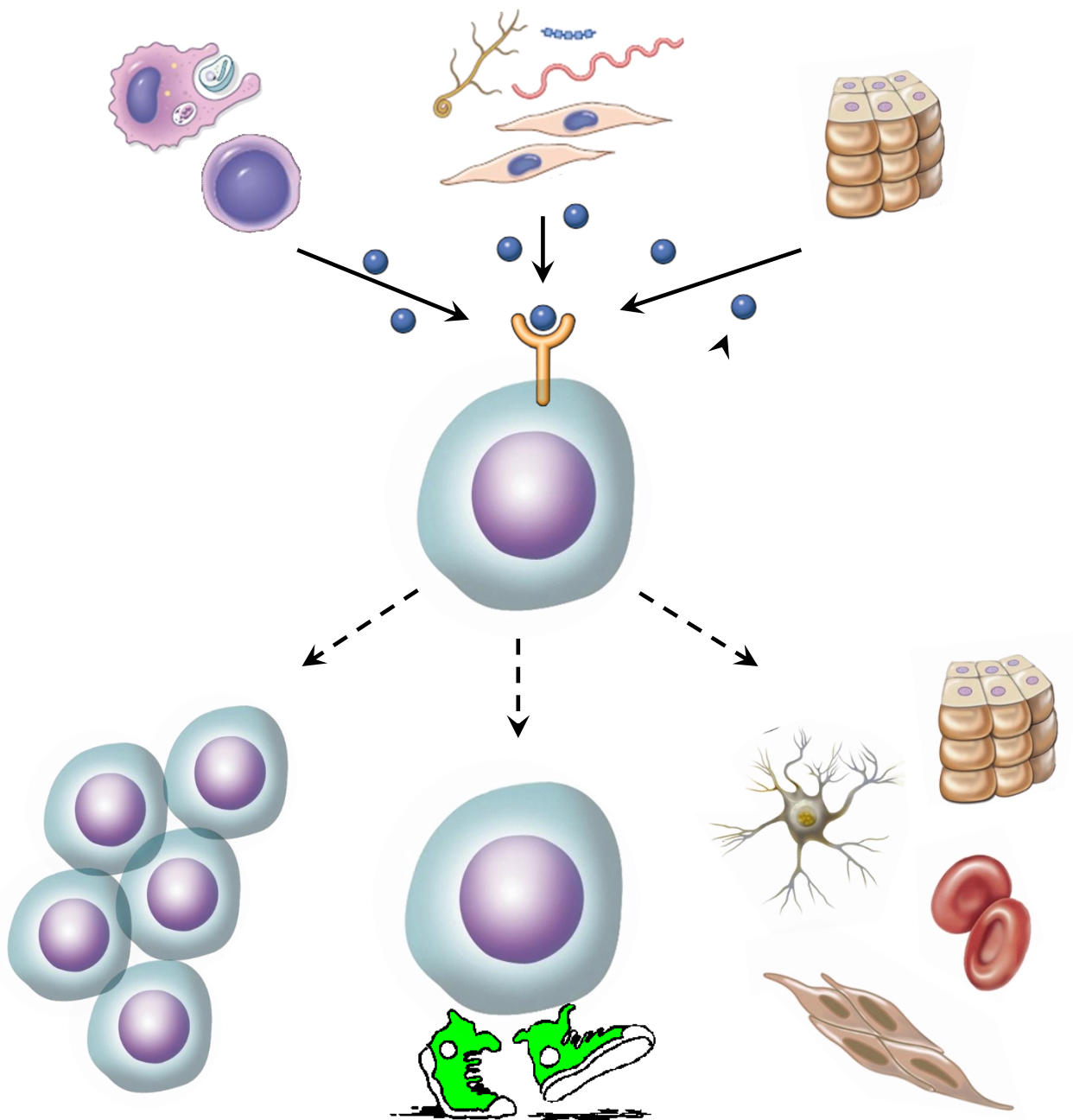
Cheaper and quicker than therapeutic cloning

Due to the genetic modifications during reprogramming the safety of using iPS cells in patients is uncertain

Still in research



Cell proliferation - Growth factors



Growth factors

Mostly proteins from:

- Lymphocytes
- Macrophage
- Stromal cells
- Parenchymal cells

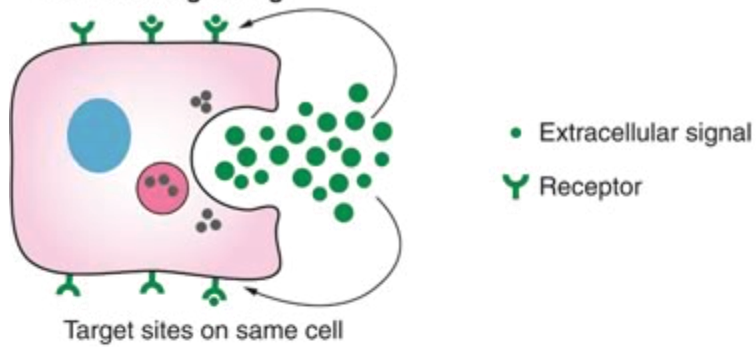
Induce cells to:

- Survive/Proliferate
- Migrate
- Differentiate

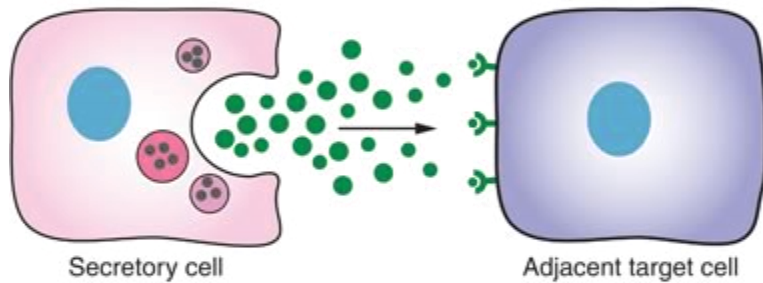
Induce proliferation through gene expression:

- Promote cell cycle entry
- Relieve cell cycle blocks
- Inhibit apoptosis
- Protein production ↑

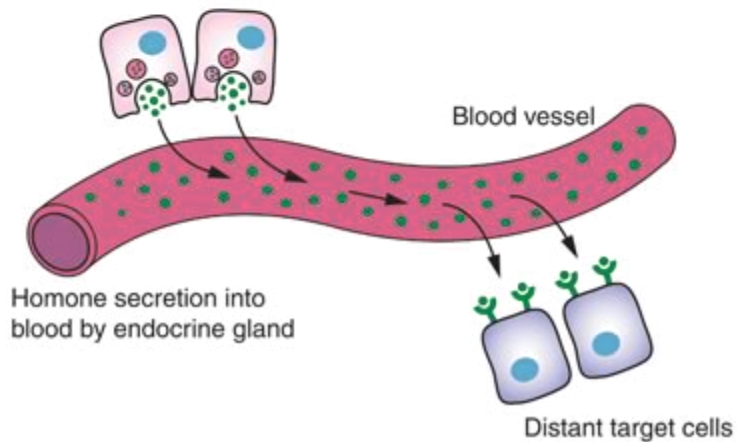
Autocrine signalling



Paracrine signalling



Endocrine signalling

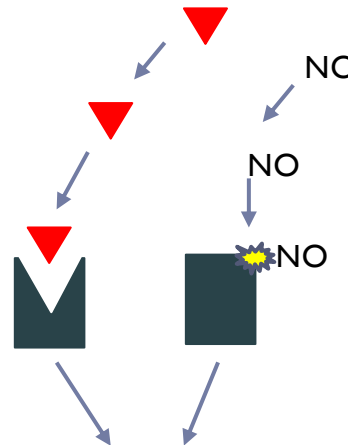


Cell signalling types

Stimulation or repression of gene expression can occur

3 types based on origin and termination of signalling molecule

2 types based on location of receptor



EGF, VEGF,
FGF, HGF

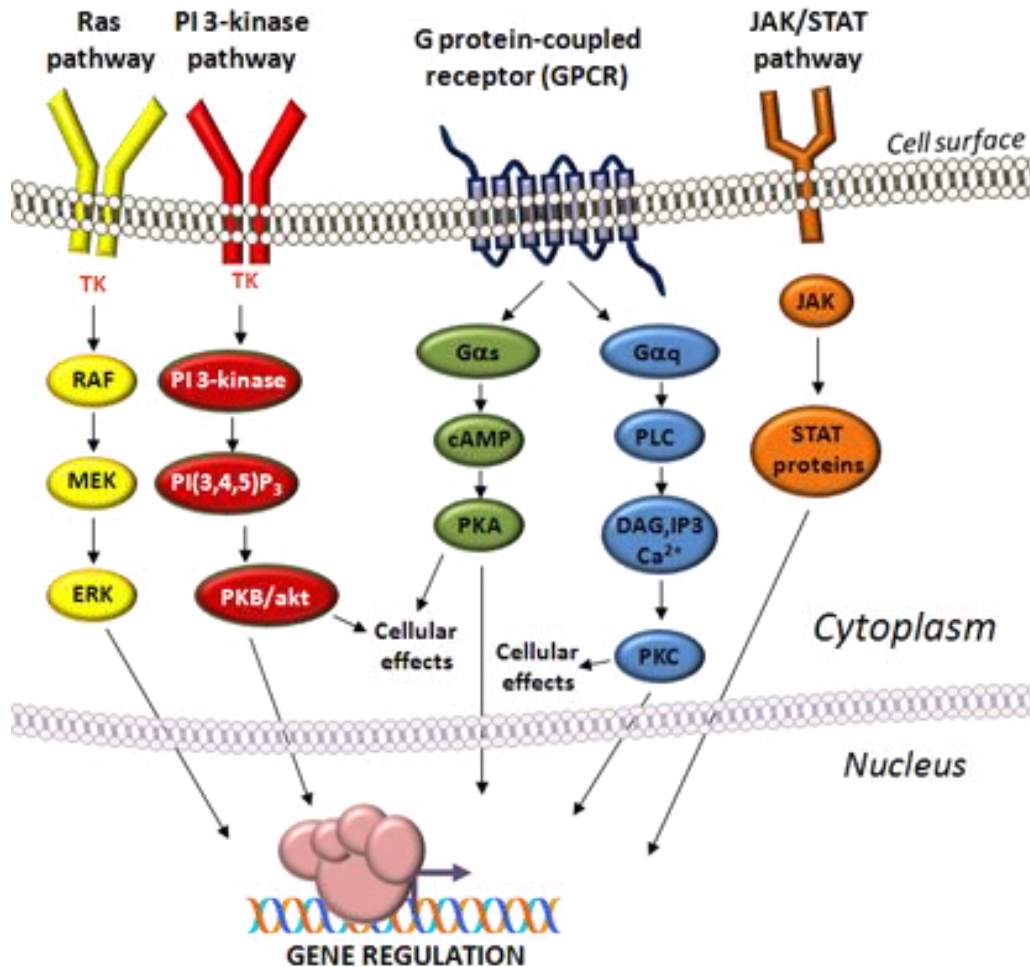
Inflammatory
mediators,
hormones,
chemokines

Cytokines
including
interferons, GH,
CSFs, EPO

Plasma membrane receptors

3 types based on type of
signal transduction:

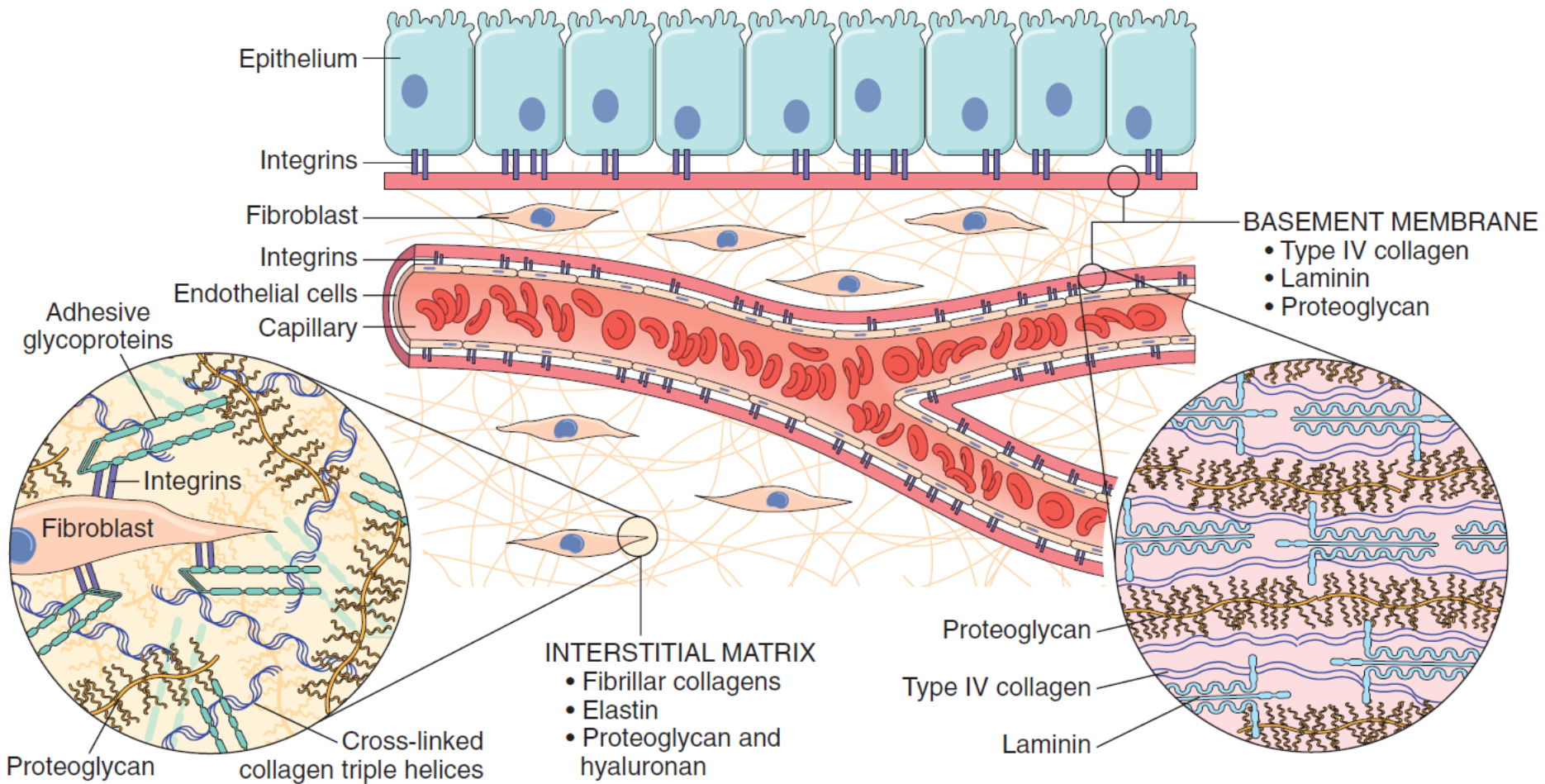
- Kinase receptors
- GPCR
- No intrinsic enzyme activity





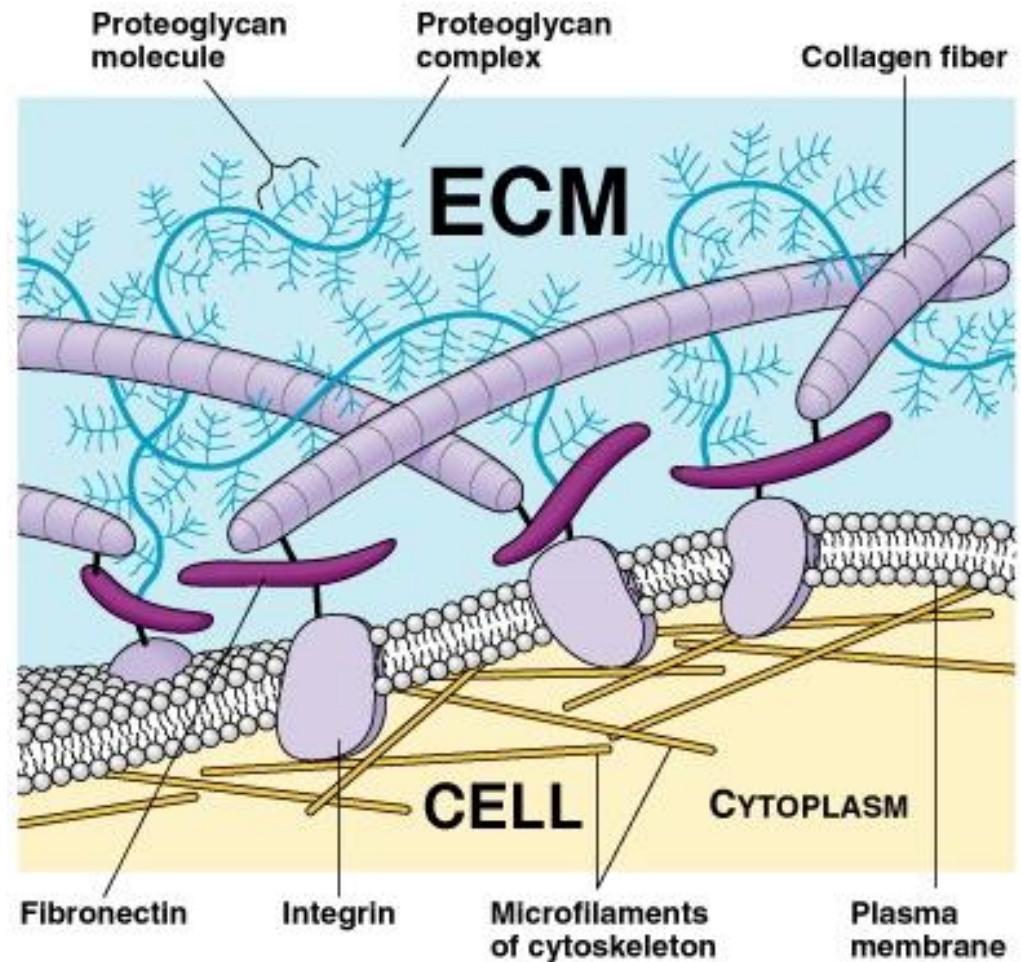
Role of the ECM

Extracellular Matrix

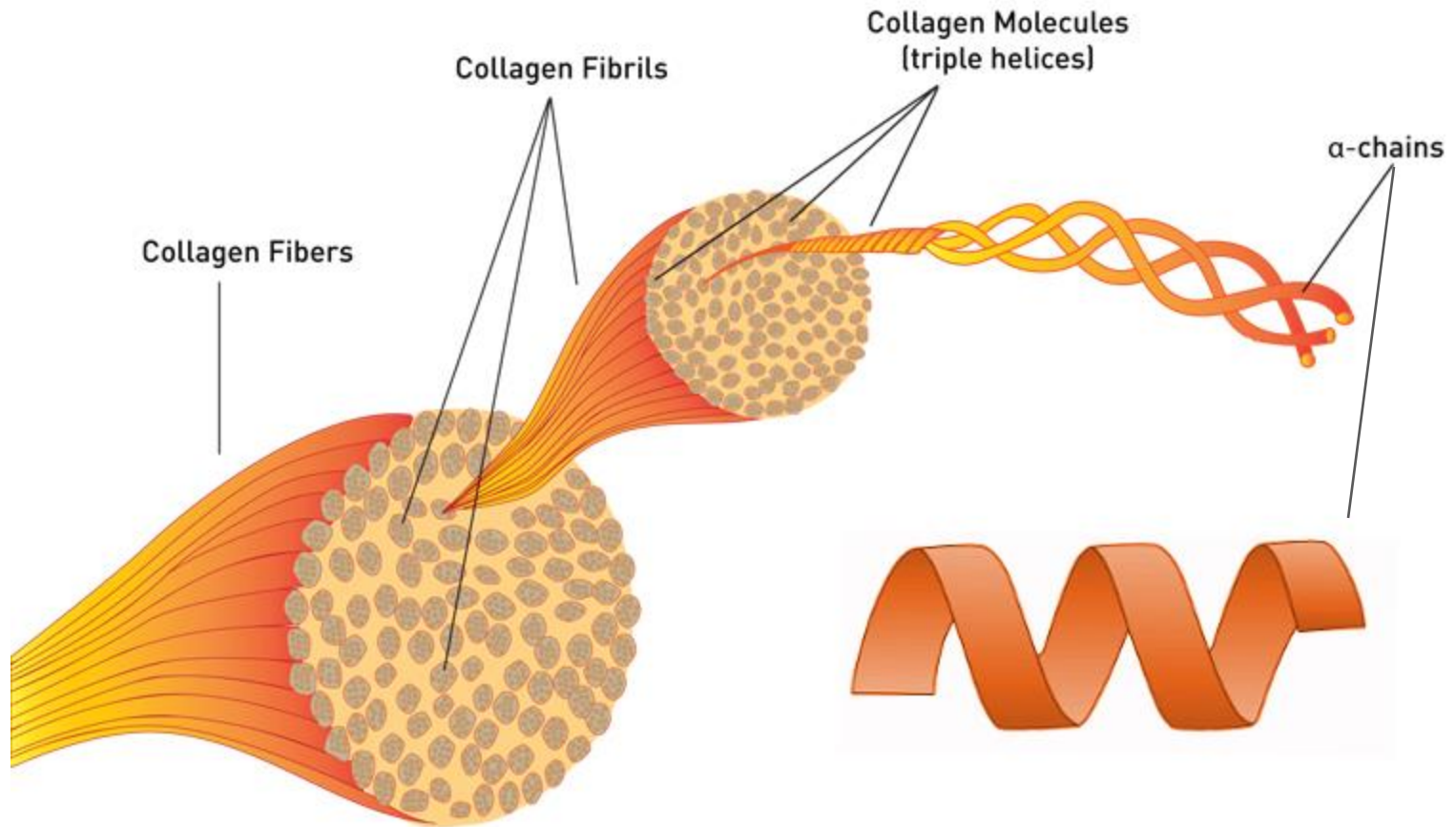


ECM components

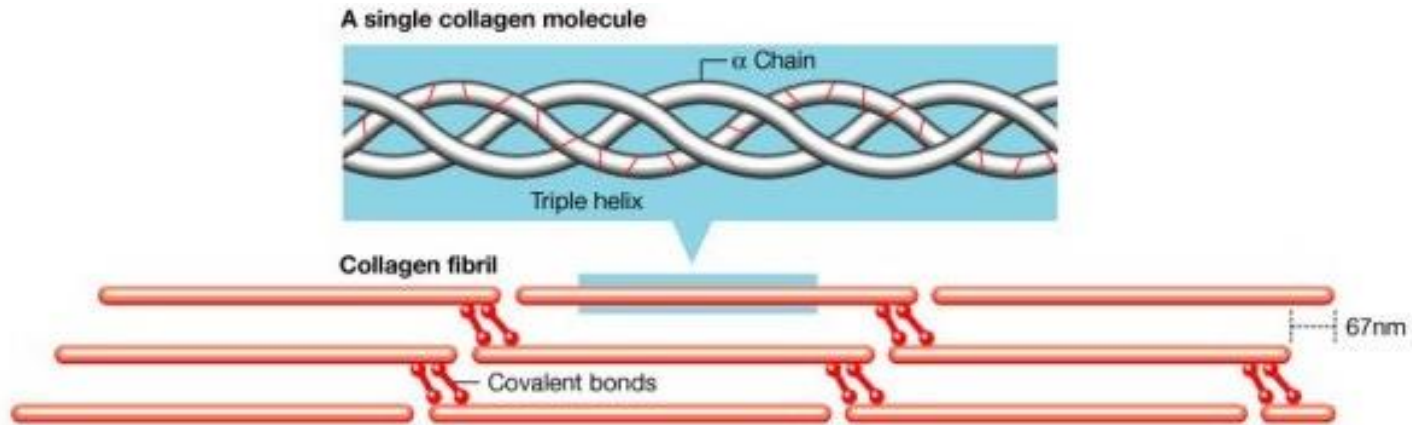
1. Fibrous structural proteins
 - collagen & elastin
 - tensile strength and recoil
2. Water-hydrated gels
 - proteoglycans & hyaluronan
 - resilience and lubrication
3. Adhesive glycoproteins
 - fibronectin & laminin
 - Matrix/matrix-cell connections



Collagen (fibrillar)



Collagen (fibrillar)

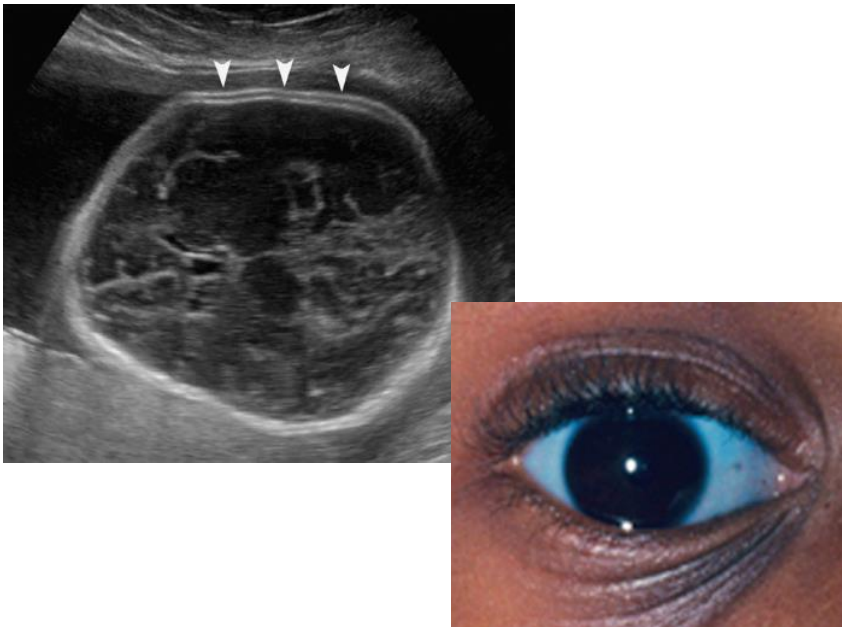


- types I, II, III, and V
- major proportion of the connective tissue in healing/scarring
- Lateral cross-linking of the triple helices catalyzed by lysyl-oxidase (Copper dependent)/lysyl-**hydroxylase** (Vit C dependent)

Examples of Collagen defects

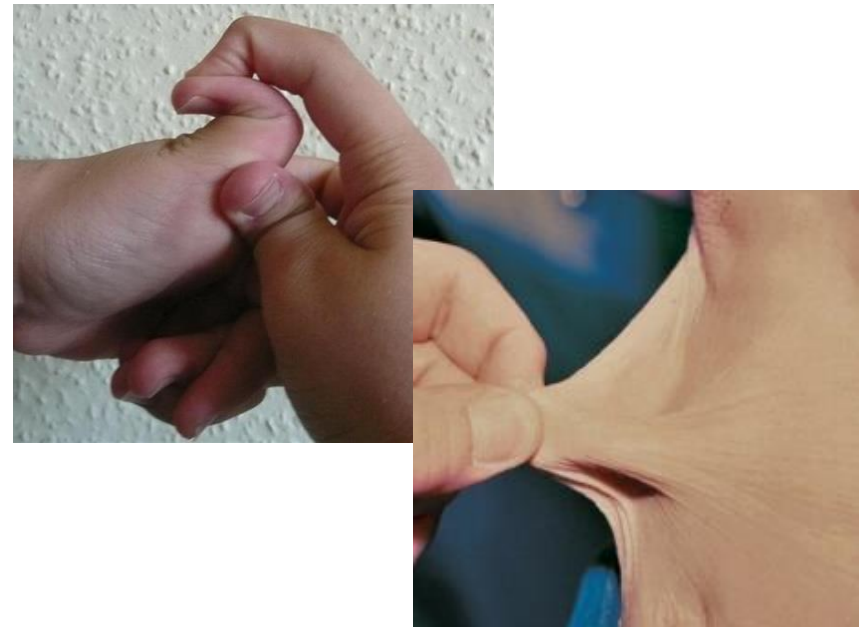
Osteogenesis Imperfecta

- ▶ aka brittle bone disease
- ▶ 8 types commonly due to a Type-I collagen deficiency

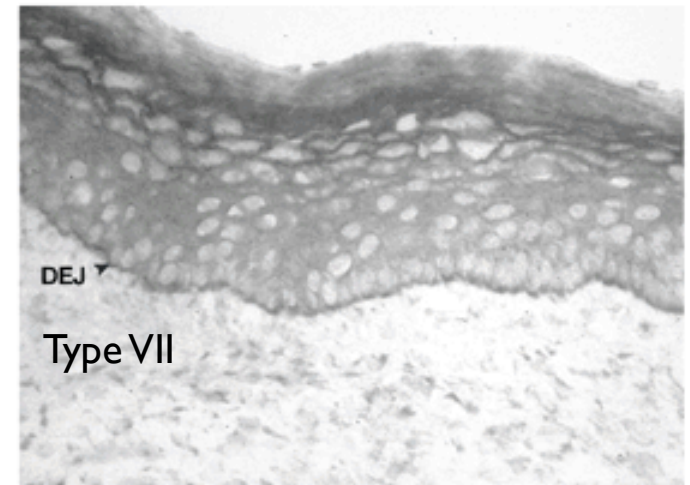
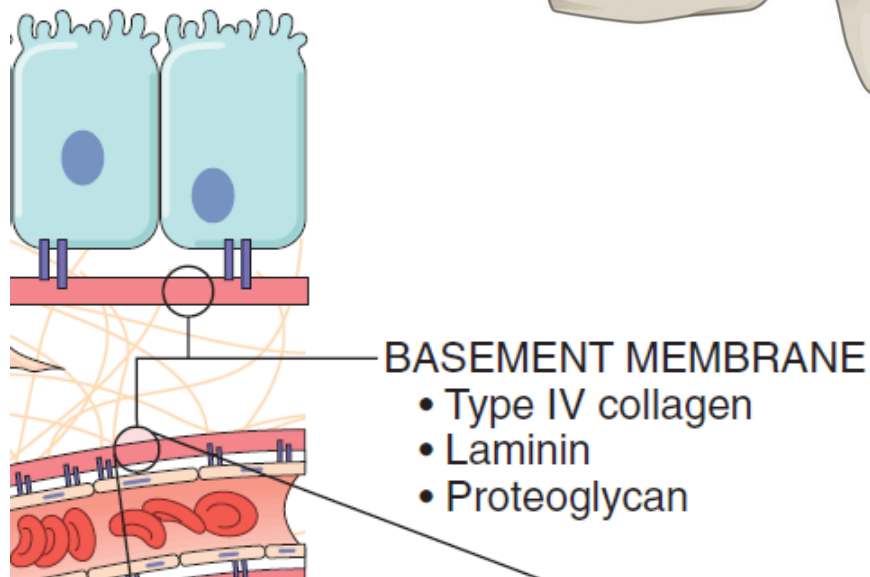
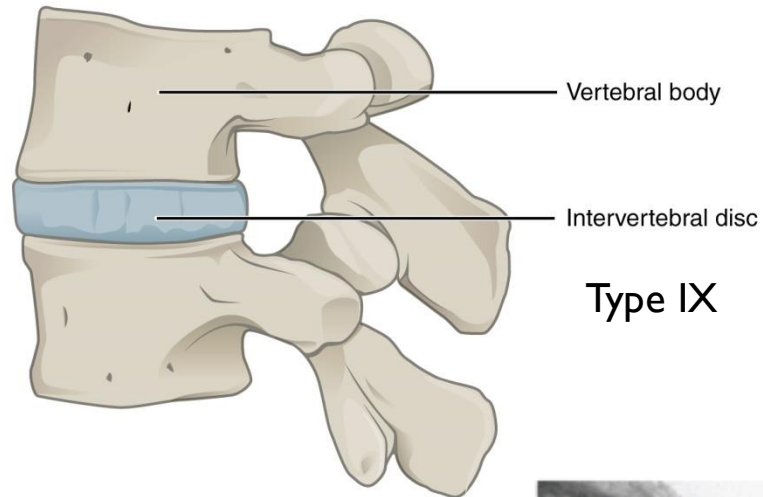


Ehlers-Danlos Syndrome

- ▶ Hyperextensible skin
- ▶ Lax joints
- ▶ Vascular defects

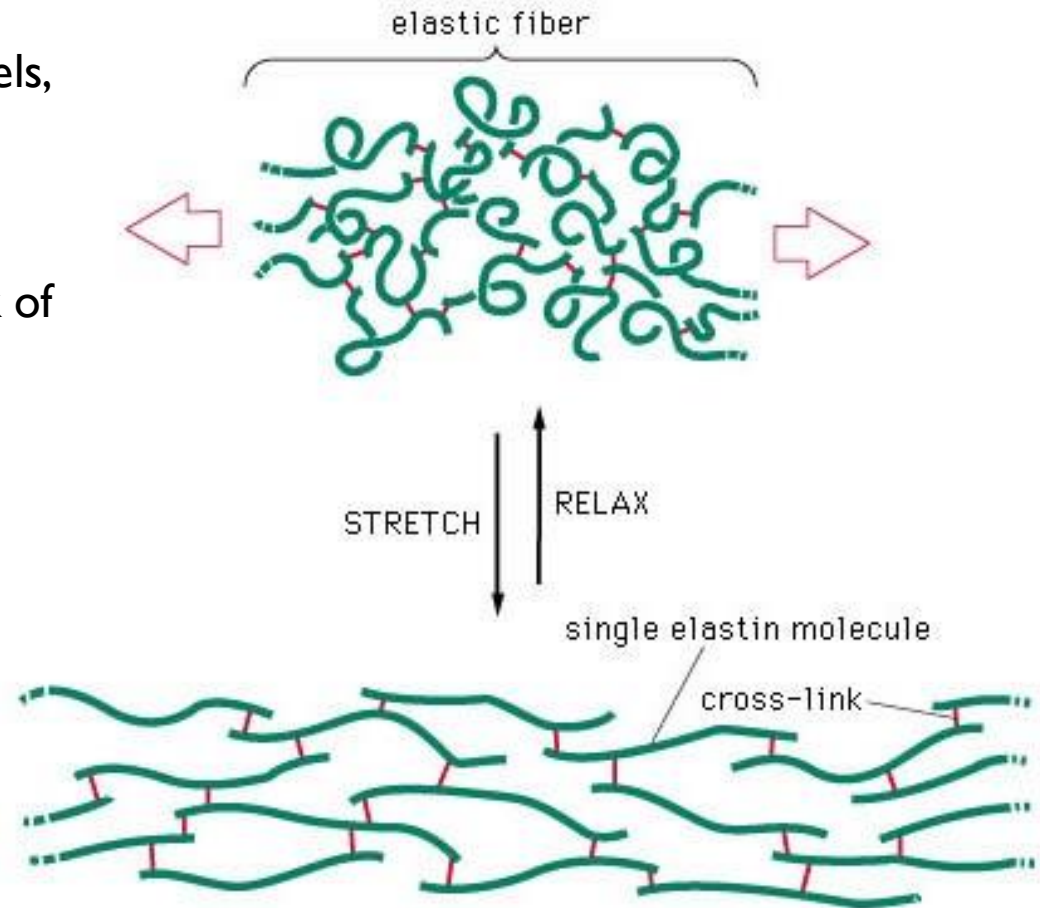


Collagen (nonfibrillar)



Elastin

- Important in the walls of large vessels, the uterus, skin, and ligaments
- The central core of elastin is surrounded by a mesh-like network of fibrillin glycoprotein
- *FBN1* mutation = Marfan Syndrome

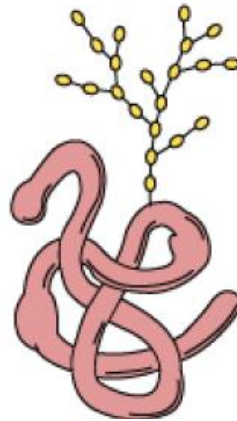
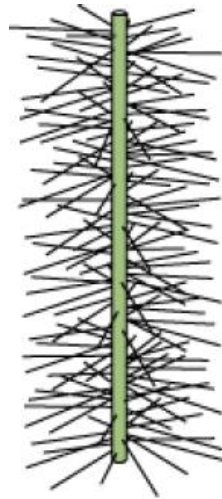


Proteoglycans and Hyaluronan

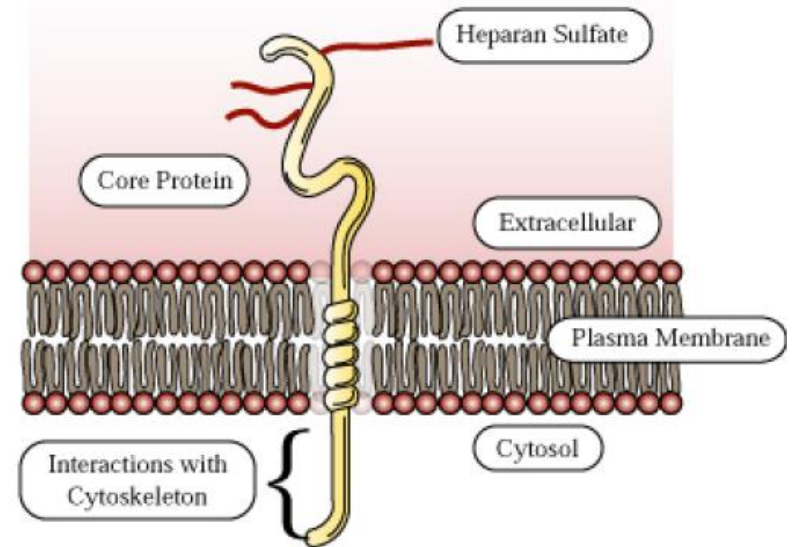
↓
highly hydrated compressible
gels conferring resilience and
lubrication, and serve as
reservoirs for growth factors

Proteoglycans have a protein
core to which
glycosaminoglycans are attached

Glycoproteins are globular
proteins with branched
monosaccharide chains



↗ huge mucopolysaccharide without a
protein core, binds water, and forms a
viscous, gelatin-like matrix



Some proteoglycans are integral cell
membrane proteins that have roles in cell
proliferation, migration, and adhesion