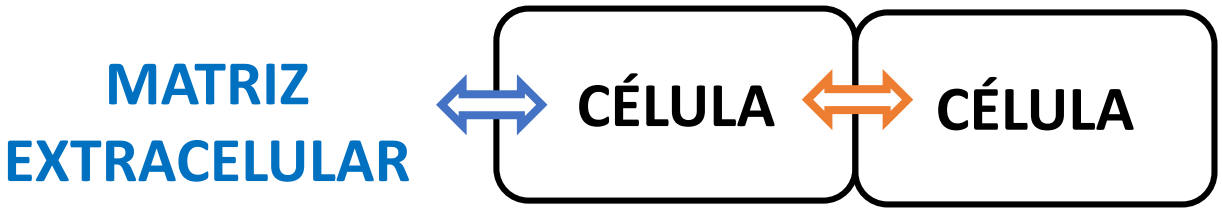
LA CÉLULA Y SU CONTEXTO



TEO16

1- identificar los componentes de la matriz y sus principales características estructurales

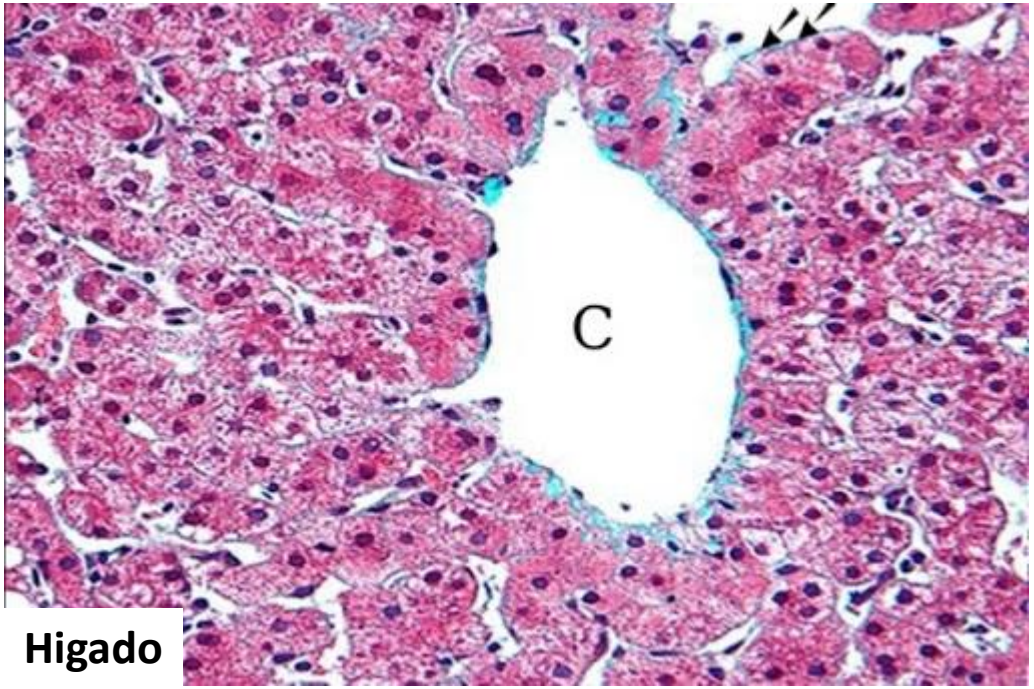
2- relacionar las características estructurales de cada elemento con su propiedades físicas - bioquímicas

3- analizar la relación entre los diferentes componentes y las células presentes en el tejido

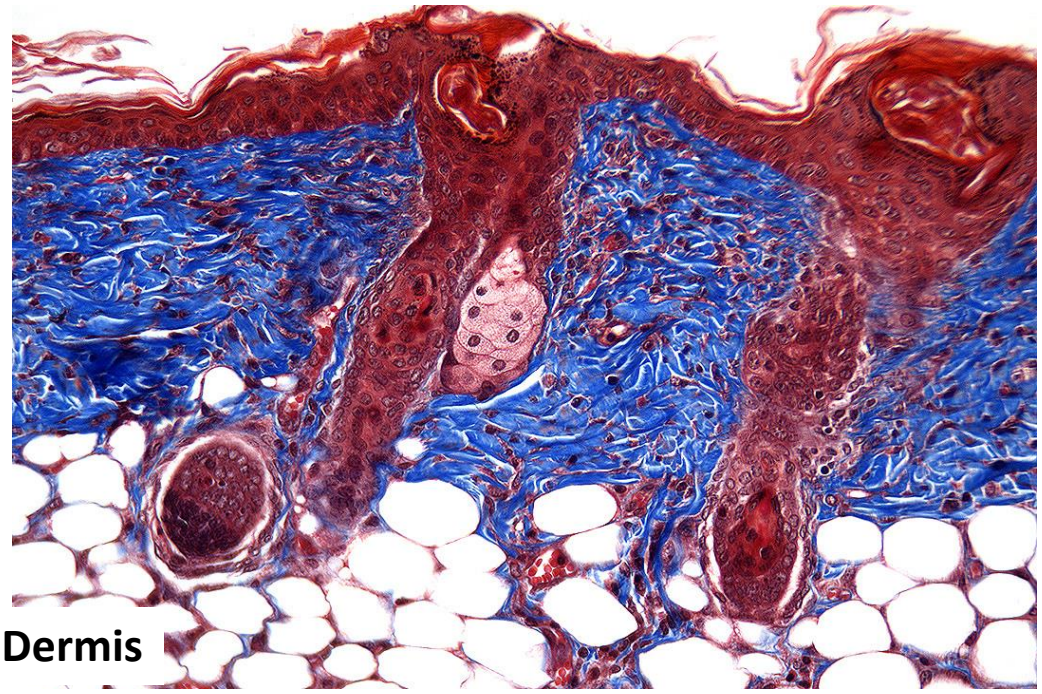
Tinción tricrómica de Masson

Colágeno

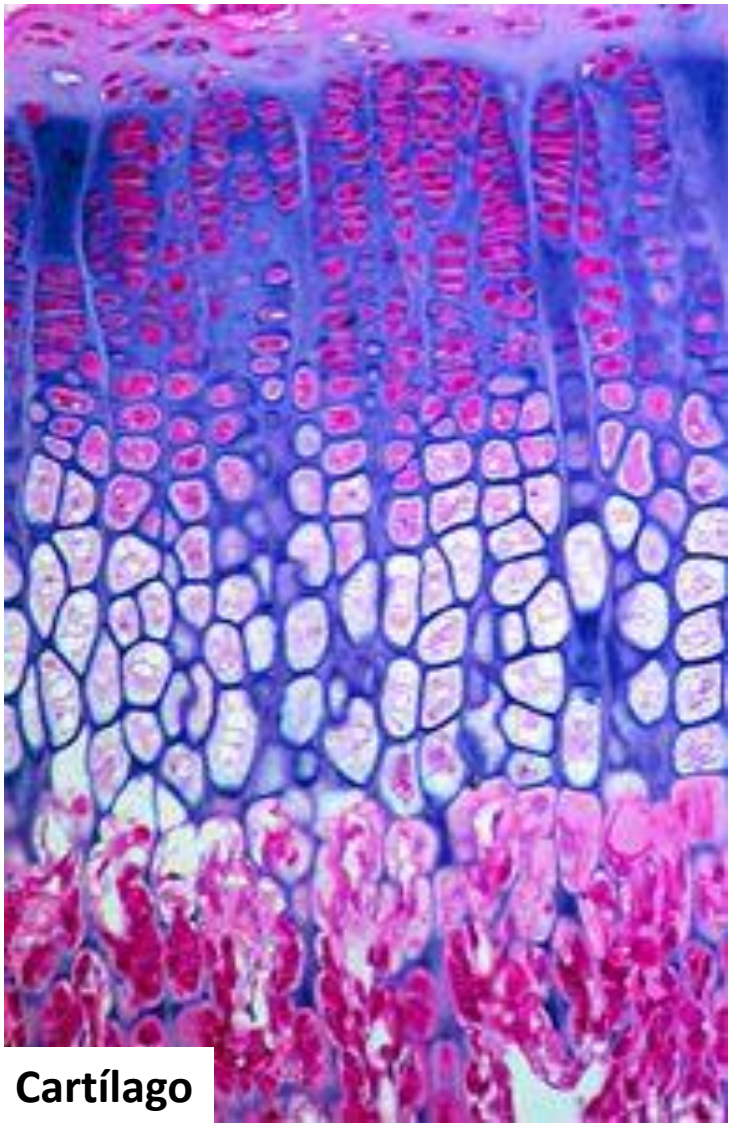
Células



Higado

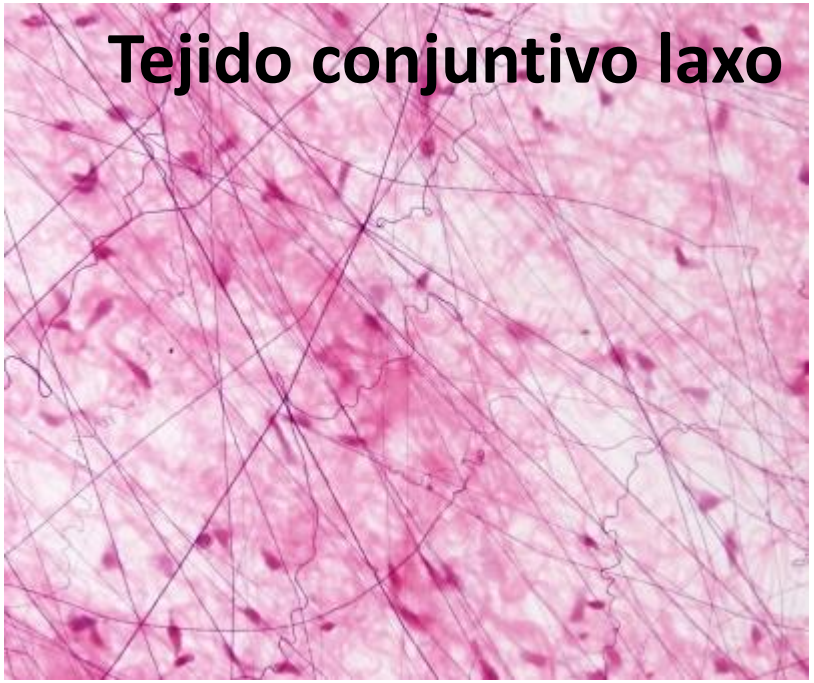


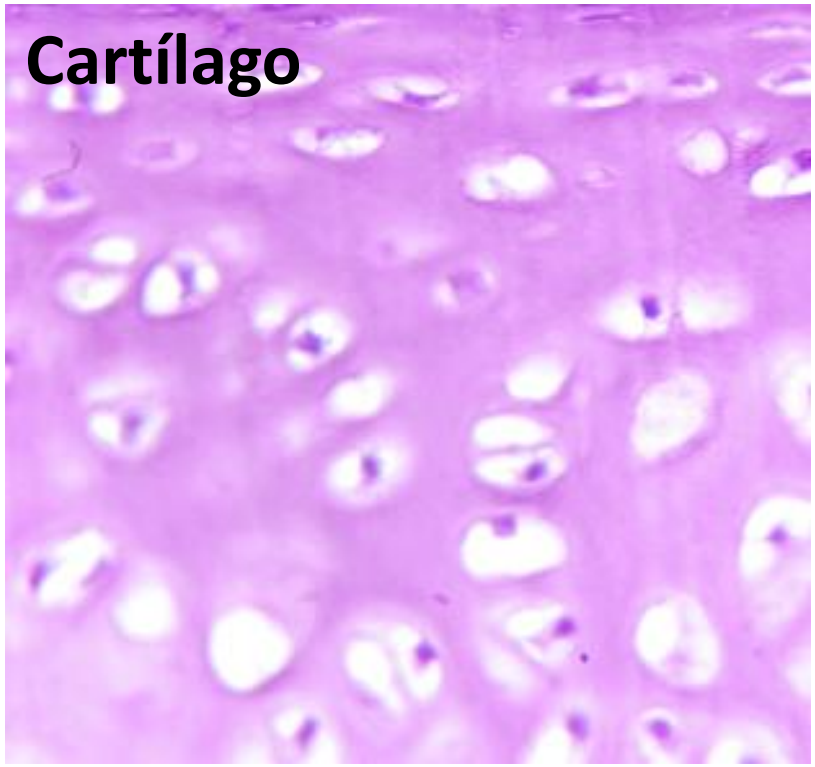
Dermis



Cartílago

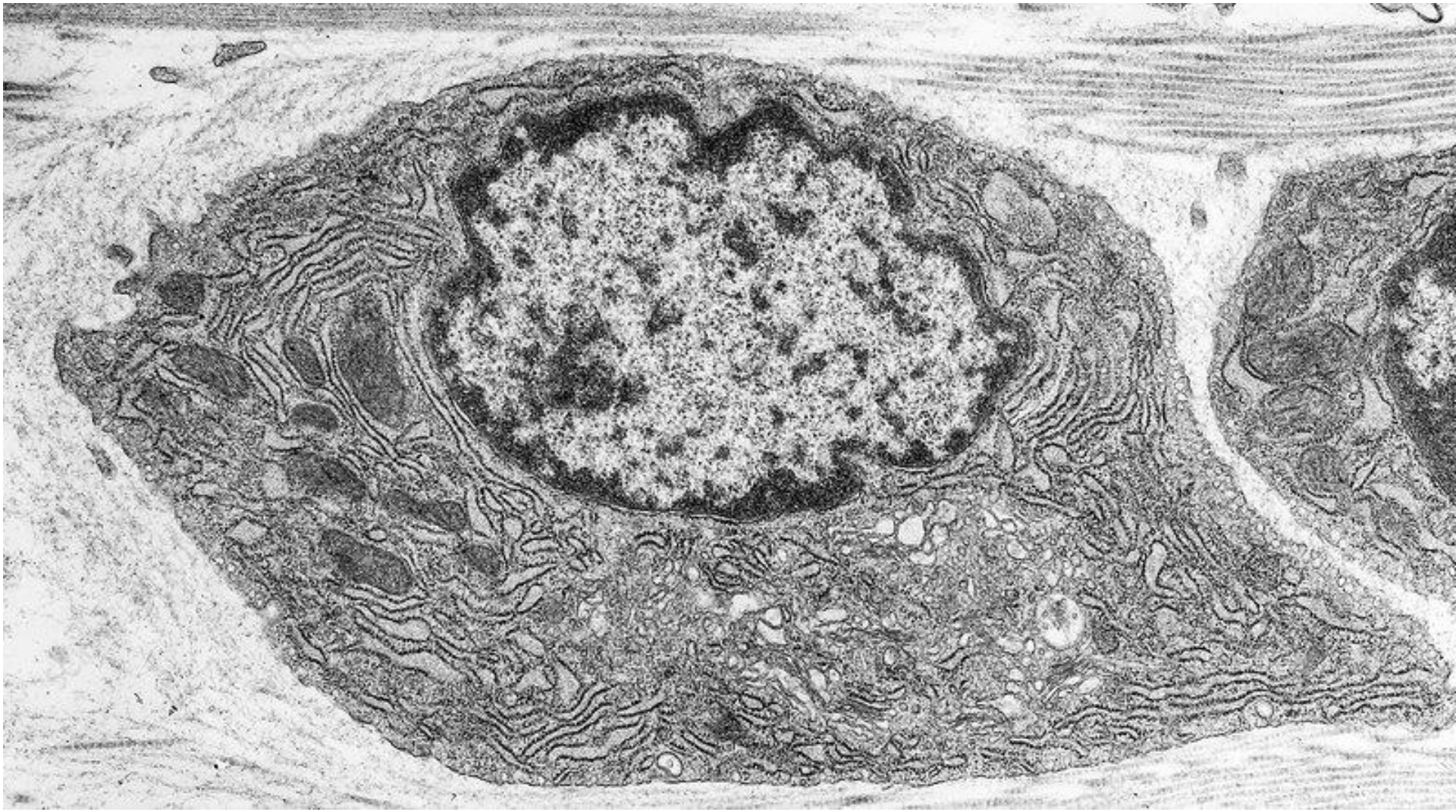
Tejido conjuntivo





Estructura: células especializadas sin contactos estables y con gran cantidad matriz extracelular.
Función: resistencia, nutrición

MATRIZ EXTRACELULAR: ¿quién la genera?

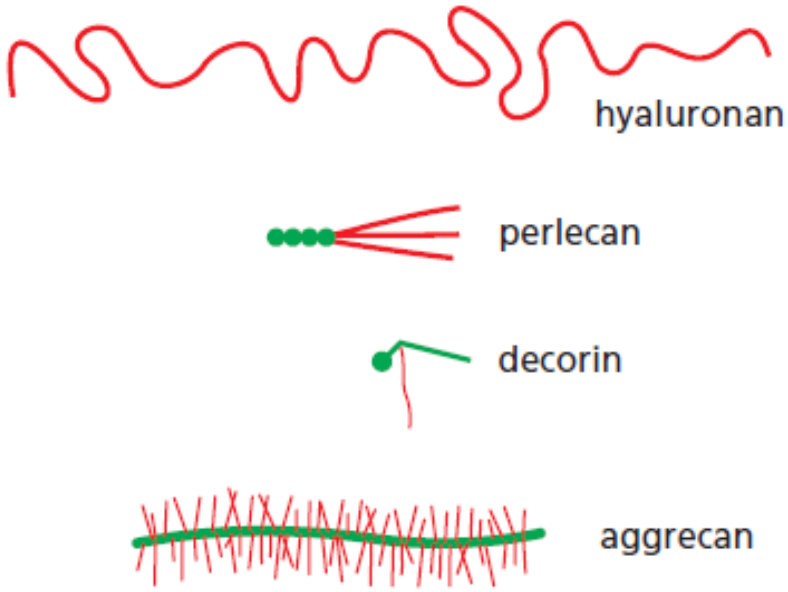


fibroblastos

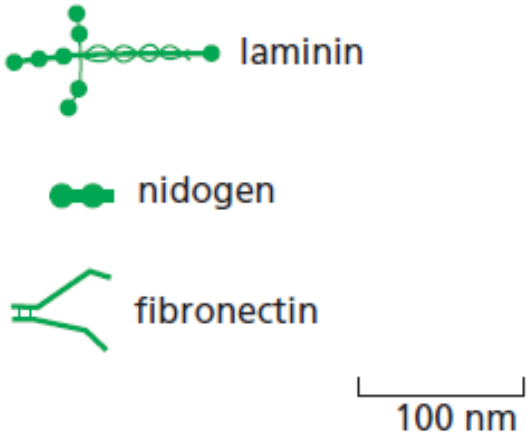
osteoblastos
condroblastos

MATRIZ EXTRACELULAR:
Componentes…..

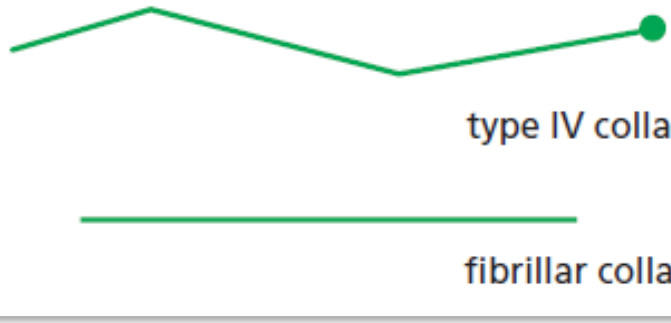
Proteoglicanos y GAGs



Glicoproteínas



colágeno



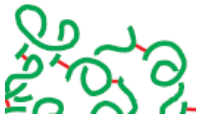
Alrededor de 300 moléculas diferentes en mamíferos

Proteoglicanos 36

Colágeno 40

Glucoproteínas >200

fibras elásticas



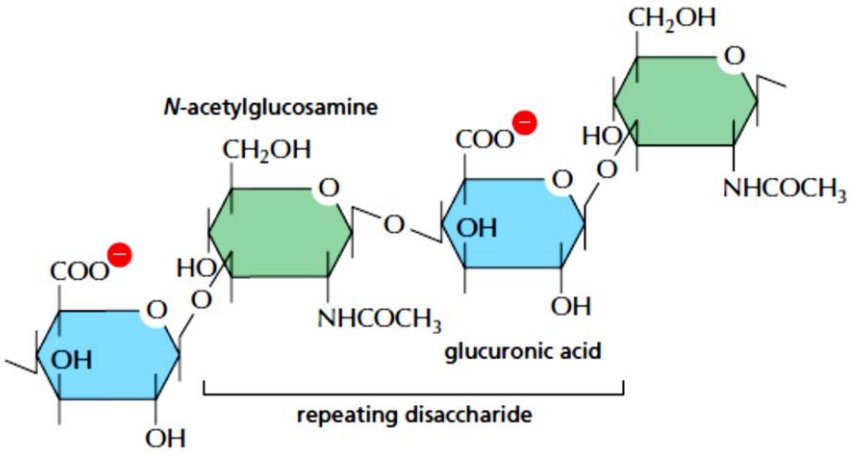
glúcidos proteína

Glucosaminoglucanos (GAGs)

Cadenas de polisacáridos **no ramificadas**, compuestas por unidades repetidas de disacáridos:

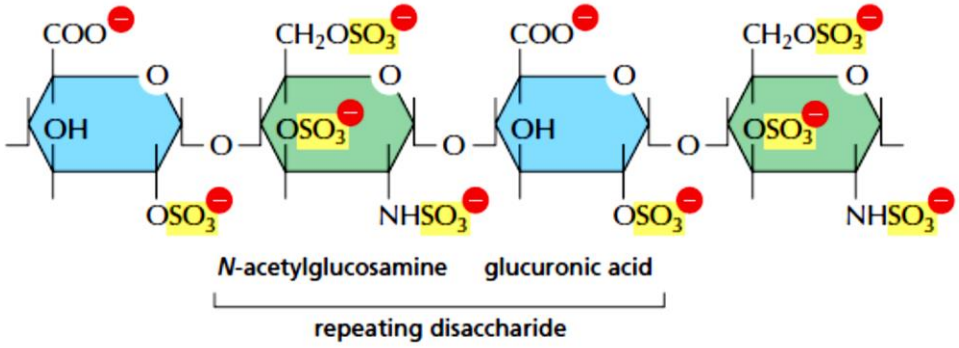
Aminoazúcar (N-acetilglucosamina o N-acetilgalactosamina) + ácido urónico (glucurónico o idurónico)

Hialuronato



x 25.000 !

Heparán sulfato



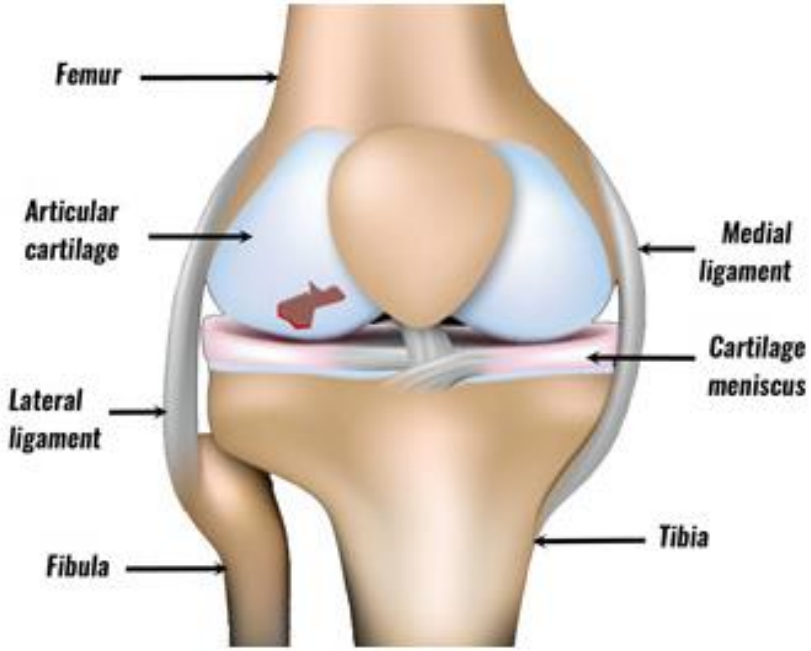
Glucosaminoglucanos (GAGs)

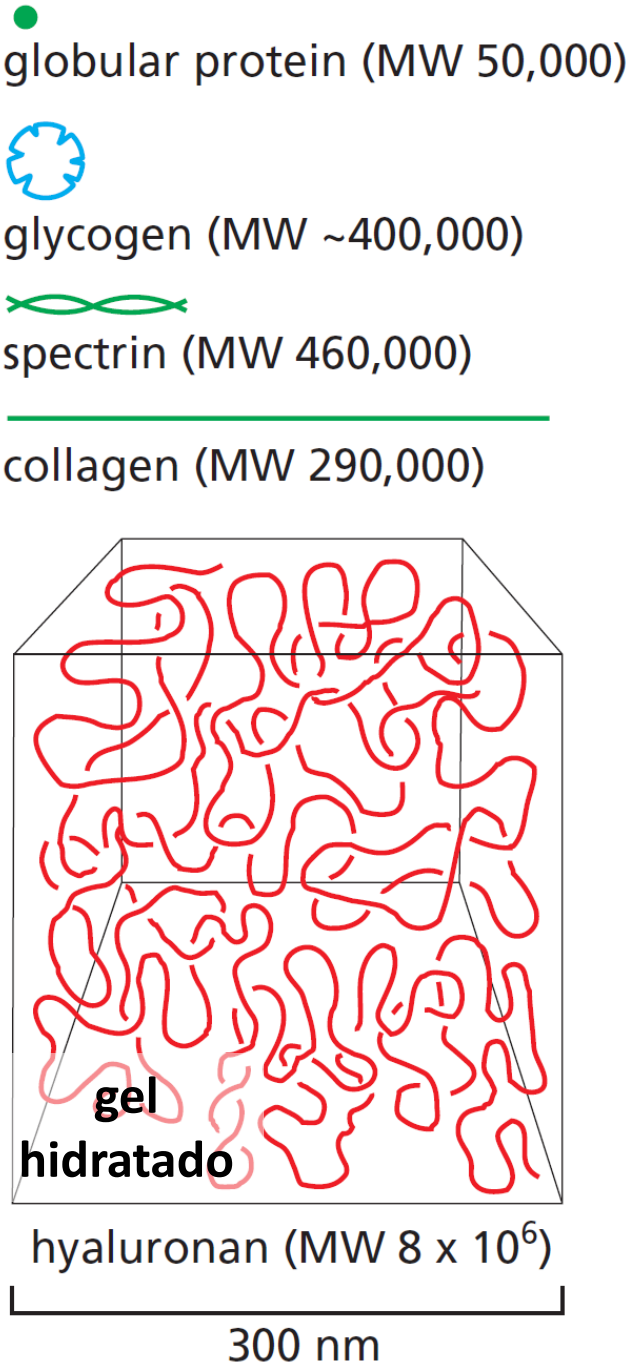
hyaluronato

chondroitin sulfato y dermatan sulfato

heparan sulfato

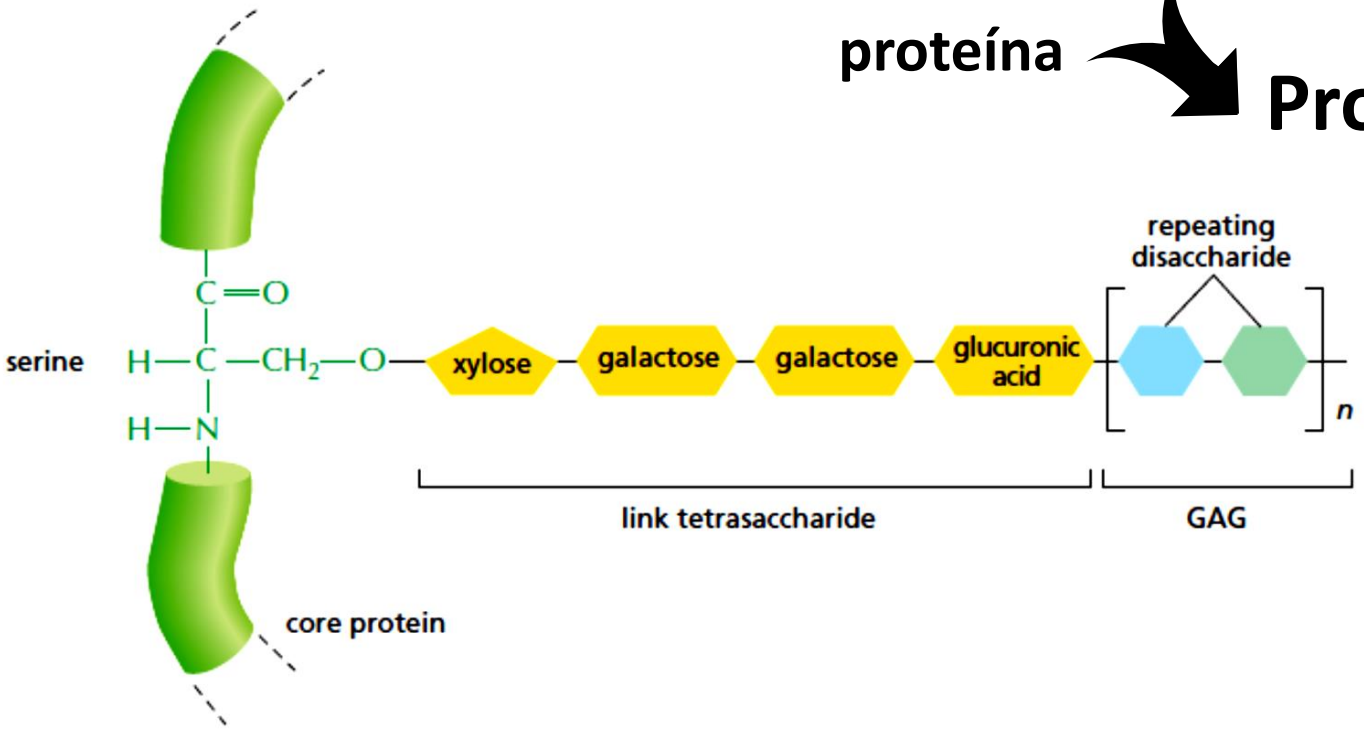
keratan sulfato



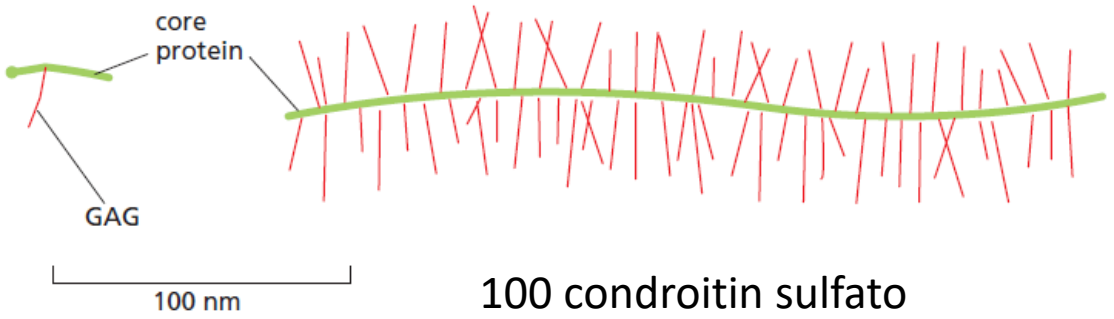


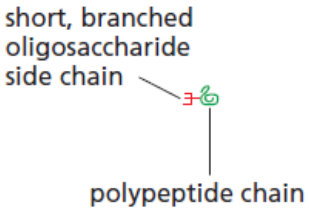
GAGs

proteína → **Proteoglicanos**



DECORIN (MW ~40,000)	AGGRECAN (MW ~3 x 10^6)	RIBONUCLEASE (MW ~15,000)

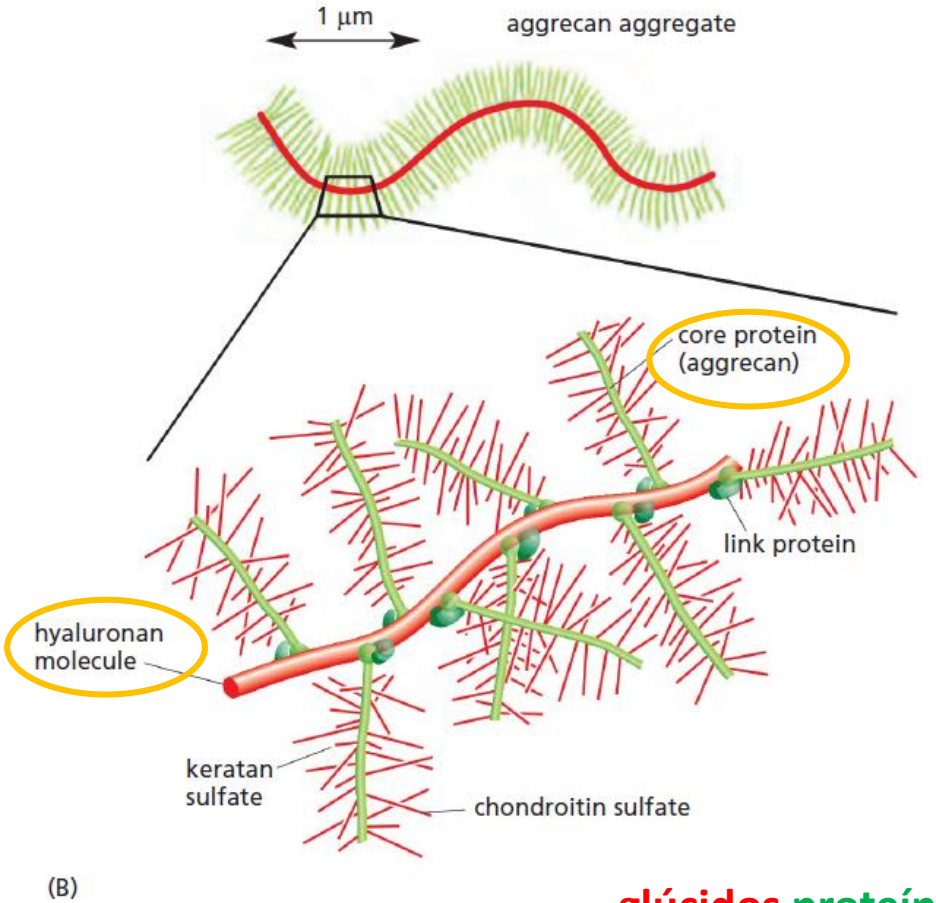




100 condroitin sulfato
30 keratan sulfato
Proteína de 3000aa

glicoproteína

Proteoglicanos



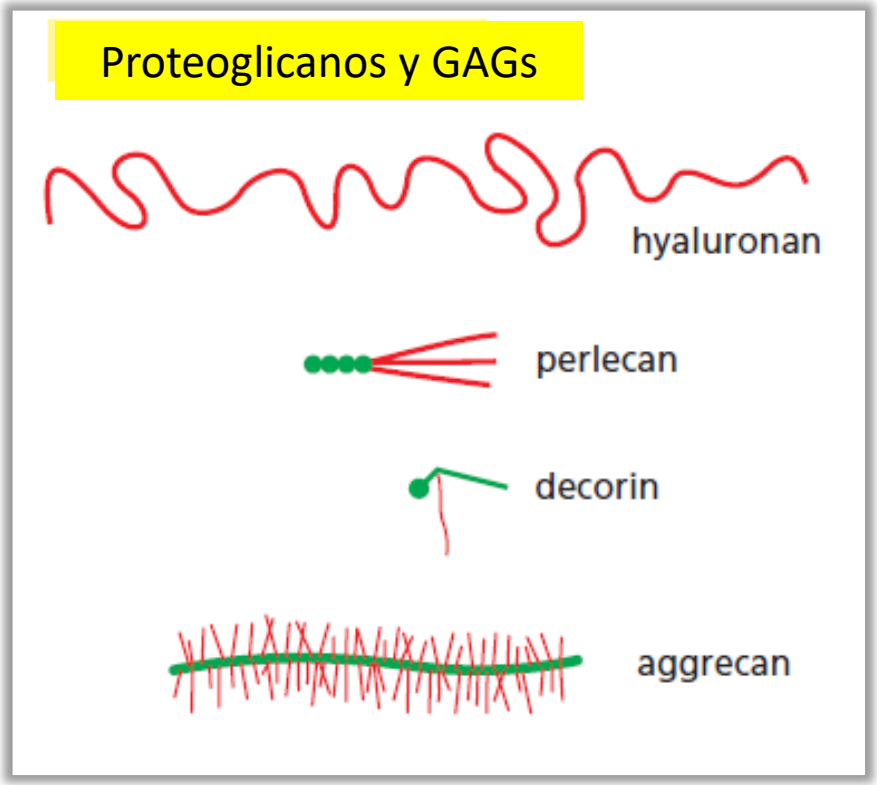
glúcidos proteína

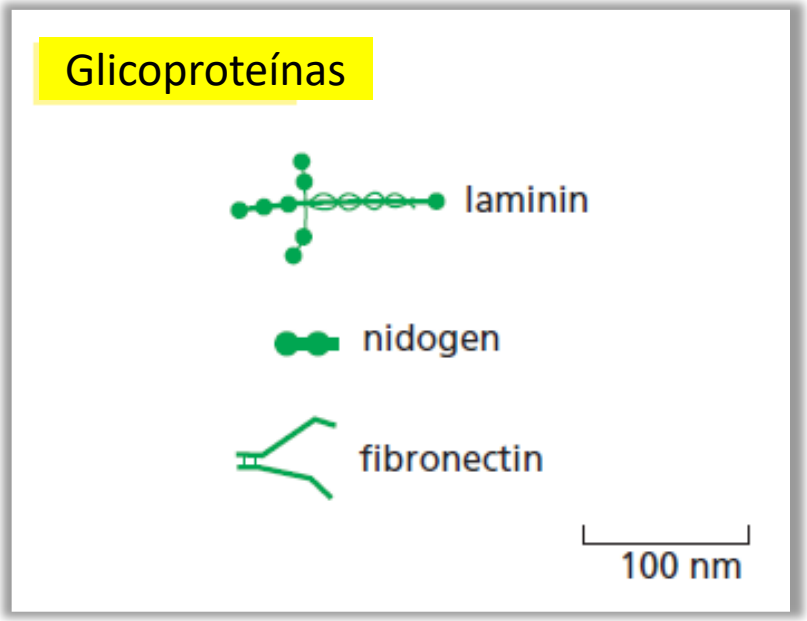
Proteoglicanos

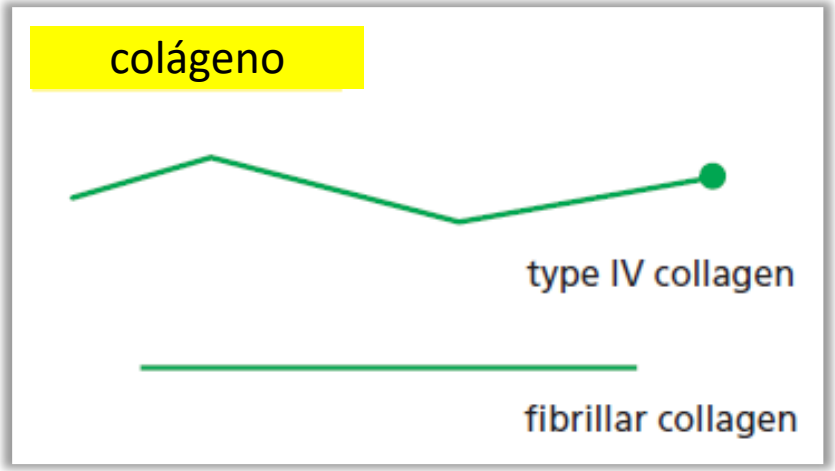
Colágeno

MATRIZ EXTRACELULAR:

Componentes…..







Alrededor de 300 proteínas en mamíferos

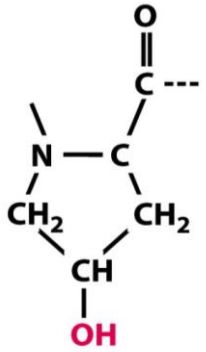
Proteoglicanos 36

Colágeno 40

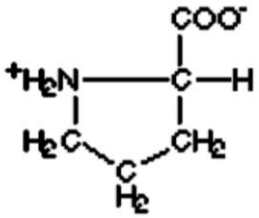
Glucoproteínas >200

glúcidos proteína

Colágeno: estructura

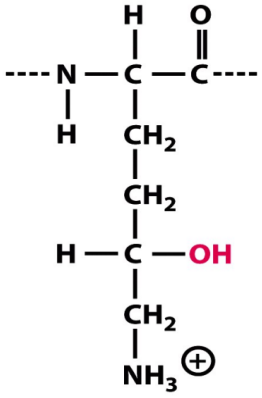


Y frecuentemente es hidroxiprolina

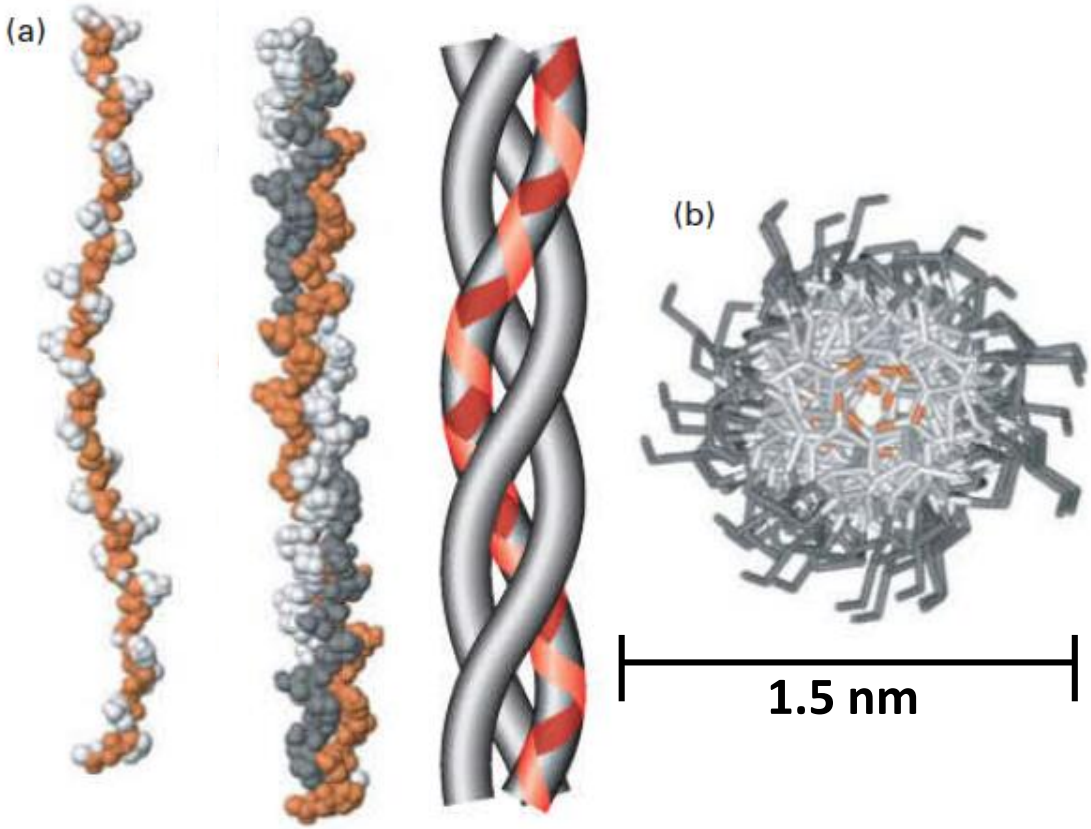


X frecuentemente es prolina

– Gly – X – Y – Gly – X – Y – Gly – X – Y –



hidroxilisina



cadena α

42 genes

hélice de tres cadenas

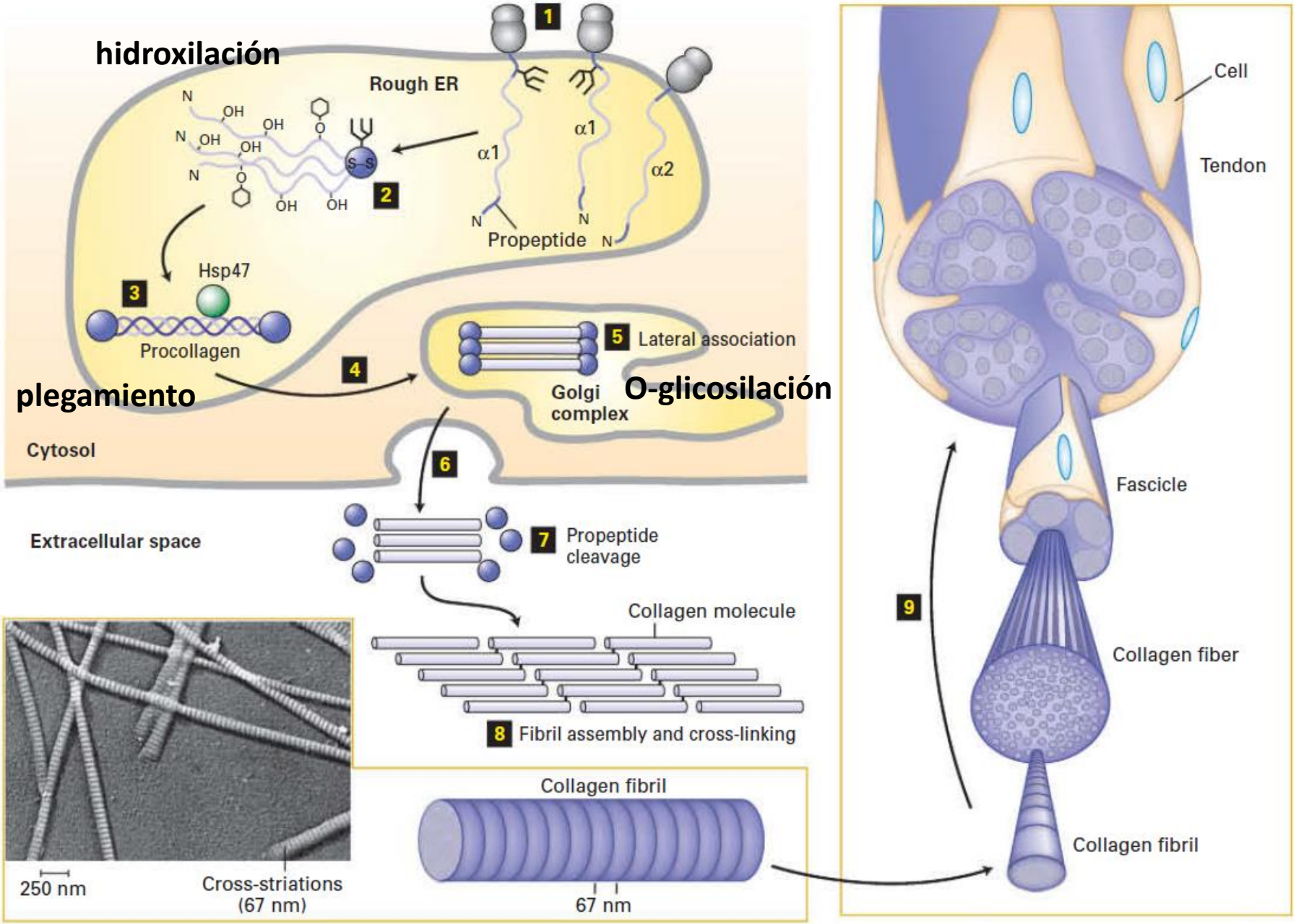
40 ≠

Tipos de colágeno…

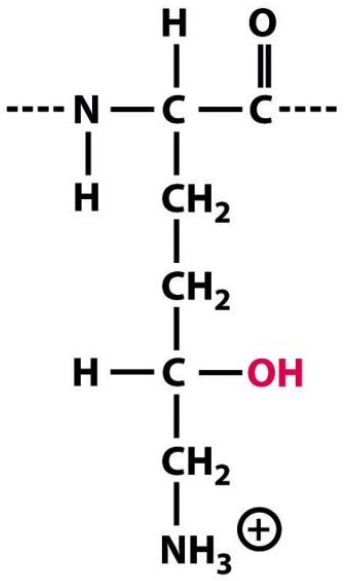
TABLE 19–2 Some Types of Collagen and Their Properties				
	Type	Polymerized form	Tissue distribution	Mutant phenotype
Fibril-forming (fibrillar)	I	Fibril	Bone, skin, tendons, ligaments, cornea, internal organs (accounts for 90% of body collagen)	Severe bone defects, fractures (*osteogenesis imperfecta*)
	II	Fibril	Cartilage, intervertebral disc, notochord, vitreous humor of the eye	Cartilage deficiency, dwarfism (*chondrodysplasia*)
	III	Fibril	Skin, blood vessels, internal organs	Fragile skin, loose joints, blood vessels prone to rupture (*Ehlers–Danlos syndrome*)
	V	Fibril (with type I)	As for type I	Fragile skin, loose joints, blood vessels prone to rupture
	XI	Fibril (with type II)	As for type II	Myopia, blindness
Fibril-associated	IX	Lateral association with type II fibrils	Cartilage	Osteoarthritis
Network-forming	IV	Sheetlike network	Basal lamina	Kidney disease (glomerulonephritis), deafness
	VII	Anchoring fibrils	Beneath stratified squamous epithelia	Skin blistering
Transmembrane	XVII	Nonfibrillar	Hemidesmosomes	Skin blistering
Proteoglycan core protein	XVIII	Nonfibrillar	Basal lamina	Myopia, detached retina, hydrocephalus

Note that types I, IV, V, IX, and XI are each composed of two or three types of α chains (distinct, nonoverlapping sets in each case), whereas types II, III, VII, XVII, and XVIII are composed of only one type of α chain each.

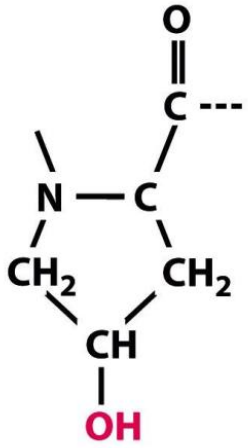
Colágeno tipo I: síntesis



Colágeno: estructura

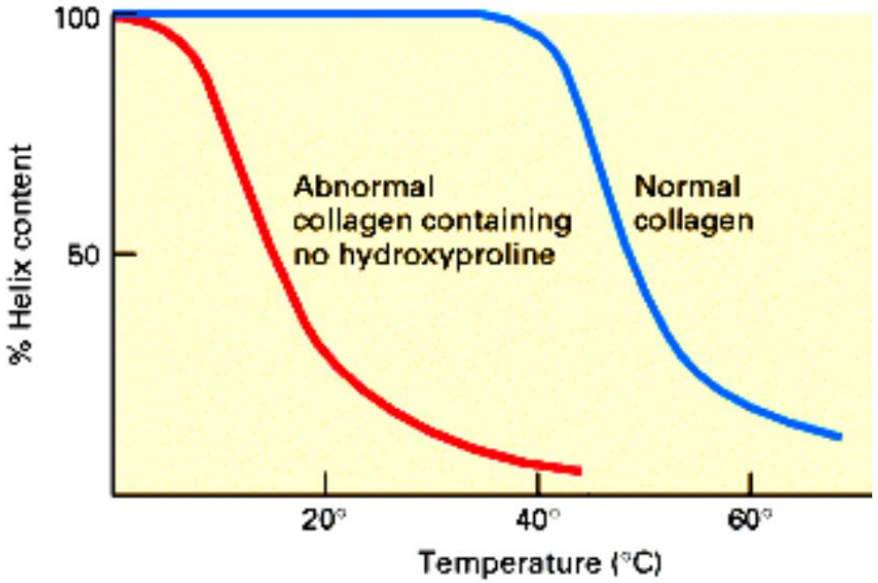


hydroxylysine in protein



hydroxyproline in protein

La hidroxilación de prolina y lisina en colágeno requiere vitamina C (ácido ascórbico) -> escorbuto

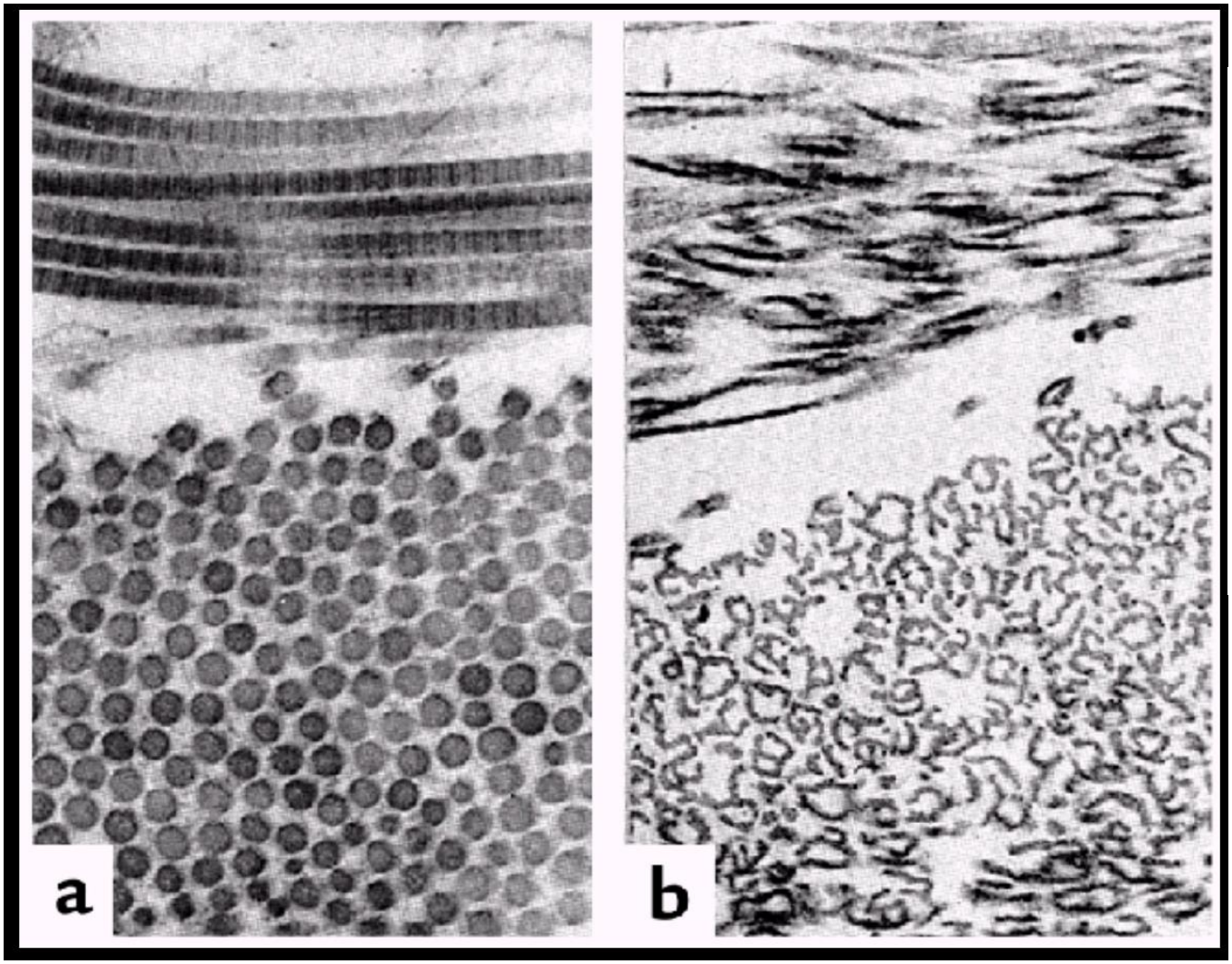


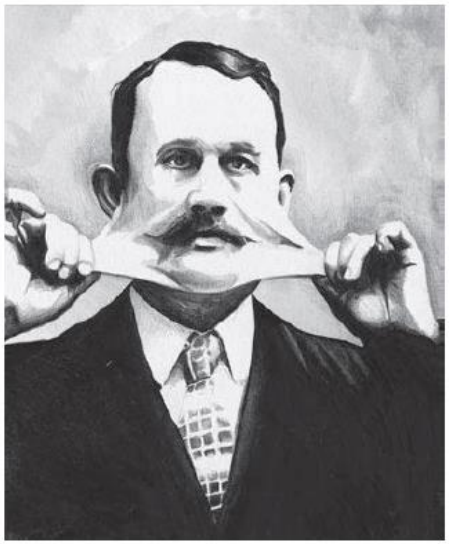
Colágeno: síntesis

Función?

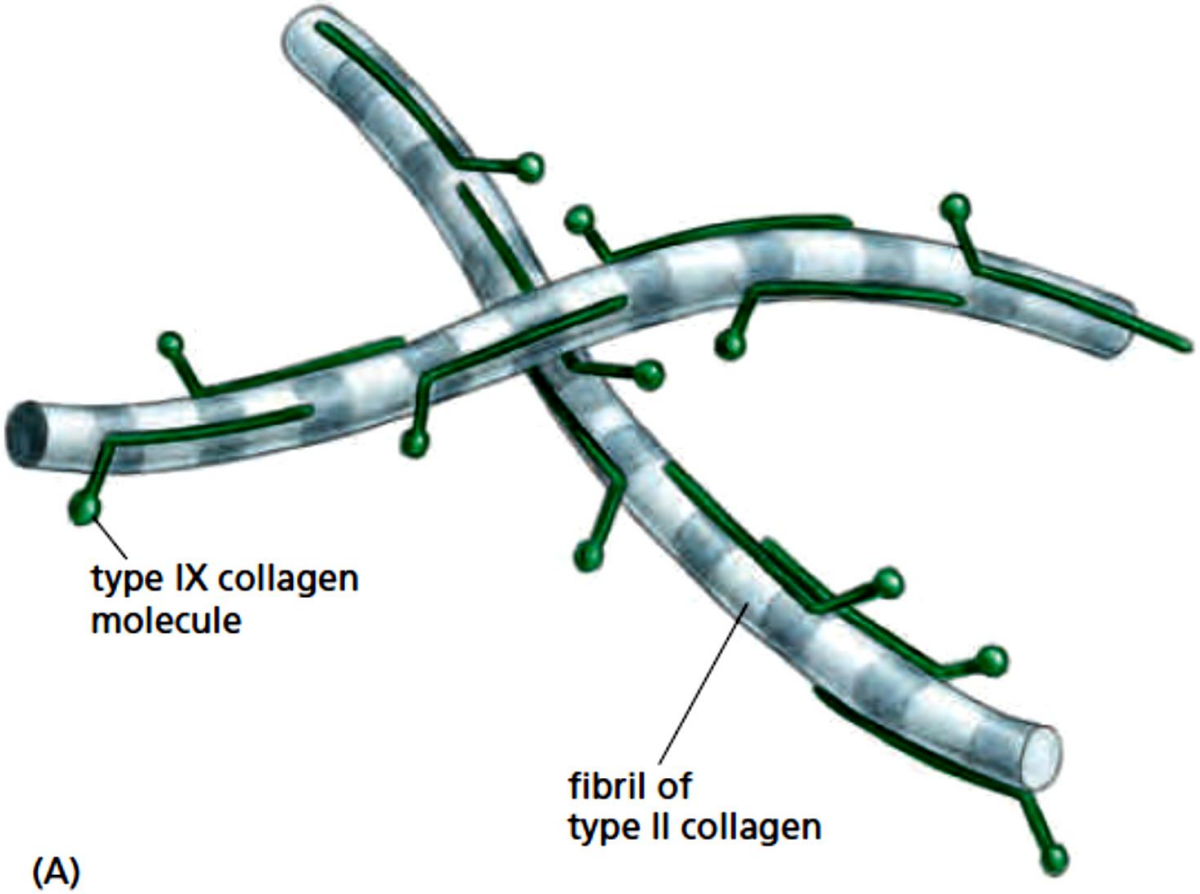
Piel normal

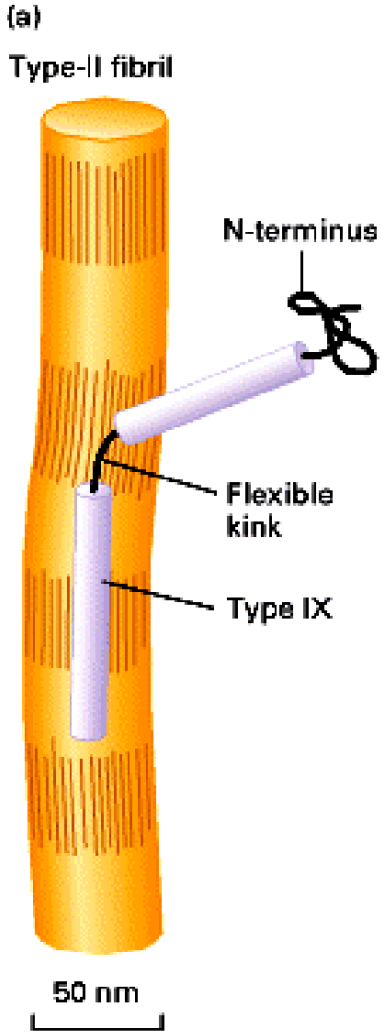
falta de
procolágeno N-peptidasa
(dermatosparaxis)



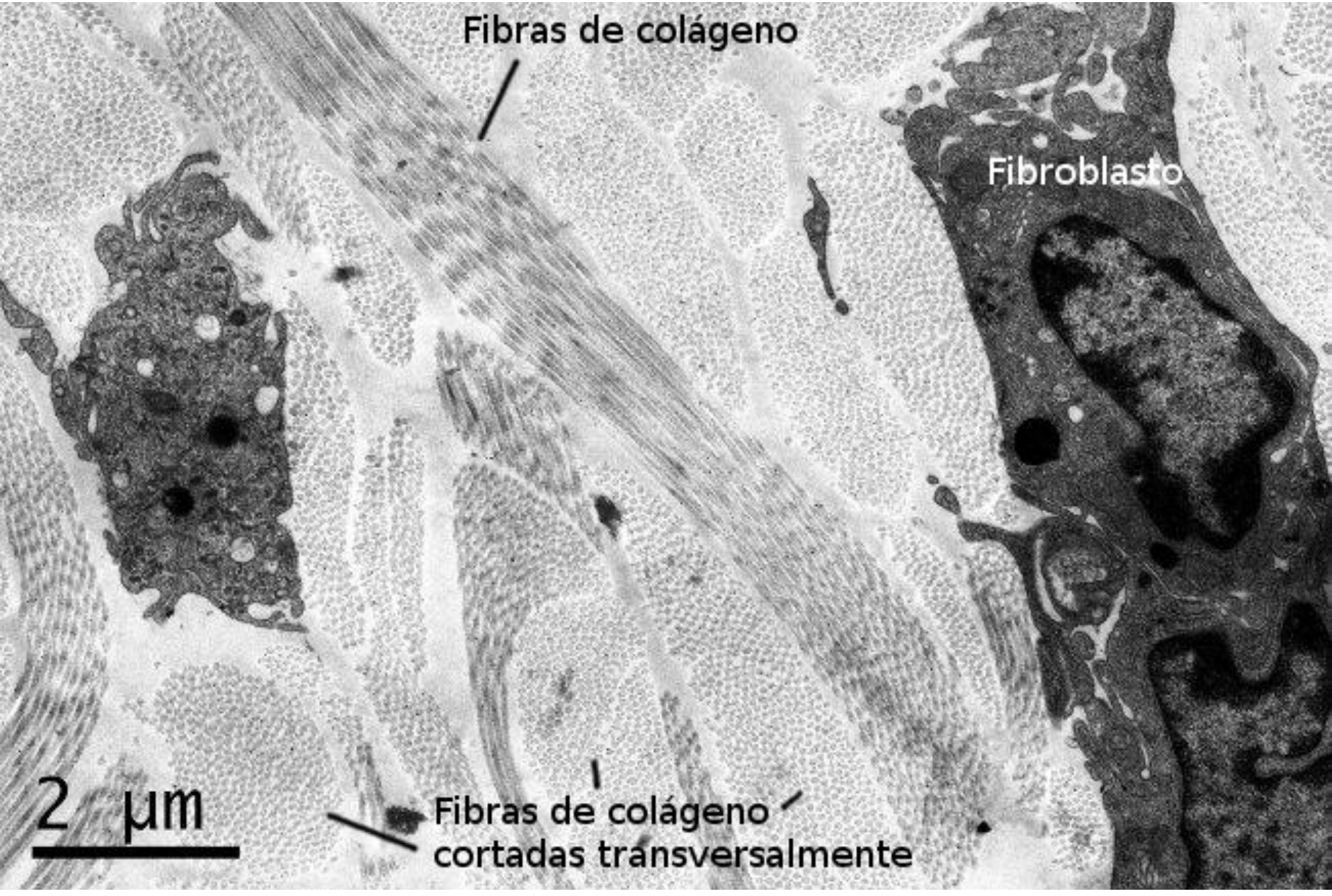


Colágeno: organización

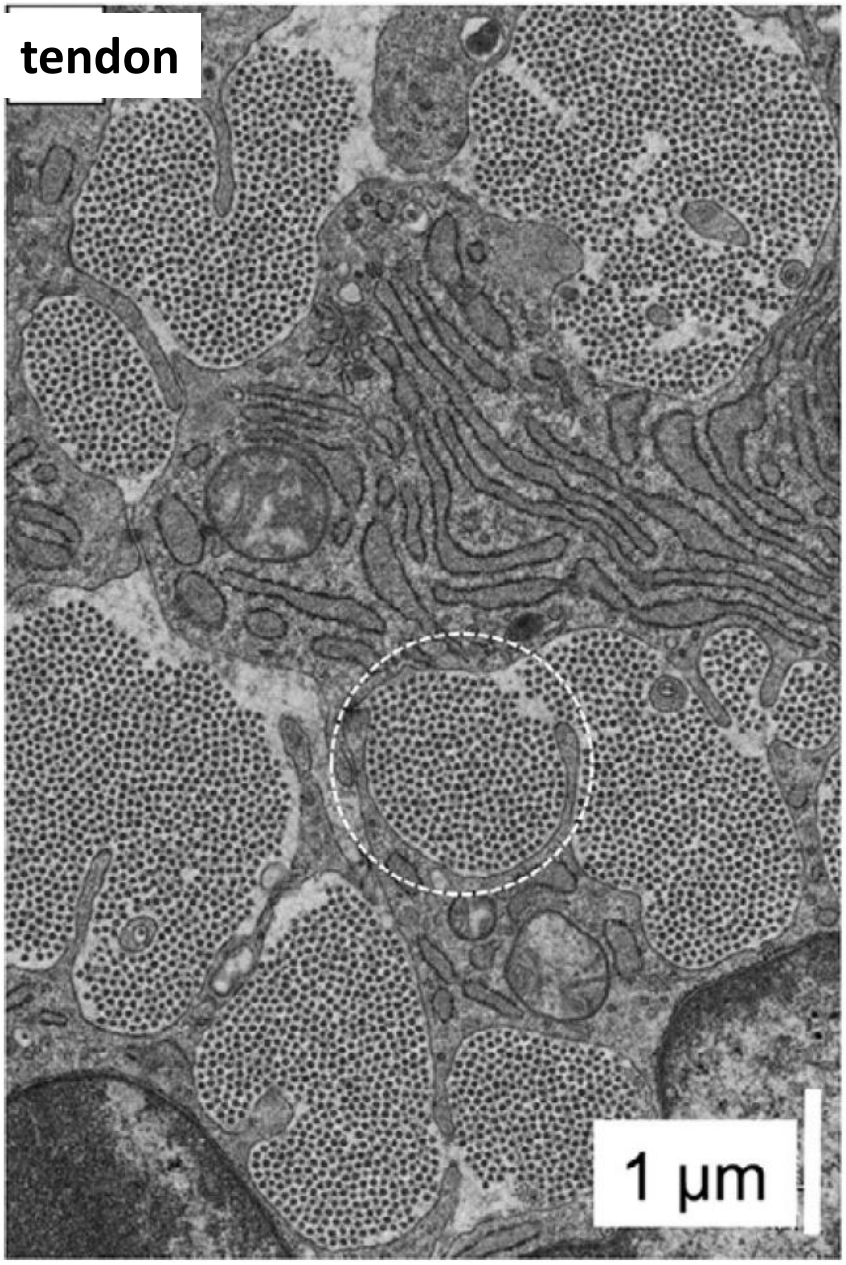


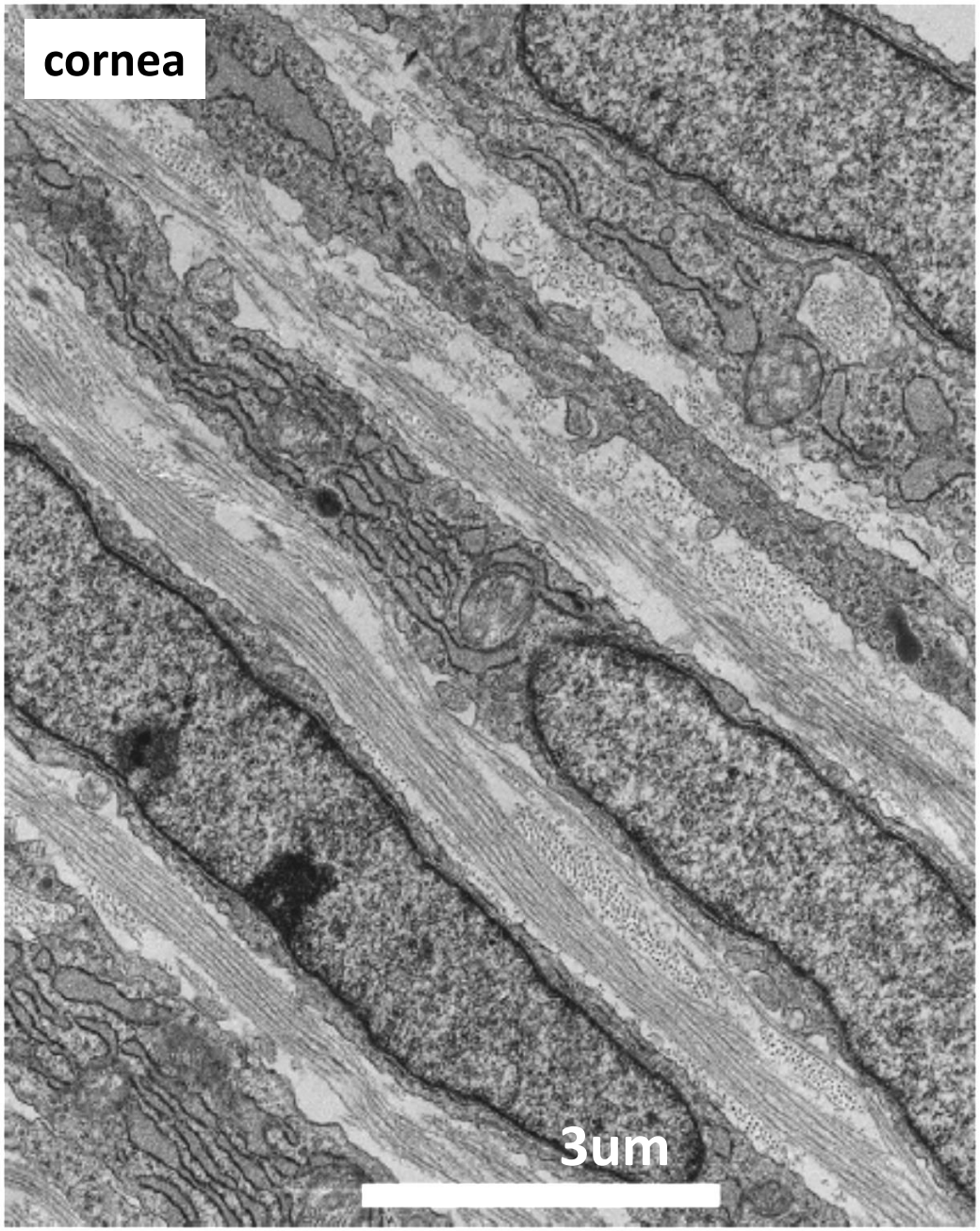


Colágeno: organización

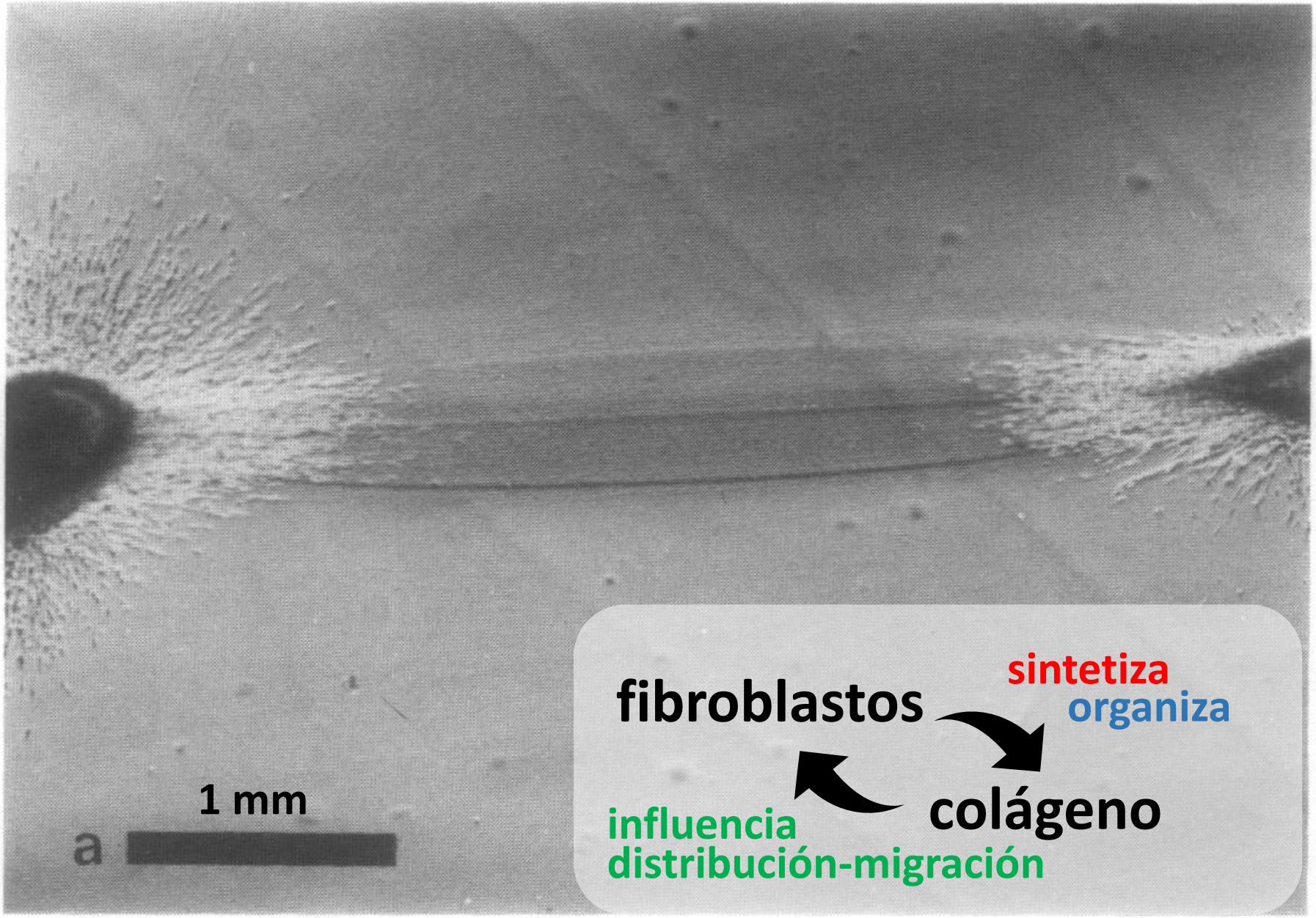


Colágeno: organización

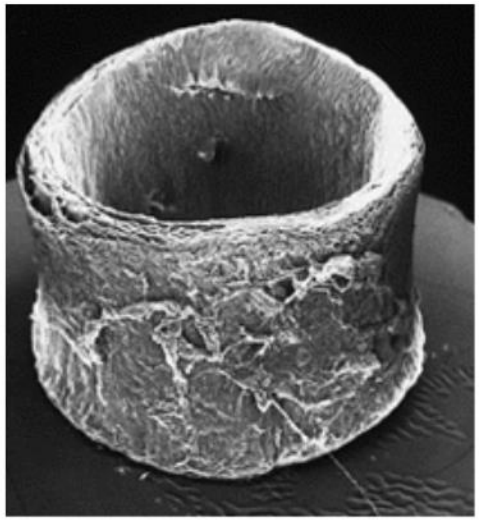




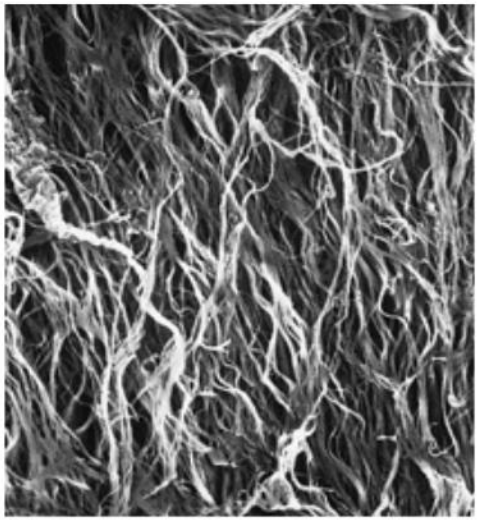
Colágeno: organización



Fibras elásticas → elasticidad

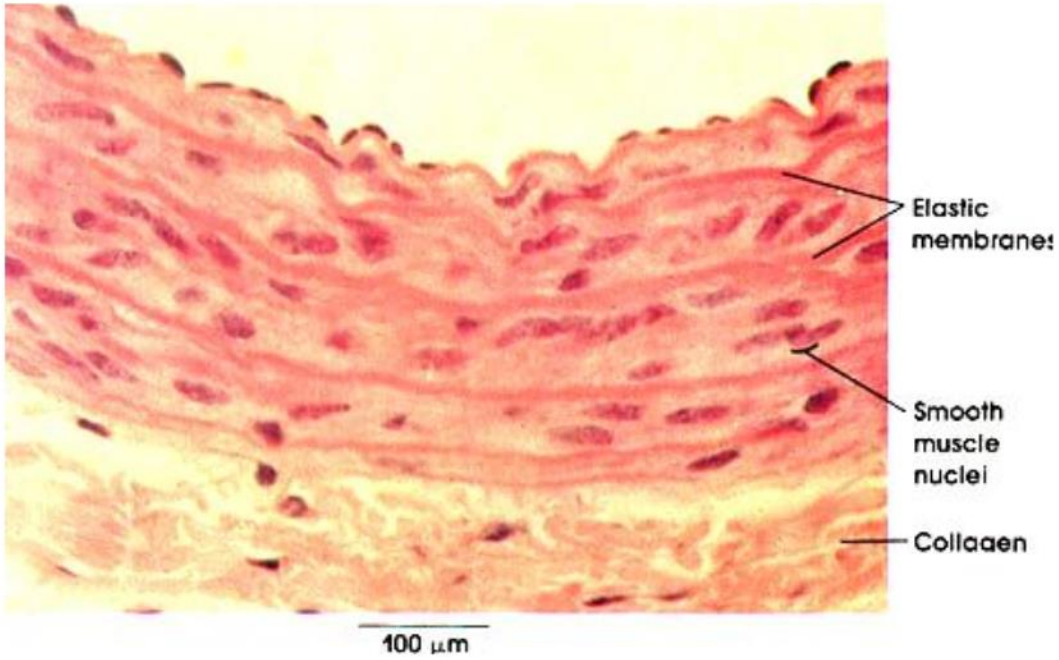


1 mm

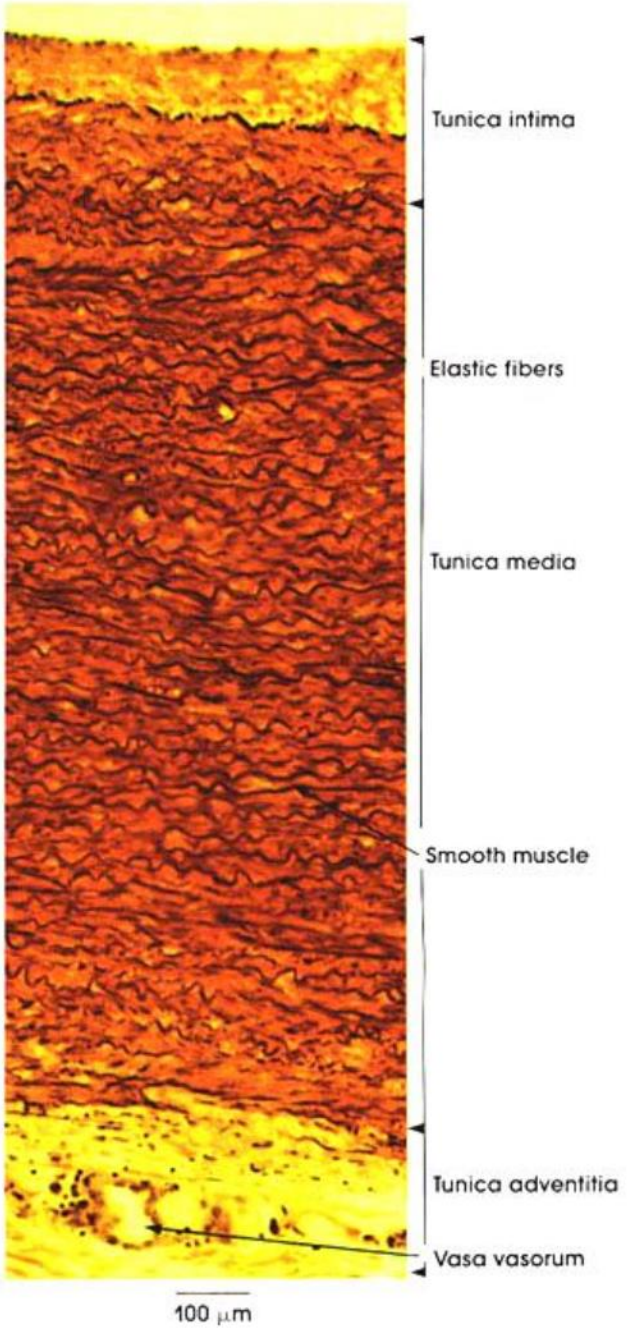


(B)

100 μm



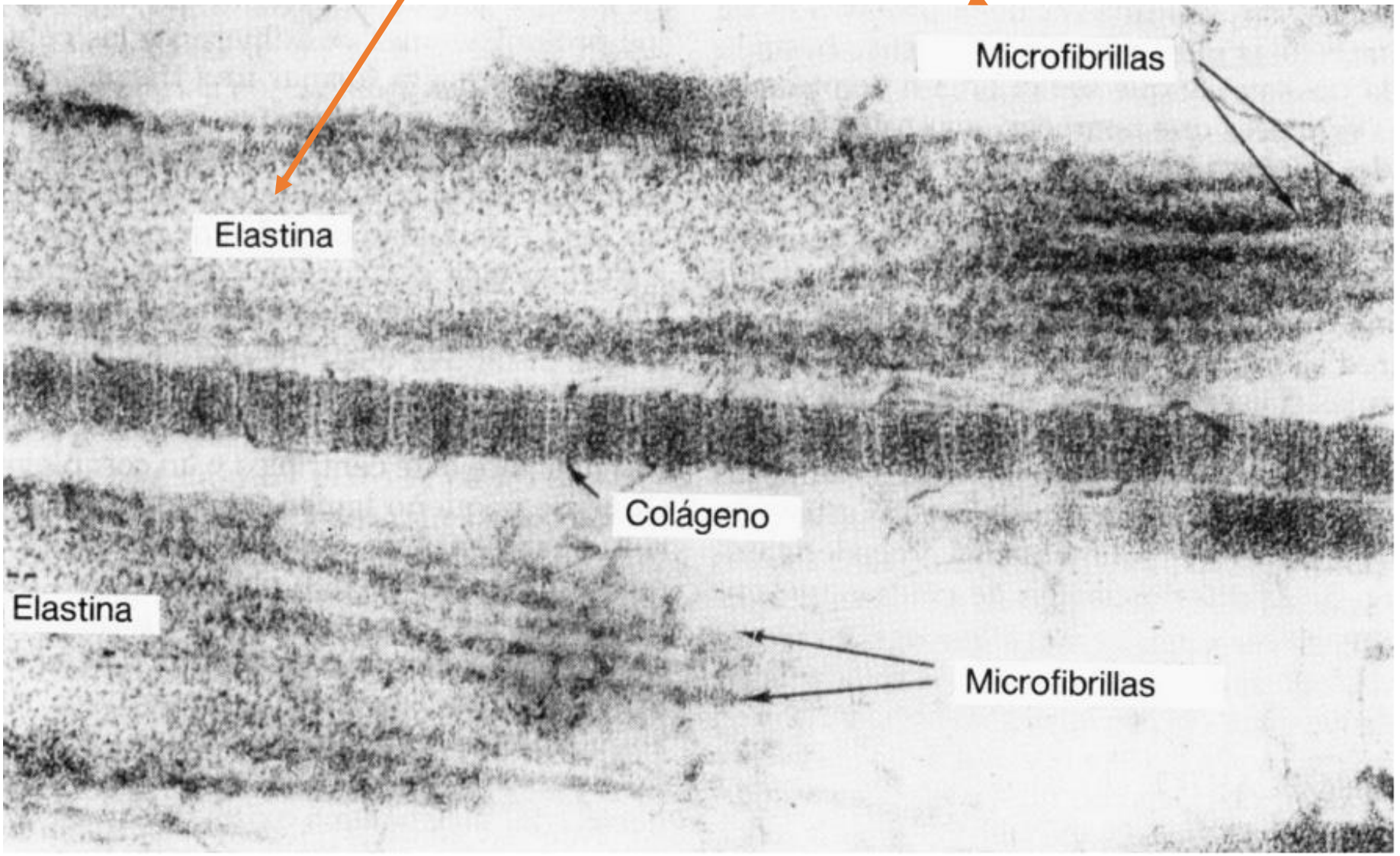
100 μm



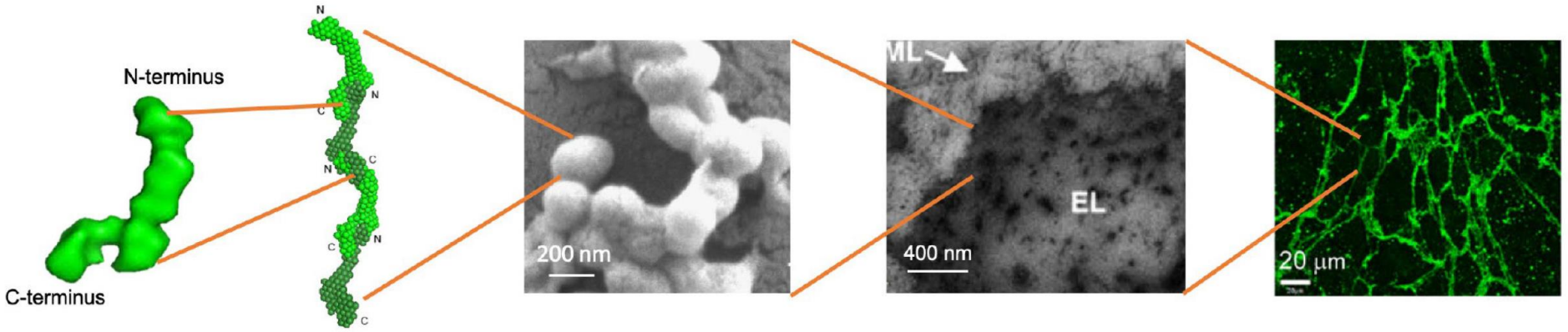
100 μm

Fibras elásticas: síntesis y organización

tropoelastina / fibrilina



Fibras elásticas: síntesis y organización



Tropoelastin monomer *15 nm*

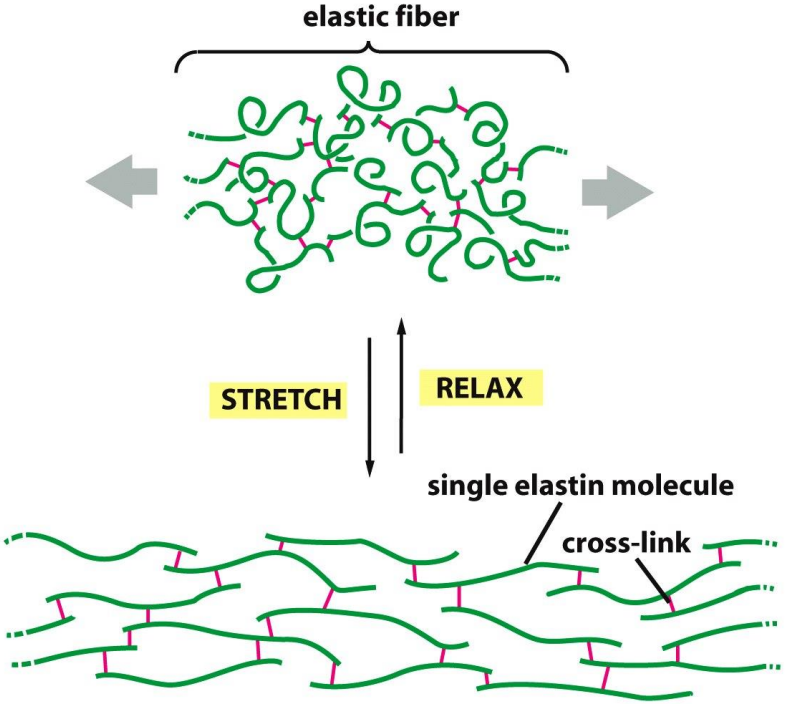
Tropoelastin multimer *>100 nm*

Spherical aggregates *~200 nm*

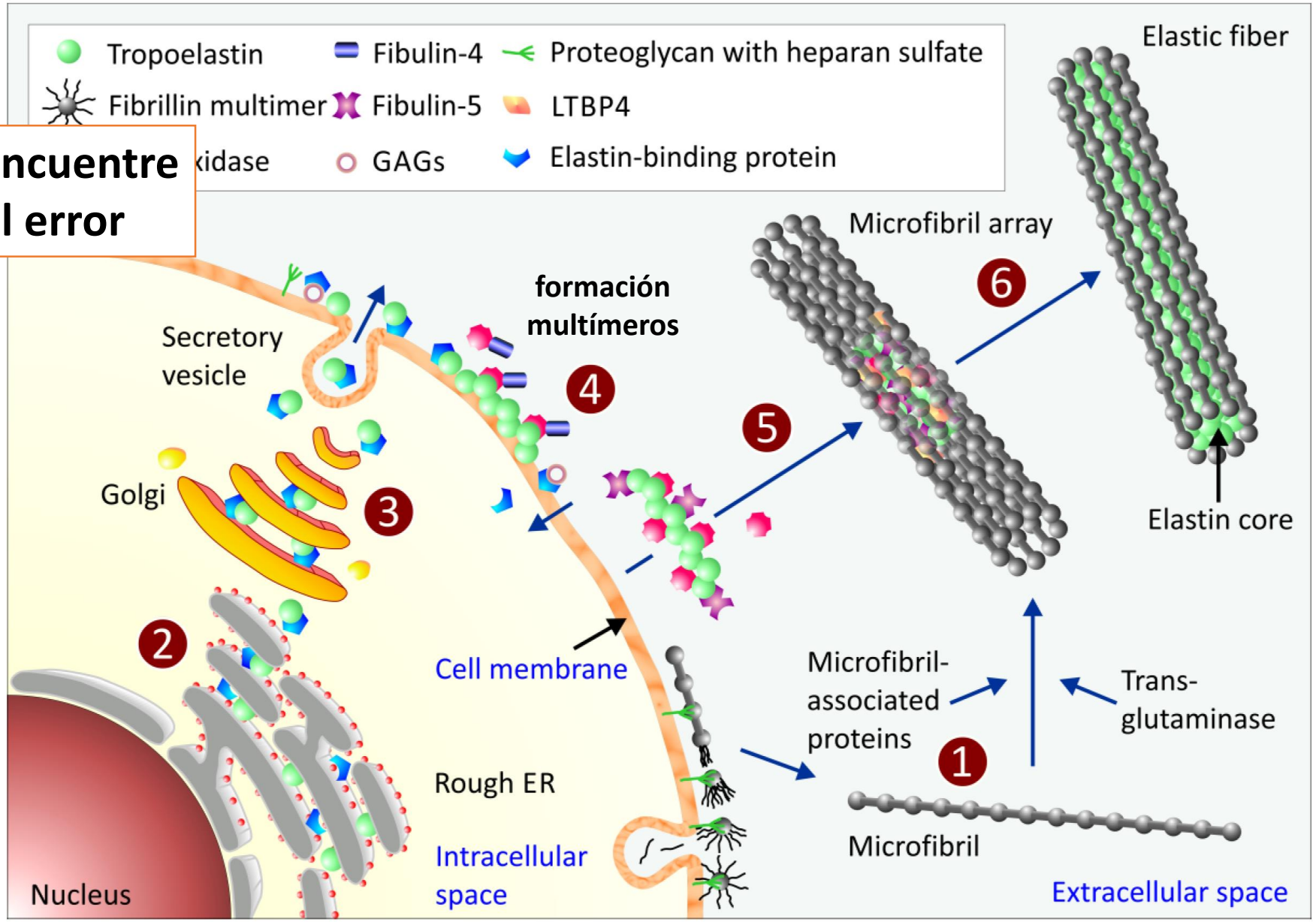
Microfibrils *1 µm*

Elastic fibers *2 µm*

Ozsvar 2021 doi: 10.3389/fbioe.2021.643110



Fibras elásticas: síntesis y organización



Schmelzer 2021 FEBs doi: 10.1111/FEBS.15899

Ejercicio - Marfan syndrome

1. Escribir 12 palabras clave (ejemplos: colágeno, fibrilina, aorta, fibra elástica, aumento de expresión) relacionadas al mecanismo que genera la disección de aorta en el Síndrome de Marfan.

2. Organizar las palabras en un este cuadro:

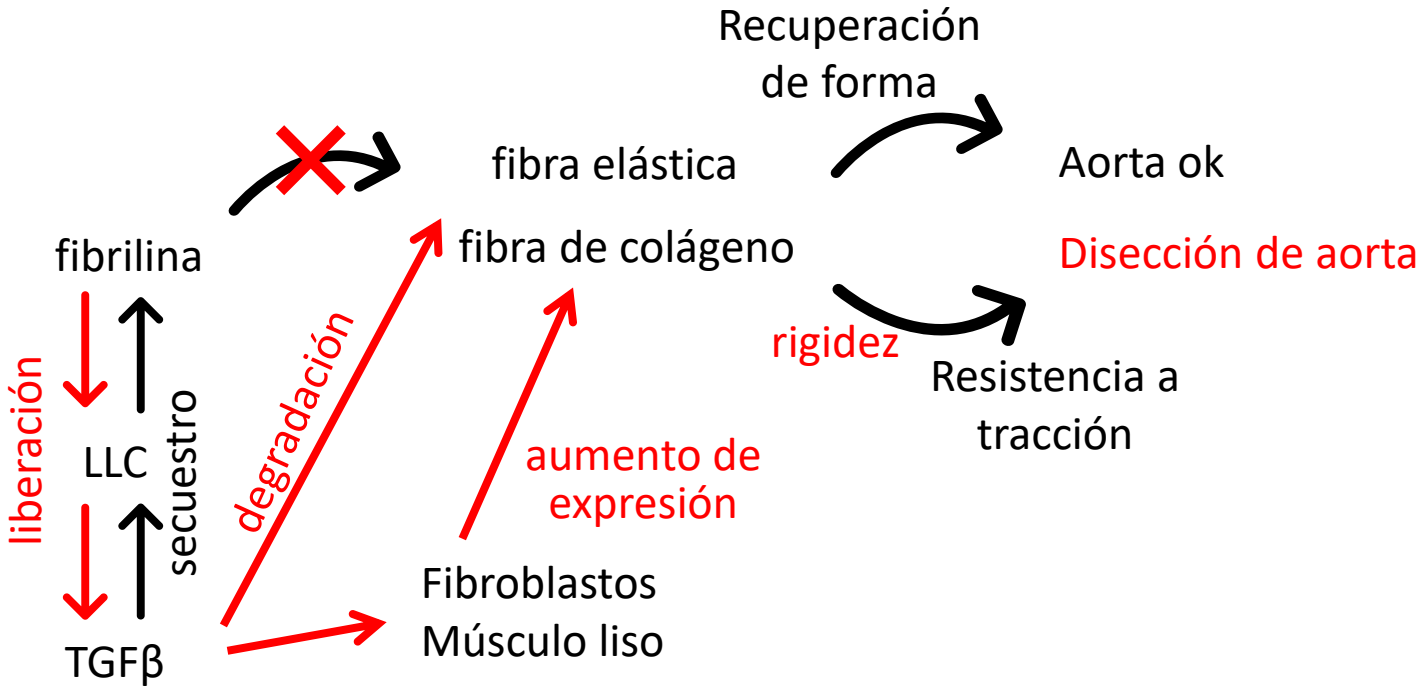
Categoría	Palabras clave
Molécula	Colágeno, fibrilina
Célula	
Tejido	Fibra elástica
Órgano	Aorta
Función	
Proceso	Aumento de expresión

3. Armar una secuencia de eventos con las palabras clave: esquema con causas y efectos en situación normal y en la situación de síndrome.

Categoría	Palabras clave
Molécula	Colágeno, fibrilina, TGFβ, LLC
Célula	Fibroblastos, músculo liso
Tejido	Fibra elástica, fibra de colágeno
Órgano	Aorta
Función	Resistencia a tracción, secuestro, liberación, rigidez, recuperación de forma
Proceso	Aumento de expresión, disección de aorta

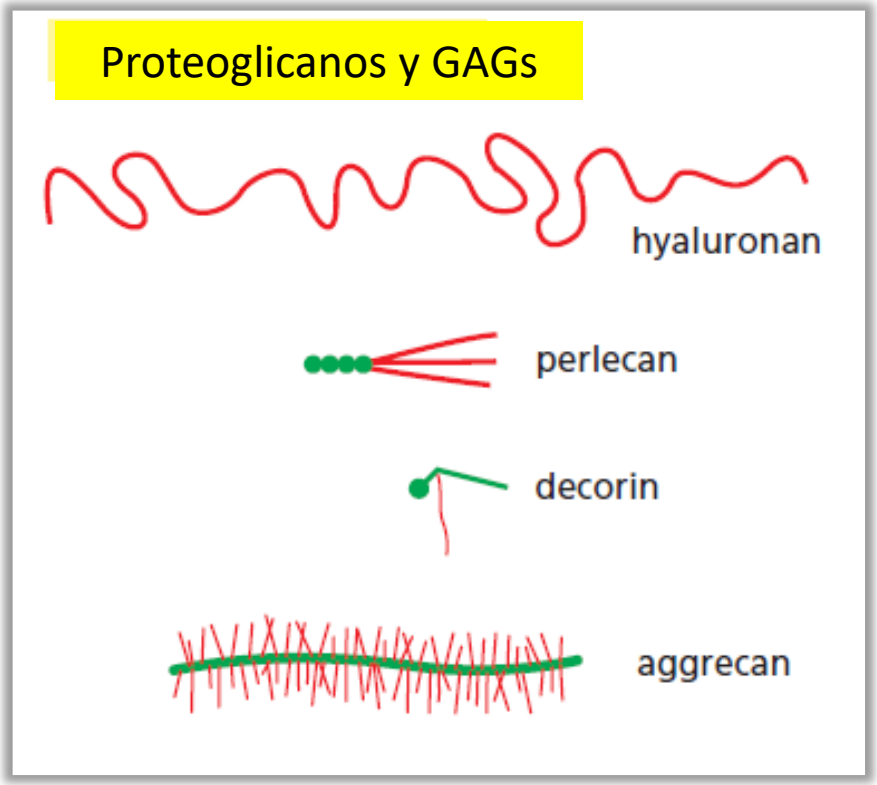
Normal

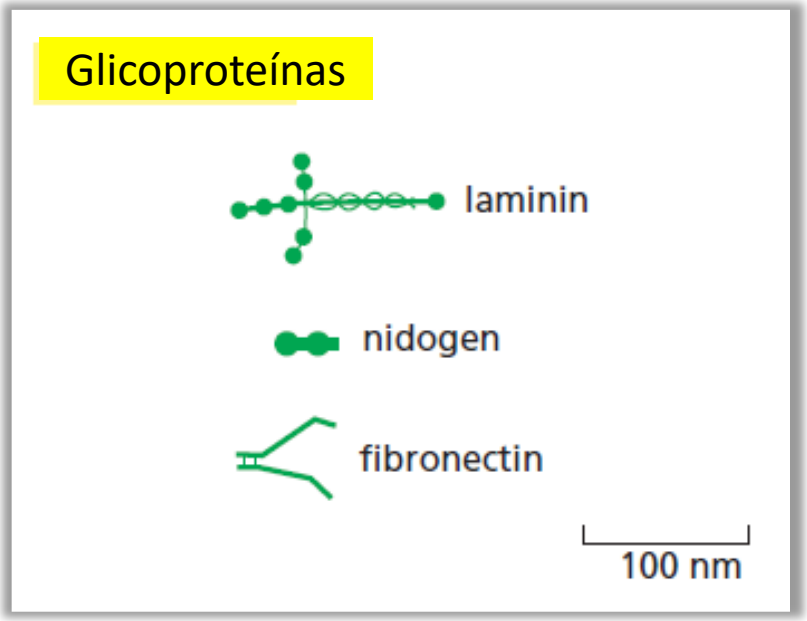
Síndrome de Marfan

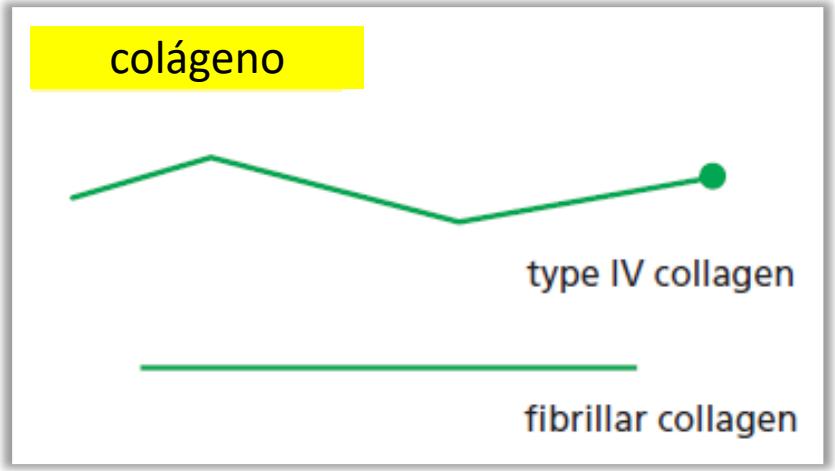


MATRIZ EXTRACELULAR:

Componentes…..







Alrededor de 300 proteínas en mamíferos

Proteoglicanos 36

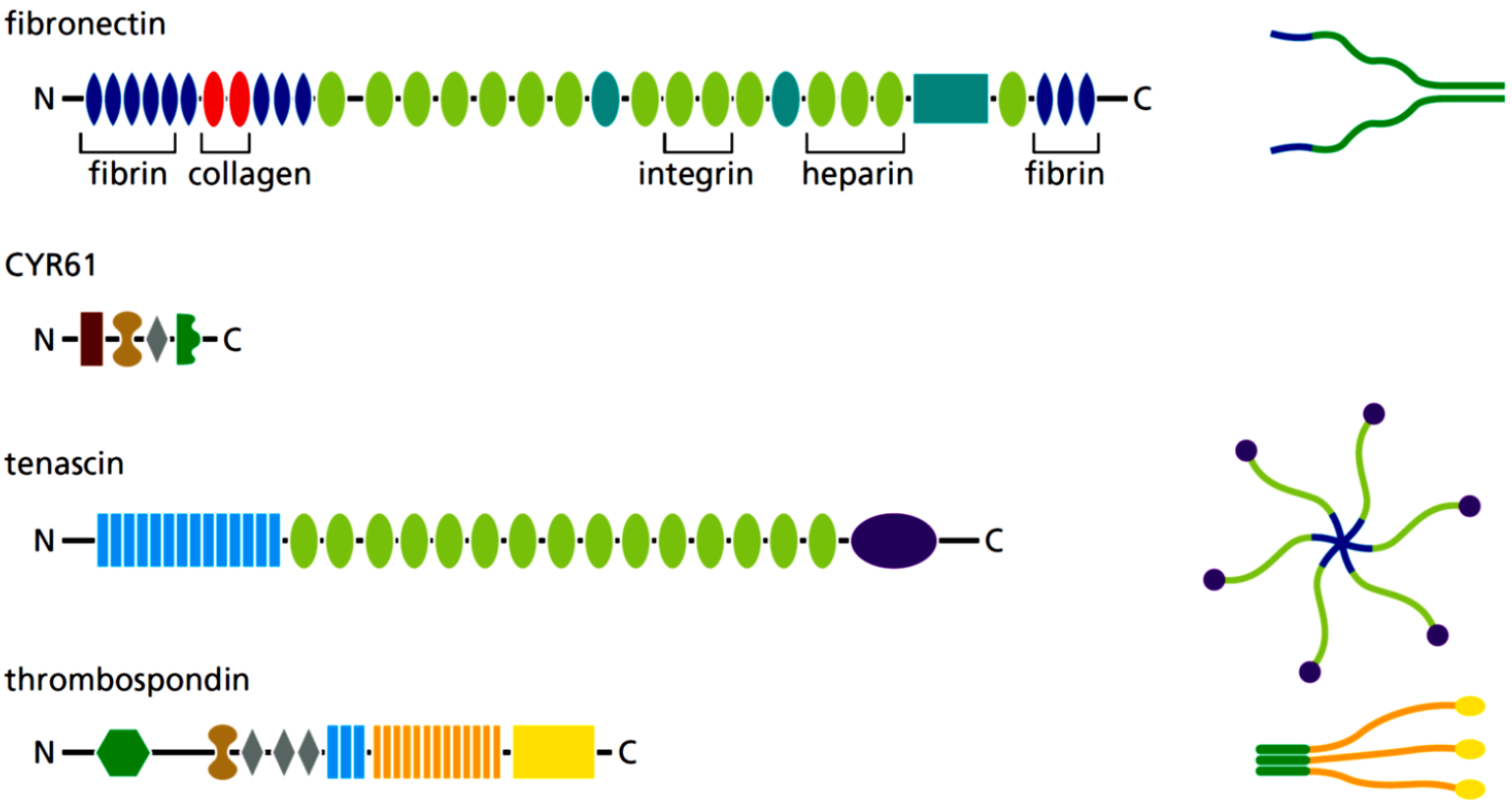
Colágeno 40

Glucoproteínas >200

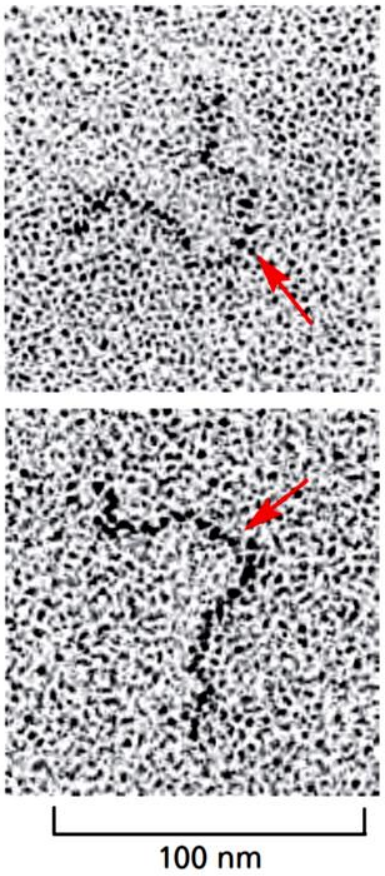
glúcidos proteína

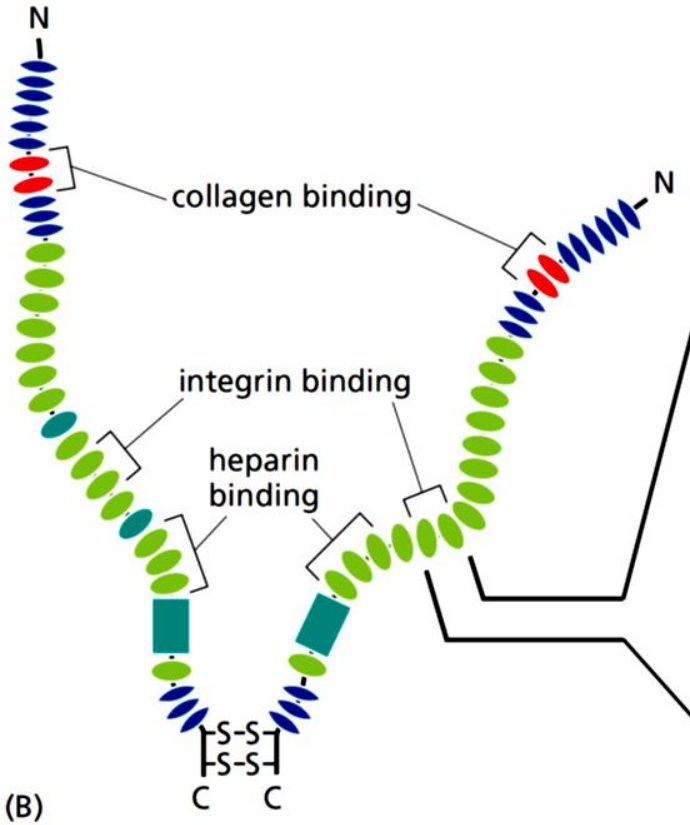
Glicoproteínas

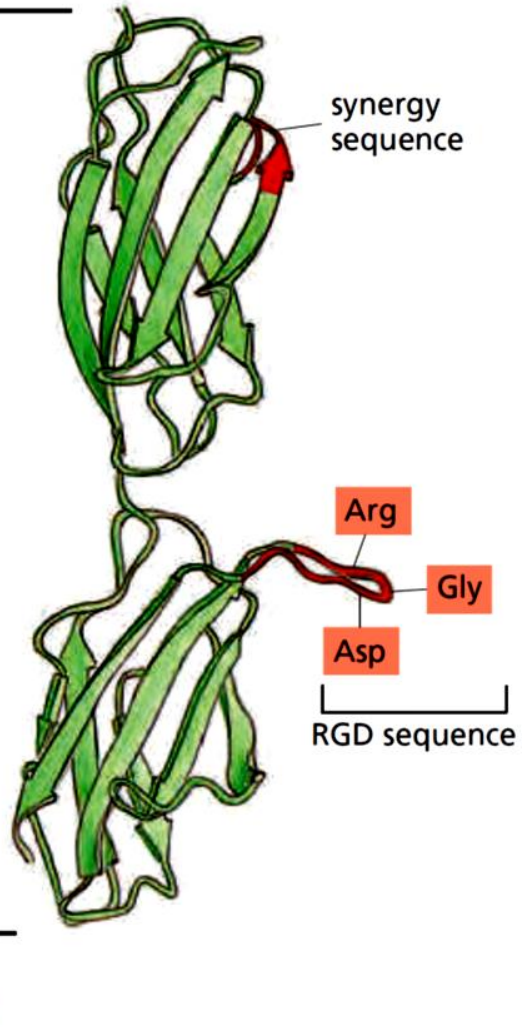
≈ 200 en mamíferos



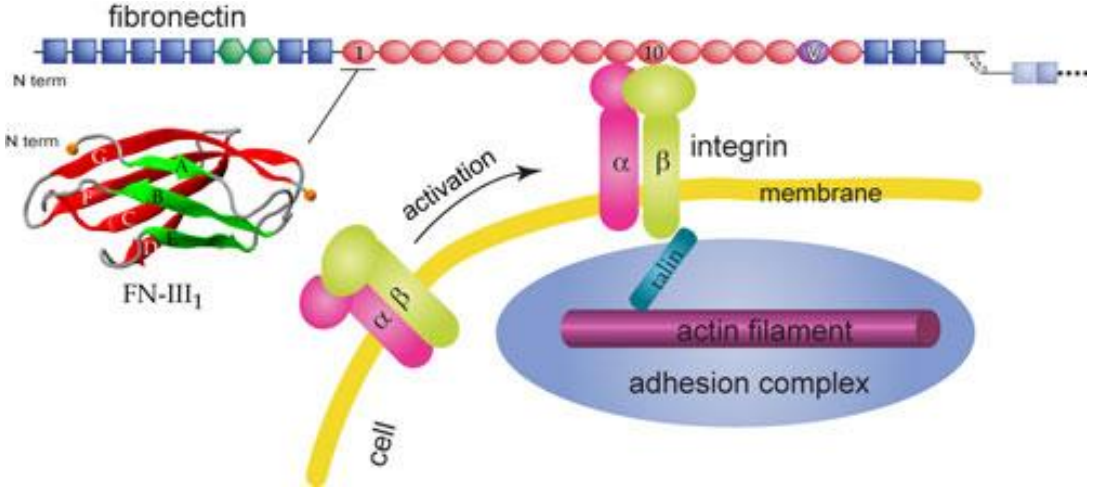
Glicoproteínas adhesivas: fibronectina





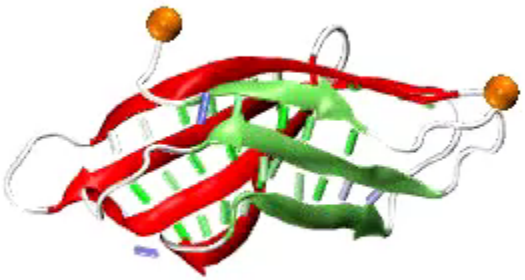


Fibronectina: dominio FN3



VIDEO

https://www.ks.uiuc.edu/Research/fibronectin/



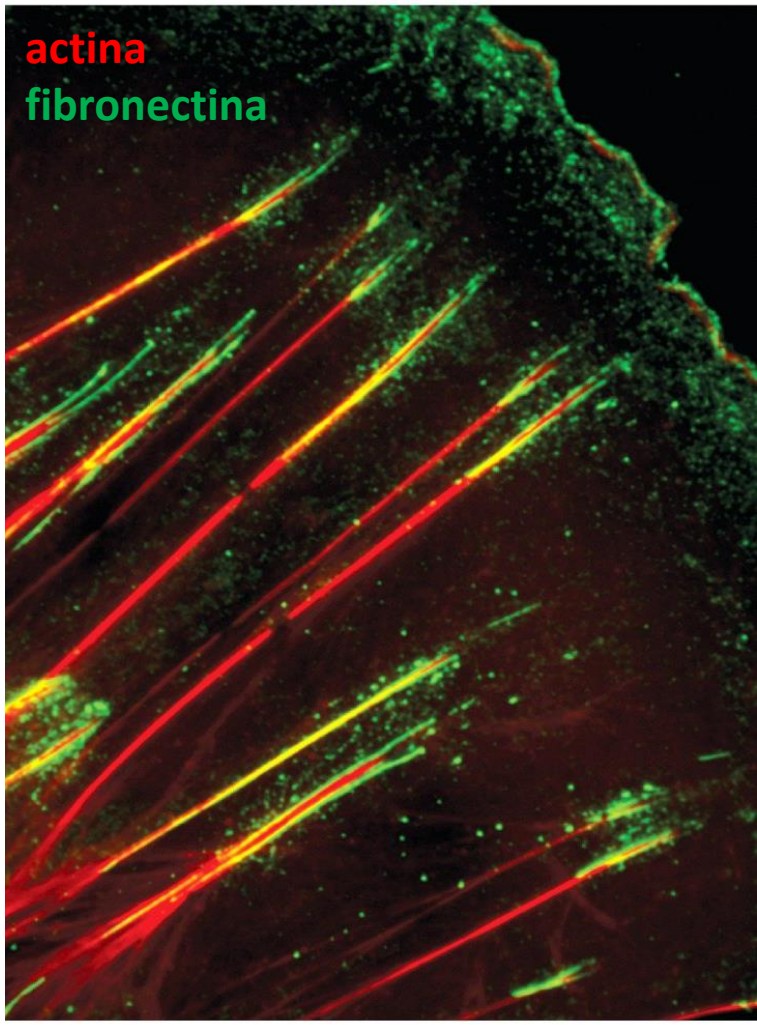
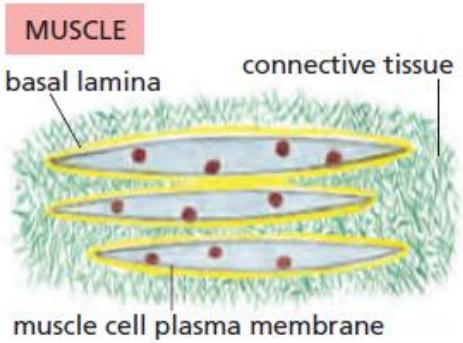
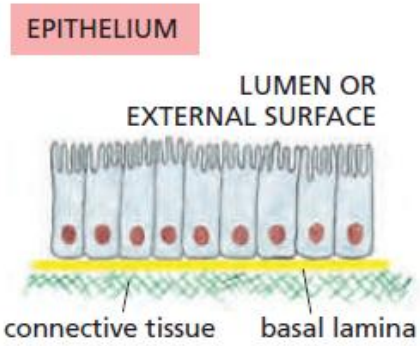


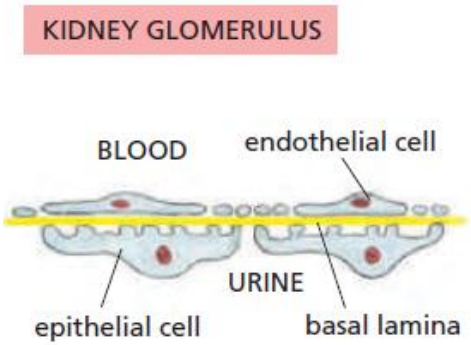
Lámina basal

¿donde?
epitelios
adipocitos
células de Schwann
células musculares
podocitos

¿para qué?
soporte mecánico
polaridad
metabolismo
migración
proliferación
diferenciación







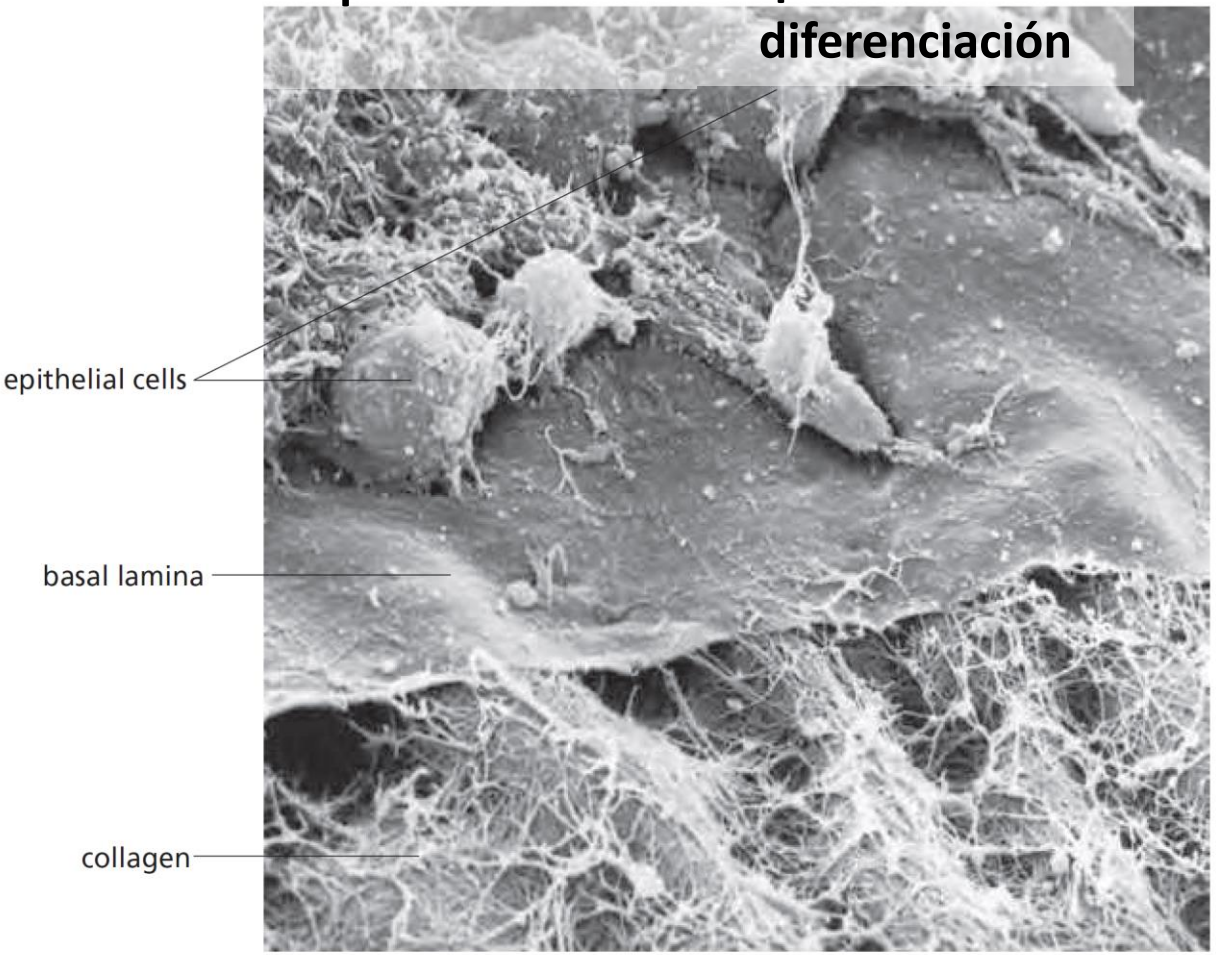


Lámina basal

Colágeno tipo IV
Perlecano (proteoglucano del tipo heparán sulfato)
Laminina - nidogeno (glucoproteinas)
Fibronectina
Colágeno tipo XVIII (forma proteoglicano)

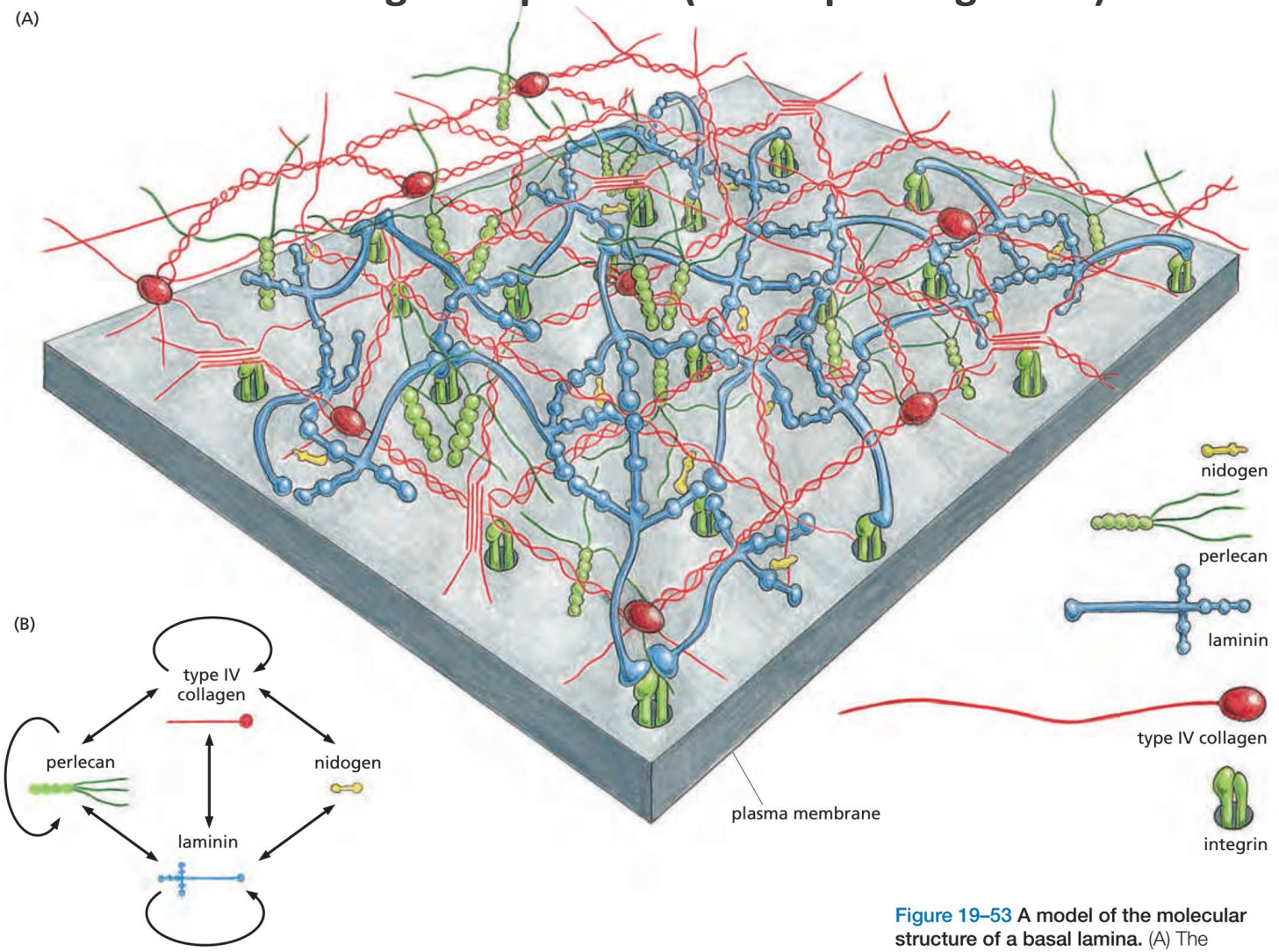


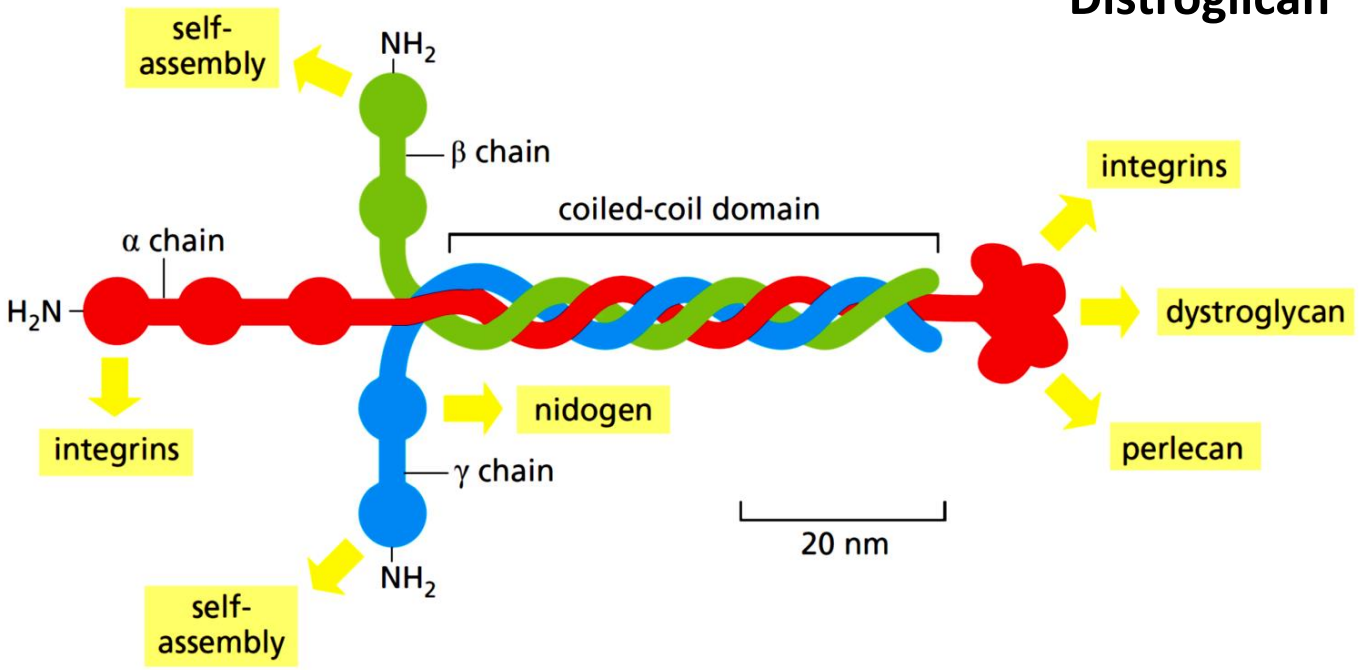
Figure 19–53 A model of the molecular structure of a basal lamina. (A) The

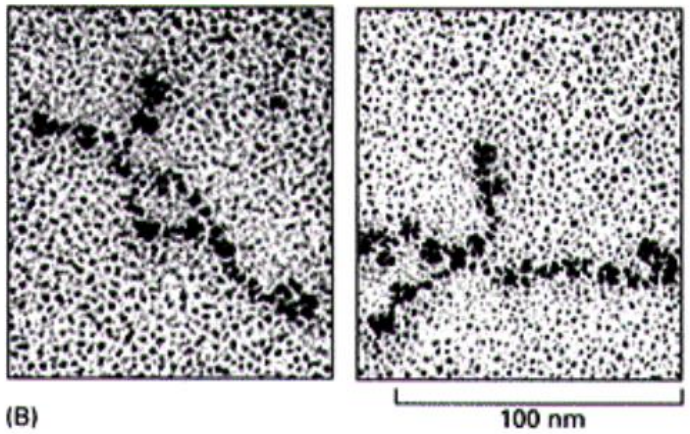
Lámina basal: lamininas

RECEPTORES de membrana:

Integrinas

Distroglican

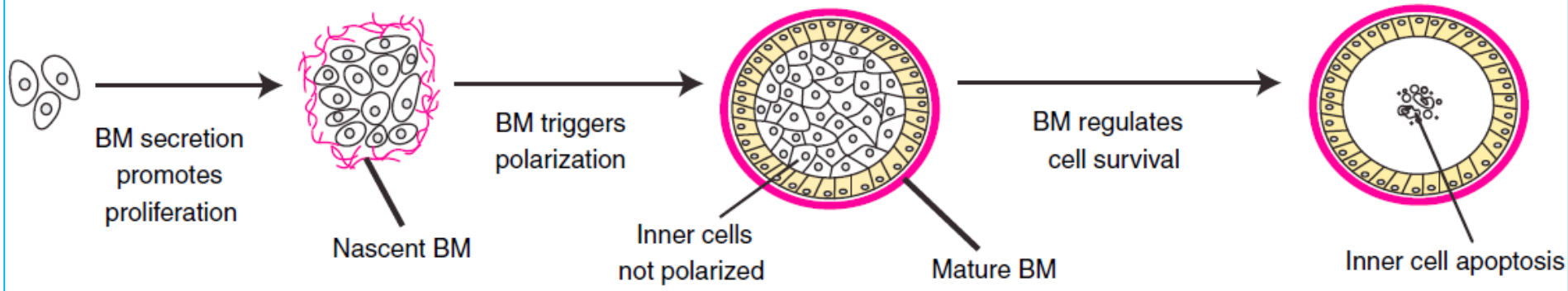




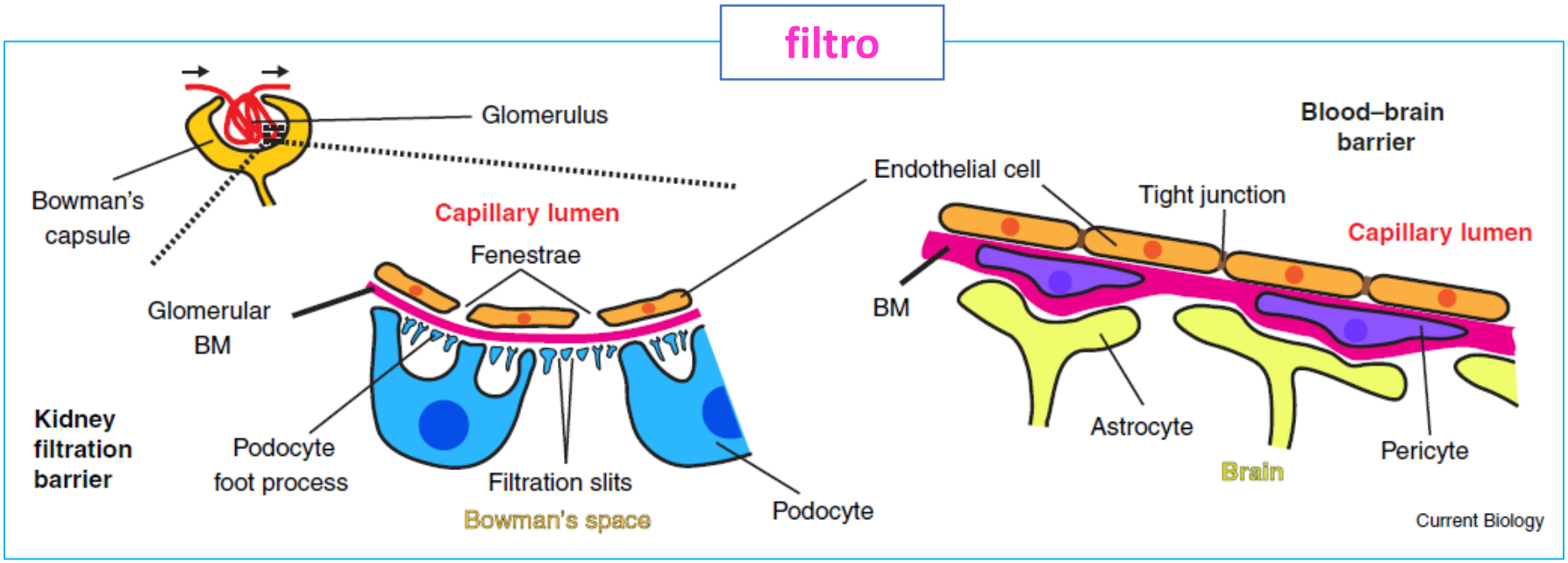
5 tipos de cadenas α
4 tipos de cadenas β
3 tipos de cadenas γ

Lámina basal

organización de epitelios



filtro



LA CÉLULA Y SU CONTEXTO

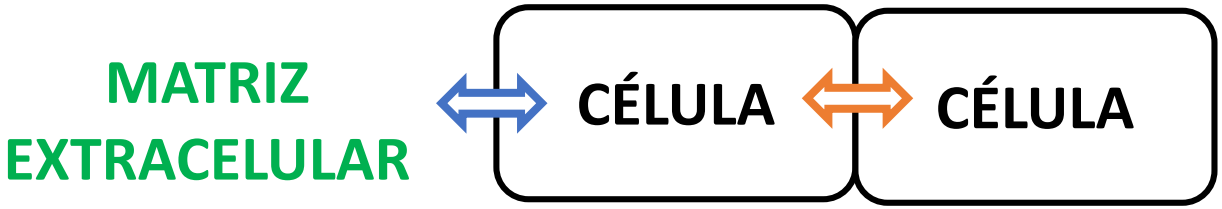
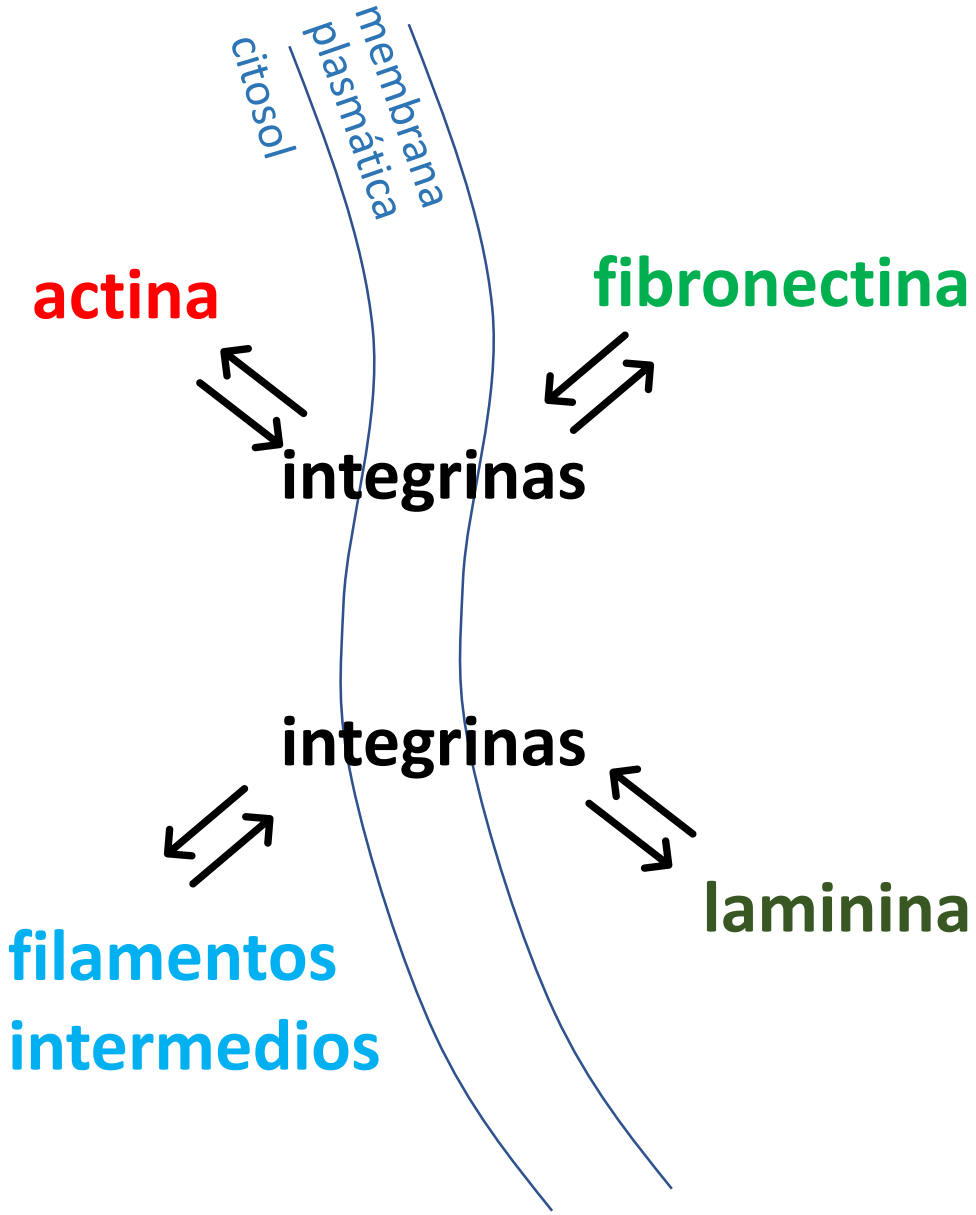
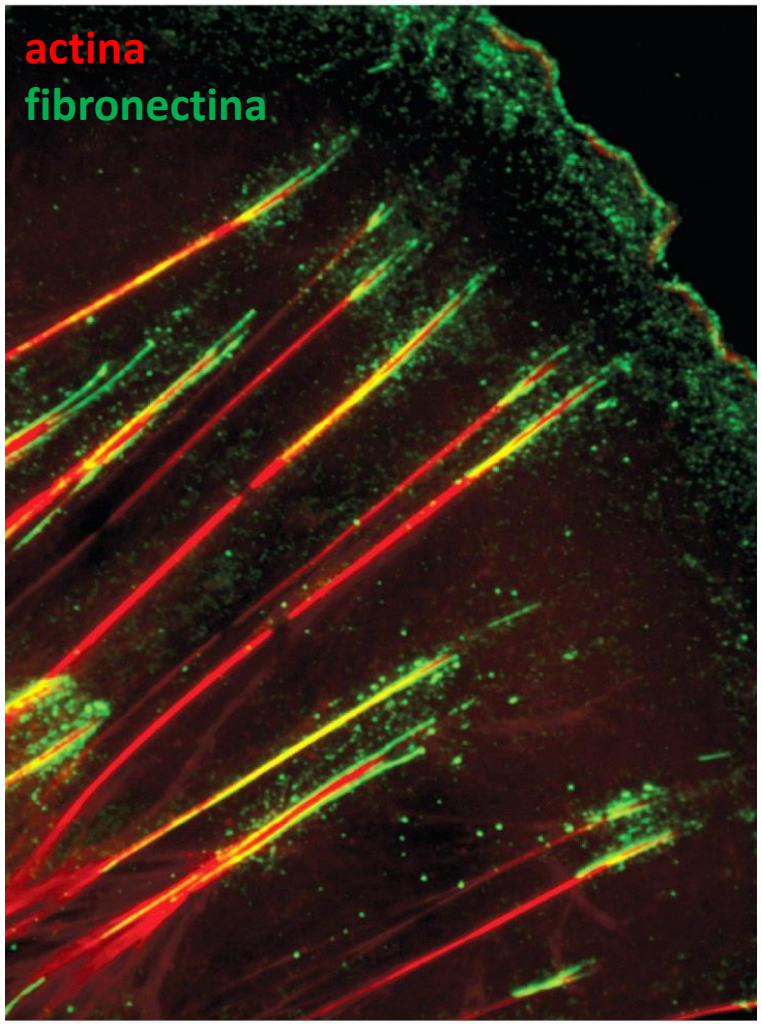


TABLE 19–1 Anchoring Junctions

Junction	Transmembrane adhesion protein	Extracellular ligand	Intracellular cytoskeletal attachment	Intracellular adaptor proteins
Cell–Cell				
Adherens junction	Classical cadherins	Classical cadherin on neighboring cell	Actin filaments	α-Catenin, β-catenin, plakoglobin (γ-catenin), p120-catenin, vinculin
Desmosome	Nonclassical cadherins (desmoglein, desmocollin)	Desmoglein and desmocollin on neighboring cell	Intermediate filaments	Plakoglobin (γ-catenin), plakophilin, desmoplakin
Cell–Matrix				
Actin-linked cell–matrix junction	Integrin	Extracellular matrix proteins	Actin filaments	Talin, kindlin, vinculin, paxillin, focal adhesion kinase (FAK), numerous others
Hemidesmosome	$\alpha_6\beta_4$ Integrin, type XVII collagen	Extracellular matrix proteins	Intermediate filaments	Plectin, BP230

Uniones célula-matriz

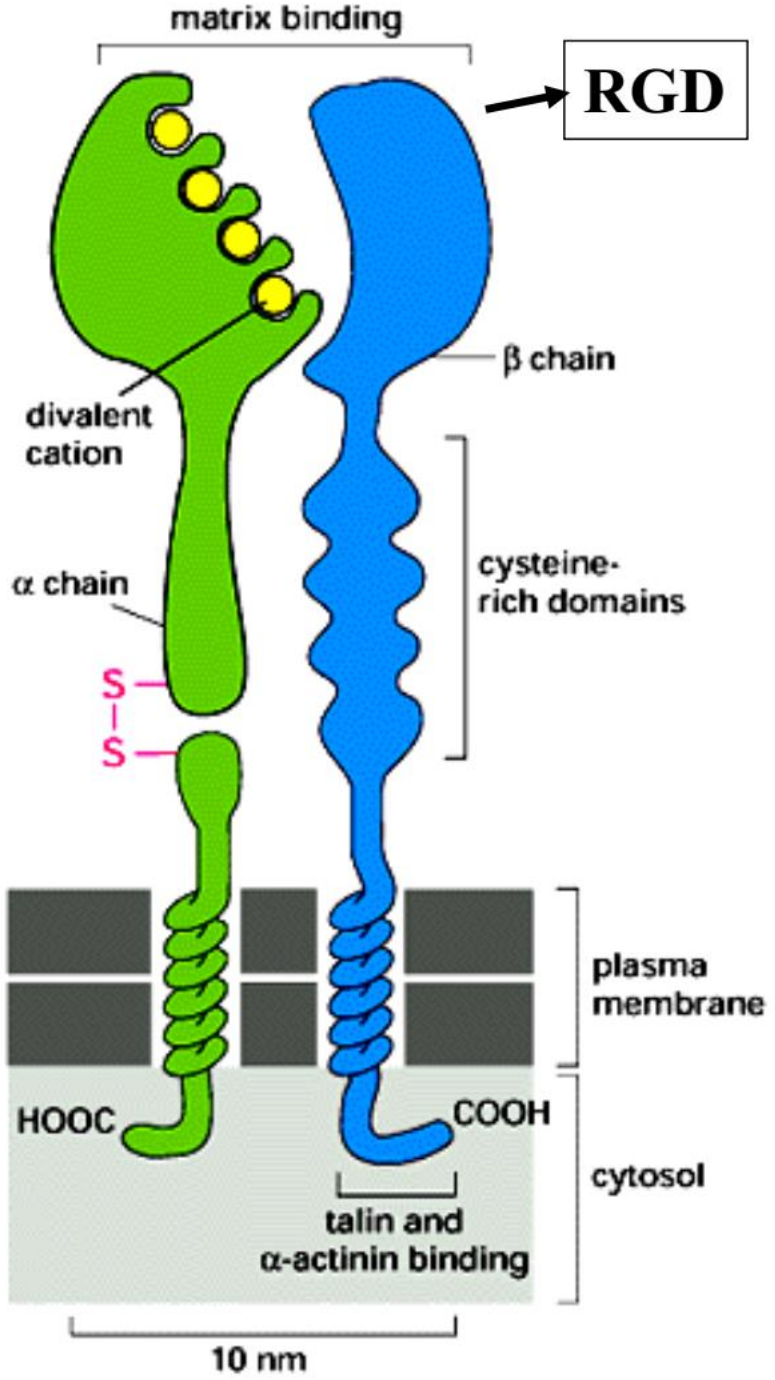




Integrinas

Ca^{2+}

Mg^{2+}

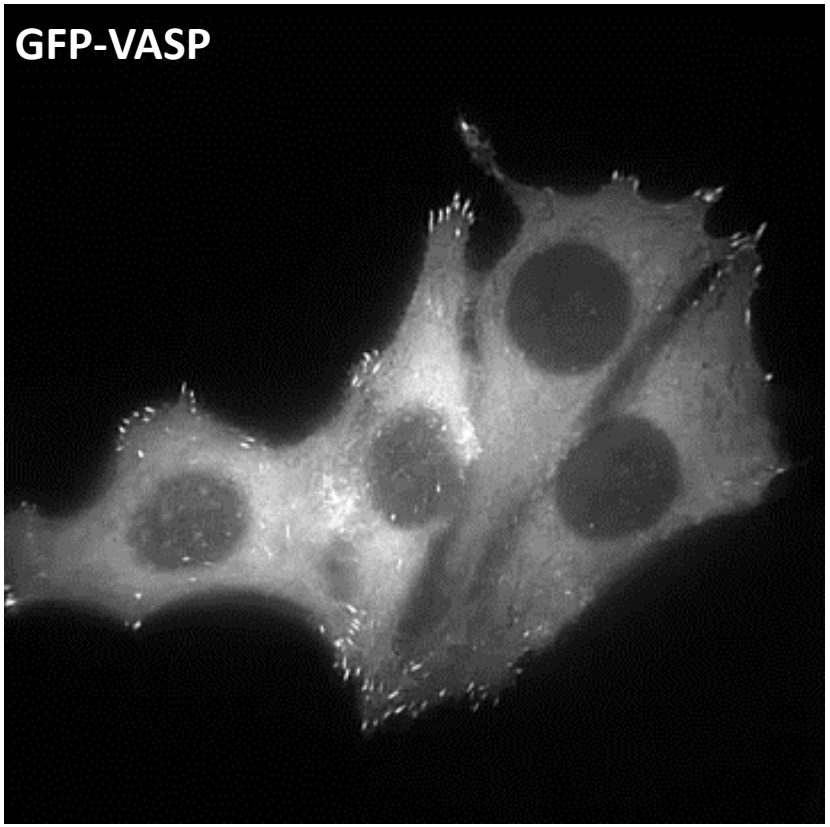


24 tipos de integrinas, formadas por combinaciones de 8 β y 18 α.

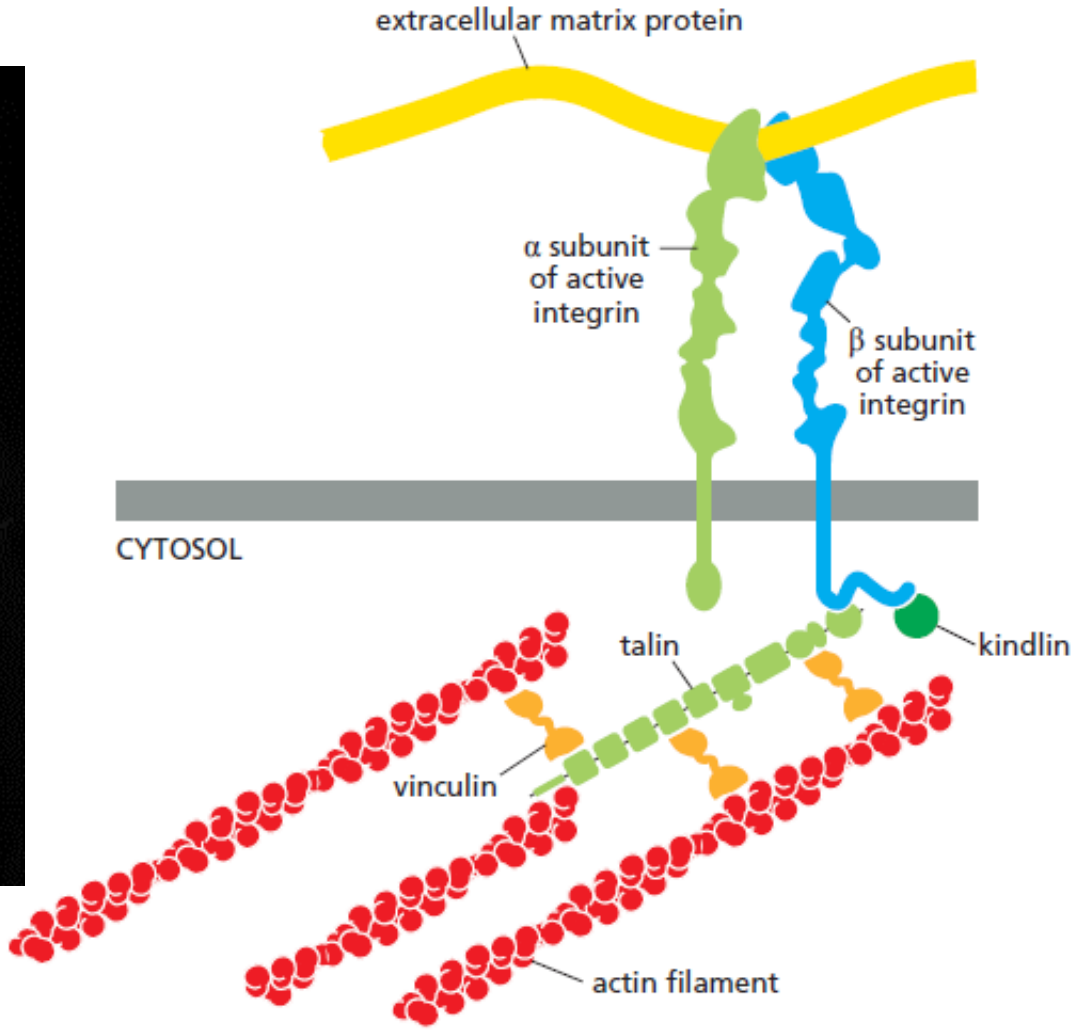
Integrinas

TABLE 19–3 Some Types of Integrins				
Integrin	Ligand*	Distribution	Phenotype when α subunit is mutated	Phenotype when β subunit is mutated
$\alpha_5\beta_1$	Fibronectin	Ubiquitous	Death of embryo; defects in blood vessels, somites, neural crest	Early death of embryo (at implantation)
$\alpha_6\beta_1$	Laminin	Ubiquitous	Severe skin blistering; defects in other epithelia also	Early death of embryo (at implantation)
$\alpha_7\beta_1$	Laminin	Muscle	Muscular dystrophy; defective myotendinous junctions	Early death of embryo (at implantation)
$\alpha_L\beta_2$ (LFA1)	Ig superfamily counterreceptors (ICAM1)	White blood cells	Impaired recruitment of leucocytes	Leukocyte adhesion deficiency (LAD); impaired inflammatory responses; recurrent life-threatening infections
$\alpha_{IIb}\beta_3$	Fibrinogen	Platelets	Bleeding; no platelet aggregation (Glanzmann's disease)	Bleeding; no platelet aggregation (Glanzmann's disease); mild osteopetrosis
$\alpha_6\beta_4$	Laminin	Hemidesmosomes in epithelia	Severe skin blistering; defects in other epithelia also	Severe skin blistering; defects in other epithelia also
*Not all ligands are listed.				

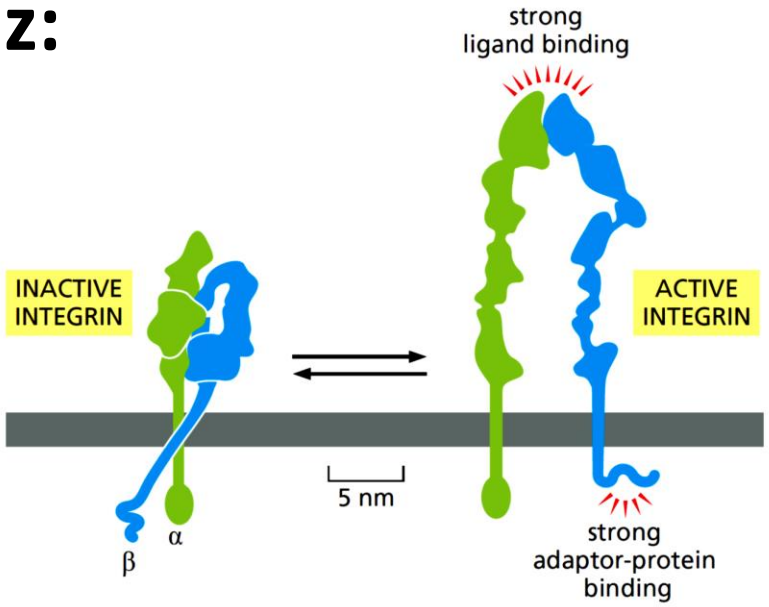
Uniones célula-matriz: contactos focales

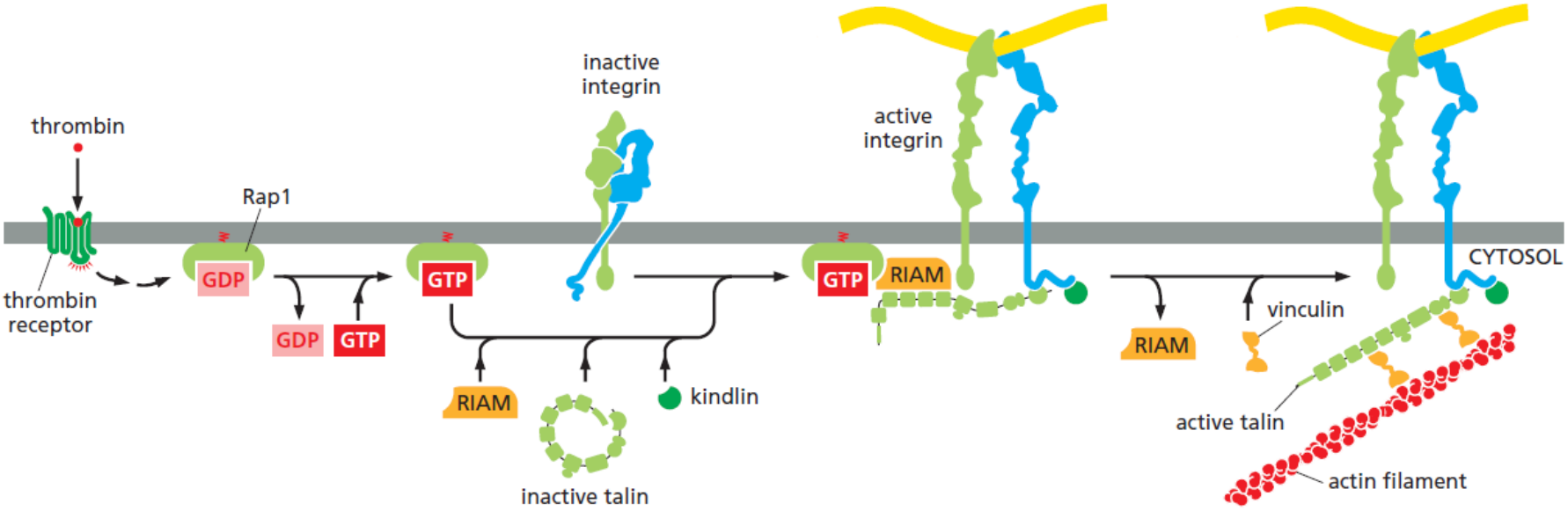


https://youtu.be/75ntMVPtP3Y

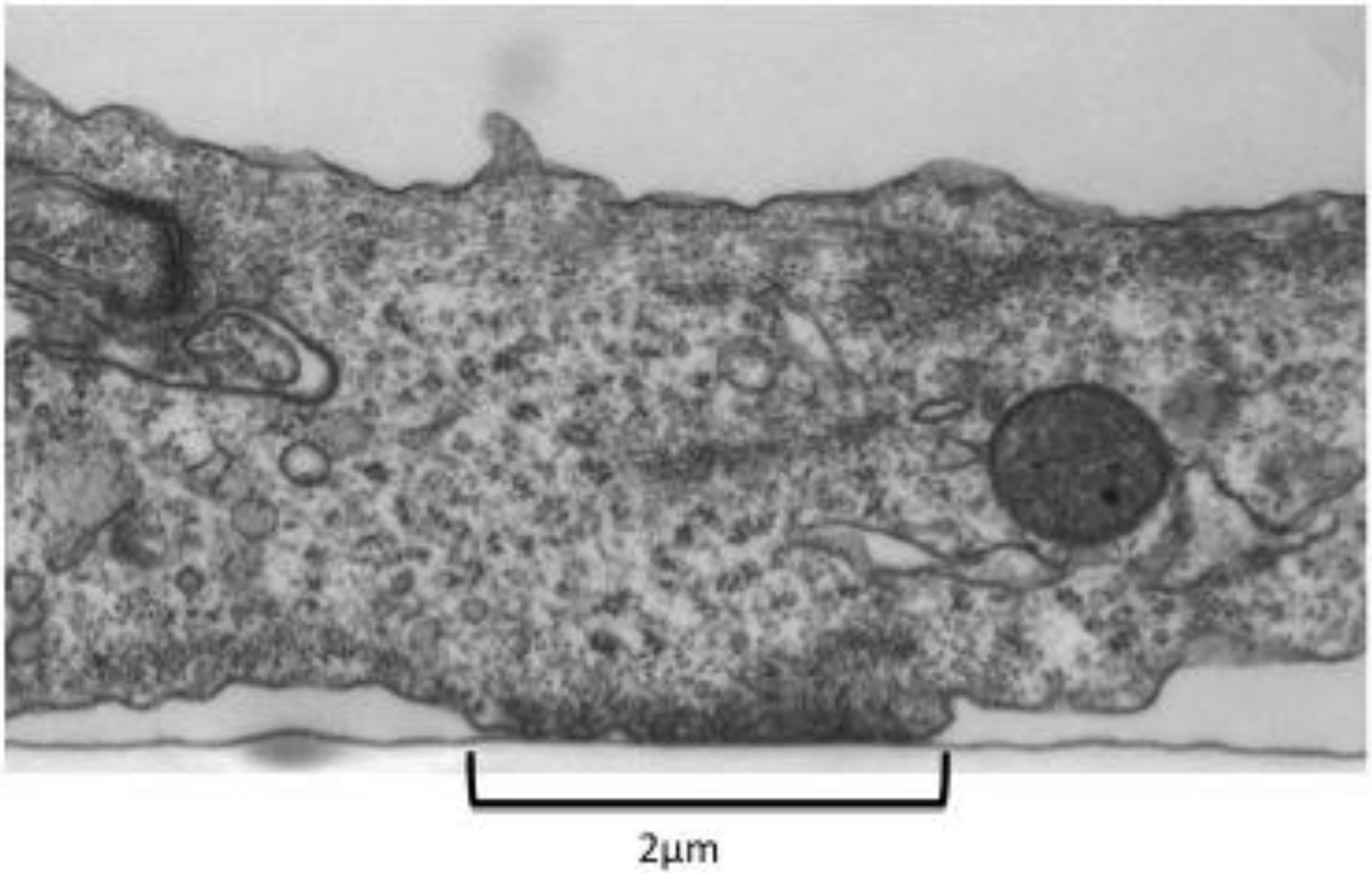


Uniones célula-matriz: contactos focales

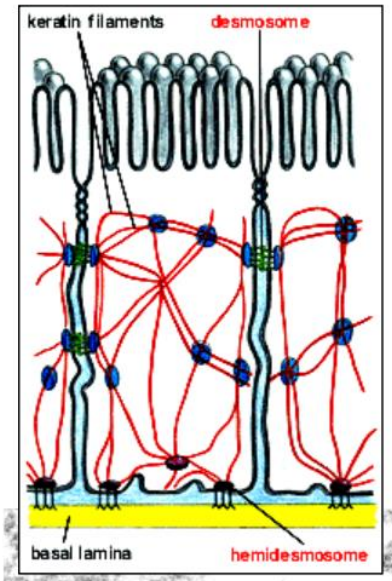


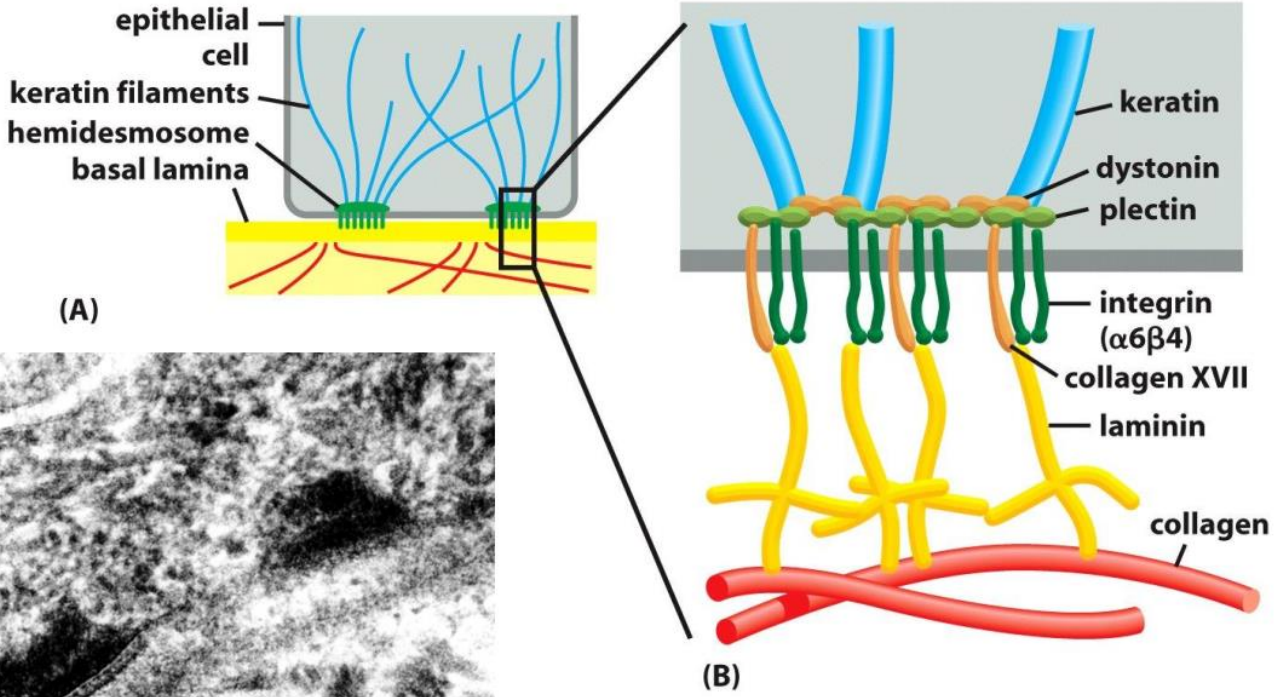


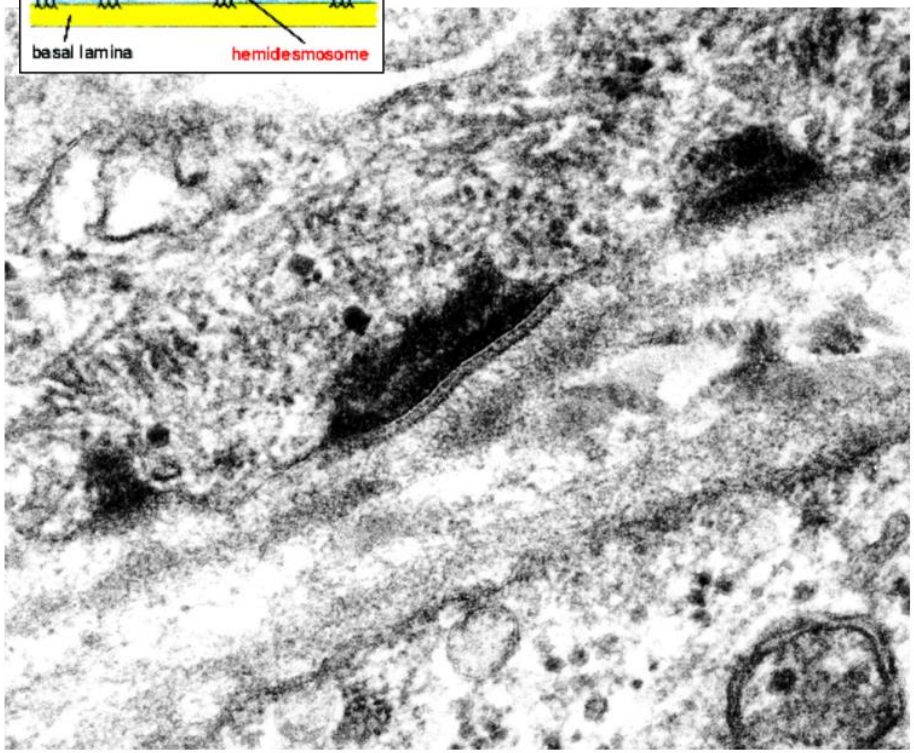
Uniones célula-matriz: contactos focales



Hemidesmosomas





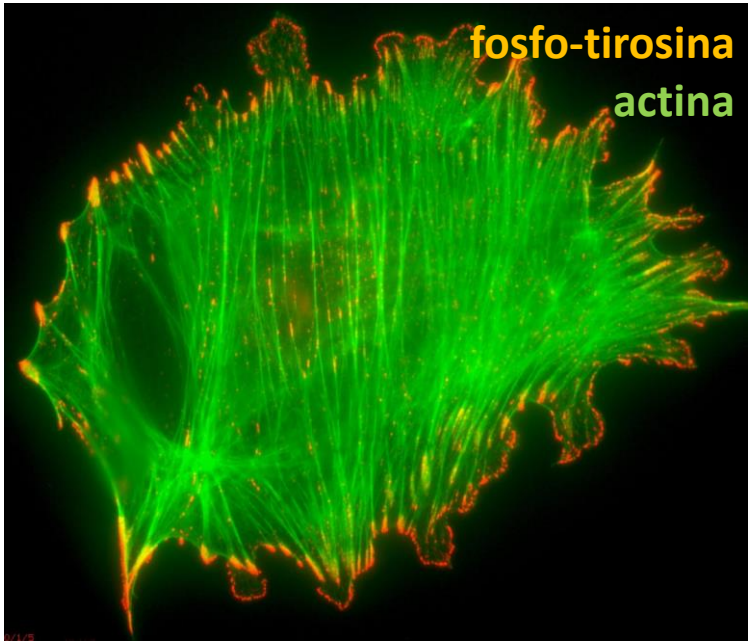


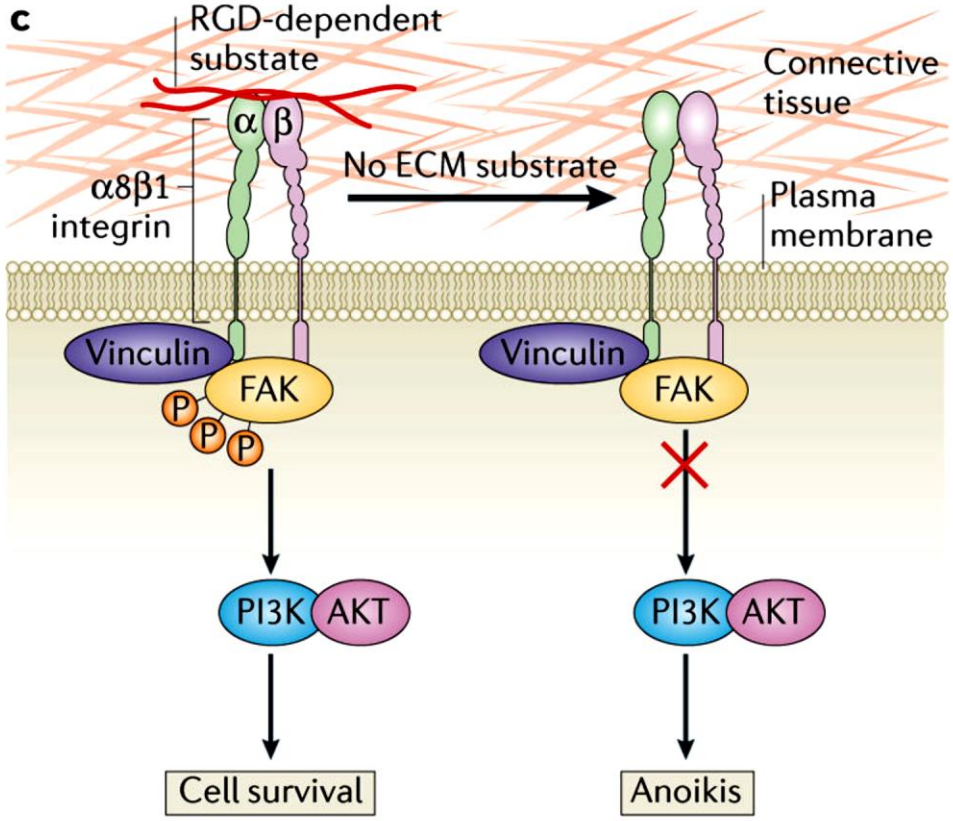
MATRIZ EXTRACELULAR:

¿es un soporte físico pasivo o activo?

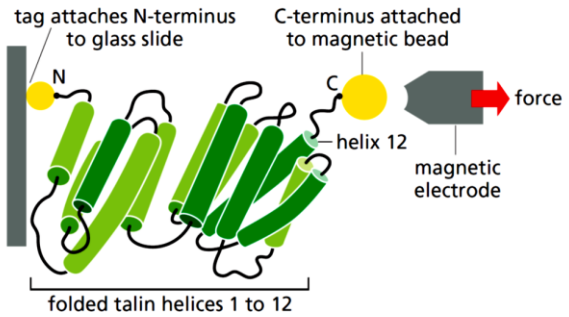
Uniones célula-matriz: señalización intracelular

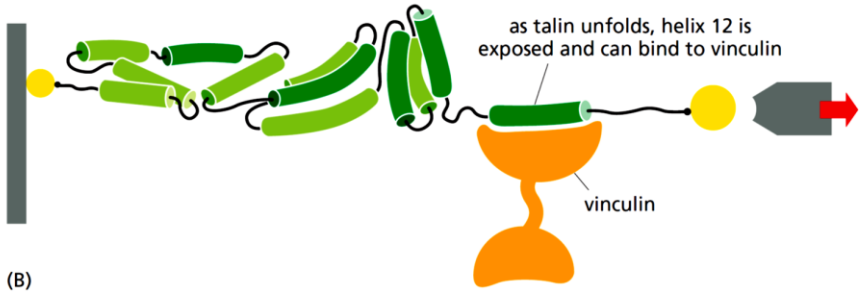
FAK - focal adhesión kinase
Src kinase
ILK - Integrin-linked kinase





Bonnans et al. *Nat Rev Mol Cell Biol*. 2014, 15(12): 786–801. doi:10.1038/nrm3904.

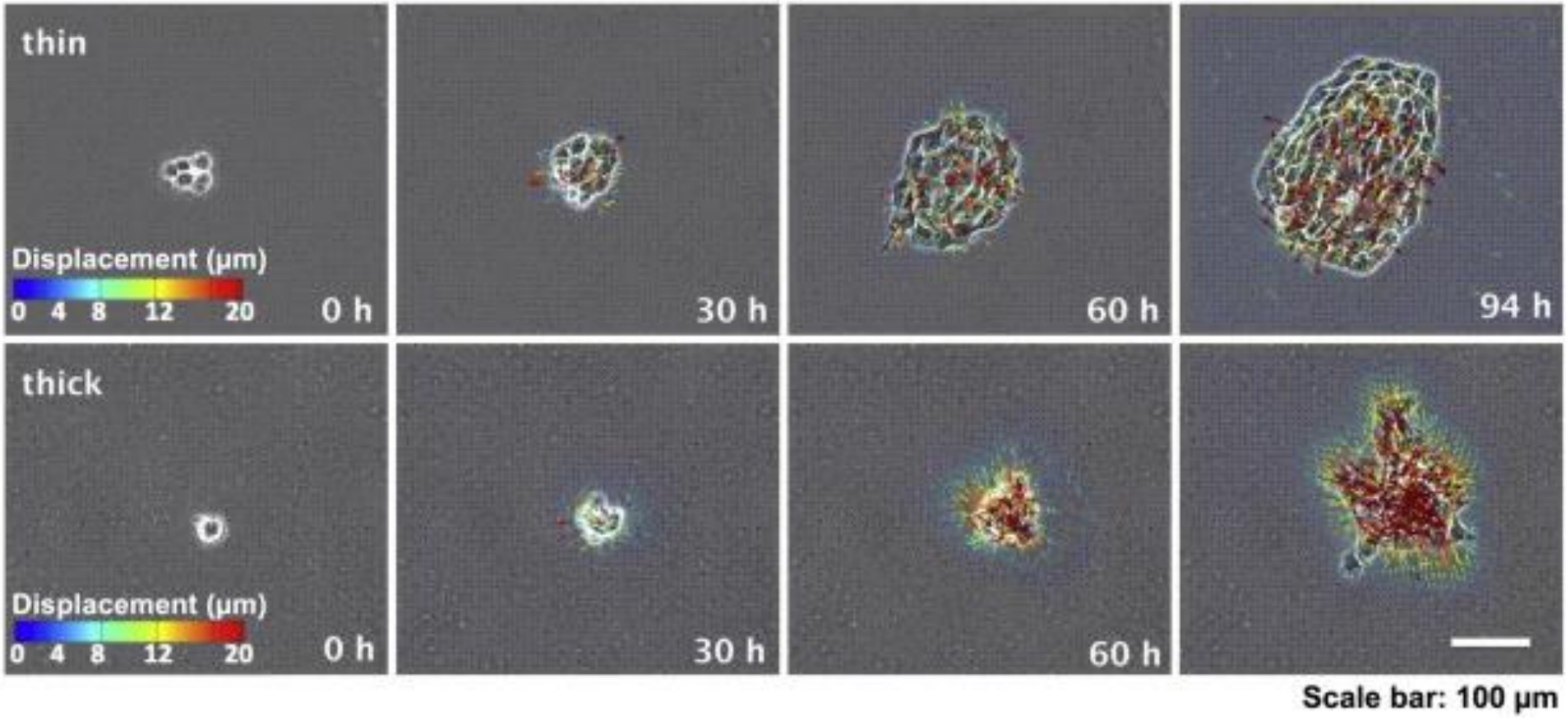




Talin: sensor de tensión

¿Cómo es la relación entre las células y la matriz extracelular?

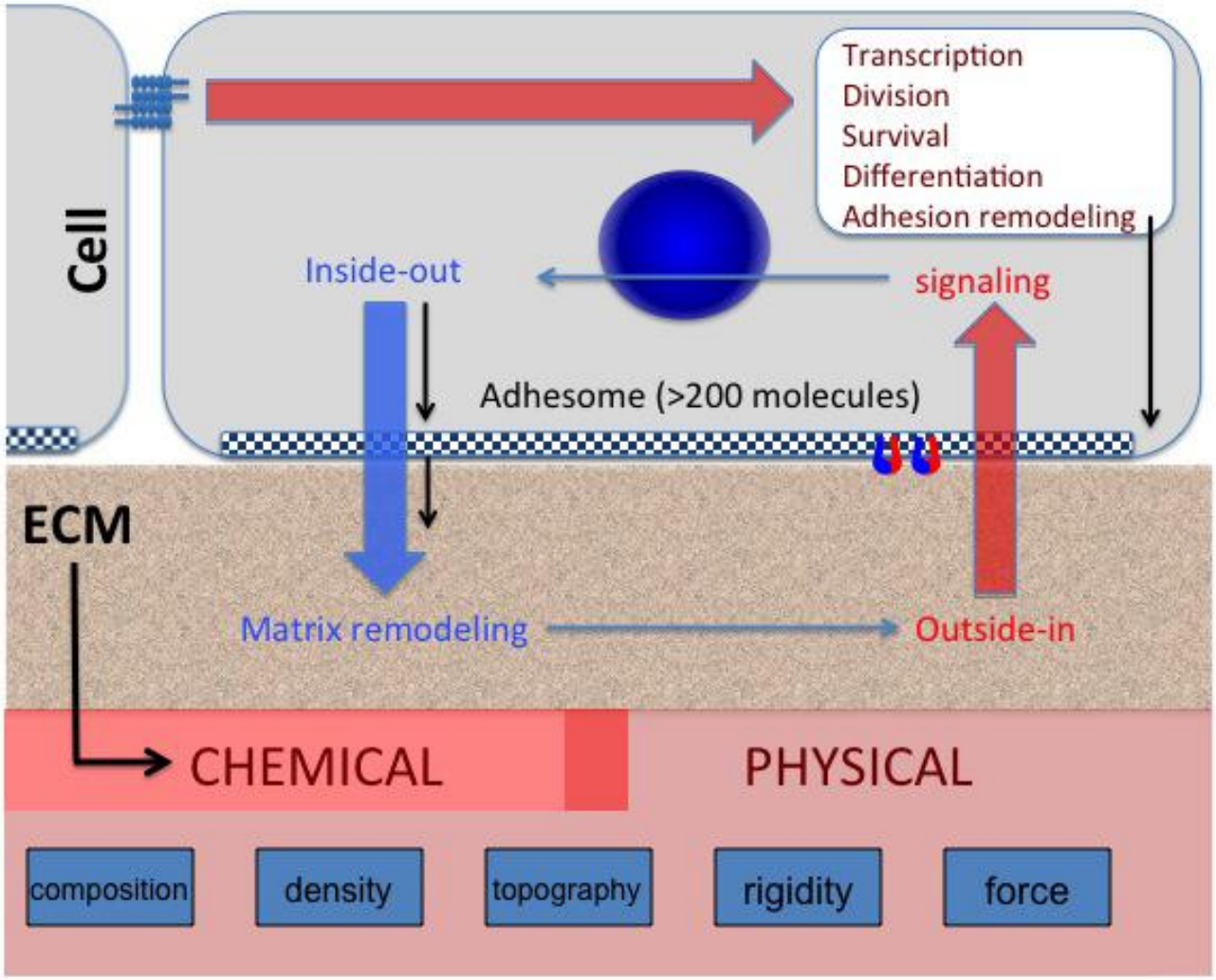
Link células



Link matriz

Tusan 2018 Biophysical J - https://doi.org/10.1016/j.bpj.2018.03.037

Relación célula-matriz: bidireccional



https://www.weizmann.ac.il/immunology/Geiger/scientific-activities/adhesion-mediated-signaling

BIBLIOGRAFÍA

- Bruce Alberts 6ª Ed - Cap. 19

- Lodish 7ª Ed - Cap. 20

- Frantz et al. (2010) The extracellular matrix at a glance. Journal of Cell Science 123, 4195-4200

- Yue (2014) Biology of the Extracellular Matrix:
An Overview. J Glaucoma 2014;23:S20–S23