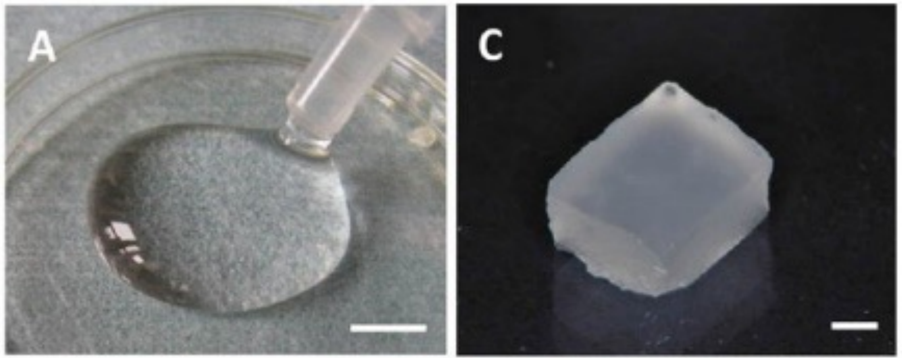
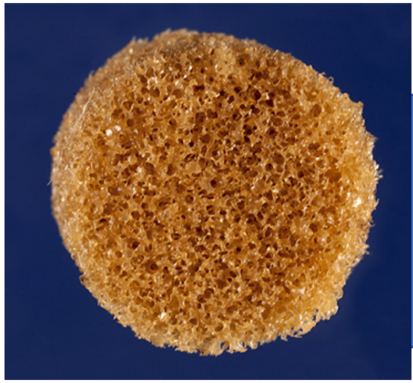
Biomimetic Scaffolds For Different Tissue Types in Tissue Engineering

The hydrogel scaffolds have biochemical similarity with the highly hydrated GAG components of connective tissues. Examples of hydrogel-forming polymers of natural origin are collagen, gelatin, fibrin, HA, alginate, and chitosan. The synthetic polymers are PLA, PPF-derived Copolymers, PEG-derivatives, and PVA.



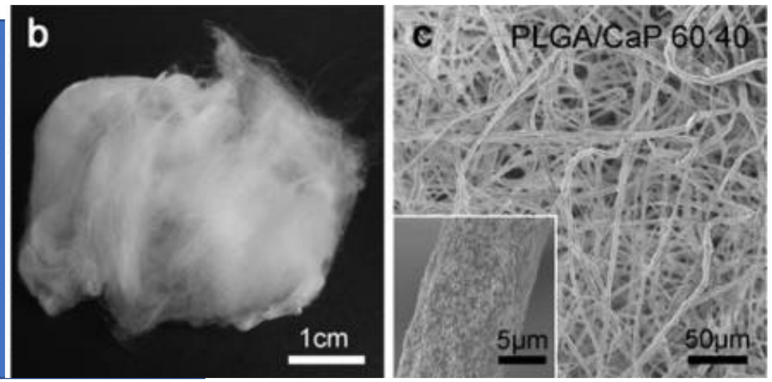


Foam porous scaffold have been used especially for growth of host tissue, bone regrowth, or organ vascularization. Synthetic biodegradable polymers such as PLLA, PGA, PLGA, PCL, PDLLA, PEE based on PEO, and PBT are used as porous scaffolding materials.

Fibrous Scaffold

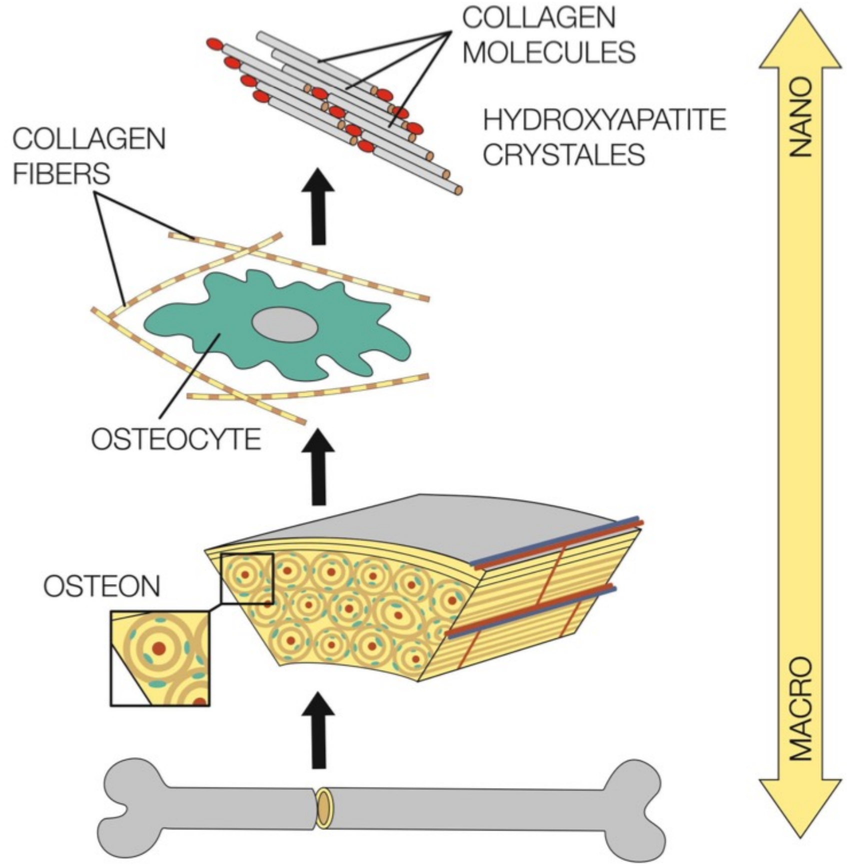
Fibrous scaffolds are used for musculoskeletal tissue engineering (bone, cartilage, ligament, and skeletal muscle), skin, vascular, neural tissue engineering, and for controlled delivery of drugs, proteins, and DNA.

Natural polymers and synthetic polymers are used such as collagen, gelatin, chitosan, HA, silk fibroin, PLA, PU, PCL, PLGA, PEVA, and PLLA-CL.



Bone Tissue Engineering

- The bone ECM consists of organic components (22 wt %), inorganic crystalline mineral components (69 wt %) and water (9 wt %).
- Organic components consist of type I, type III, type IV collagen, and fibrin. In addition, there are over 200 types of noncollagenous matrix proteins (glycoproteins, proteoglycans, sialoproteins, etc.)
- Inorganic crystalline mineral components are represented by hydroxyapatite and calcium phosphate.
- Organic components ensure flexibility, whereas inorganic components ensure strength and toughness.
- Two major types of bone structure can be distinguished: **trabecular and compact bone**. Trabecular bone is formed by a porous trabecular network and bone marrow filling a large inner space. Compact bone is made from inorganic crystalline mineral with a very low number of osteocytes, blood vessels, etc. Both types of bones are reinforced by collagen fibers.



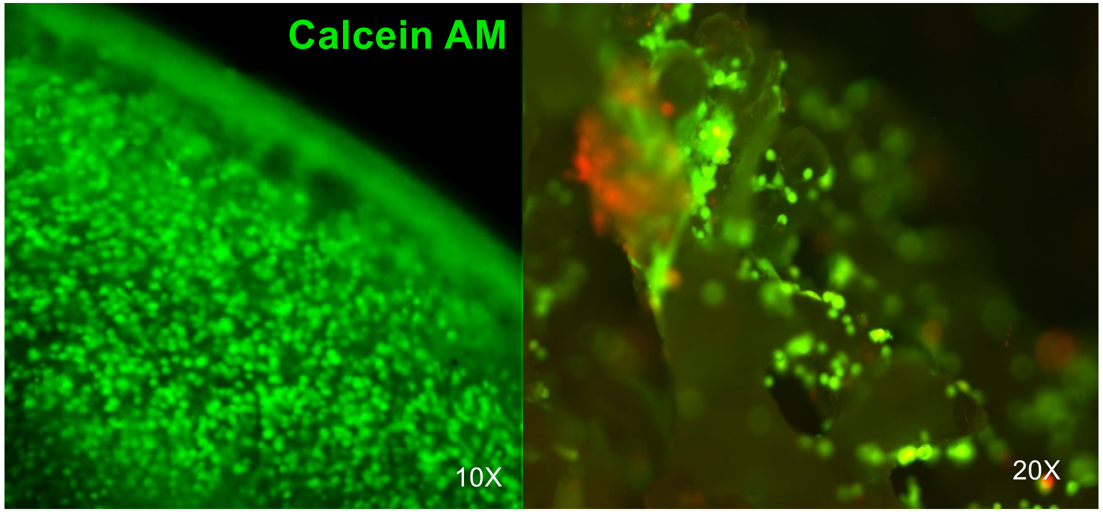
Chocholata et al., *Materials* **2019**, *12*, 568; doi:10.3390/ma12040568

Bone Tissue Engineering

Scaffold MgHA/collagen composite microstructure.

Cell viability

AEC / scaffold



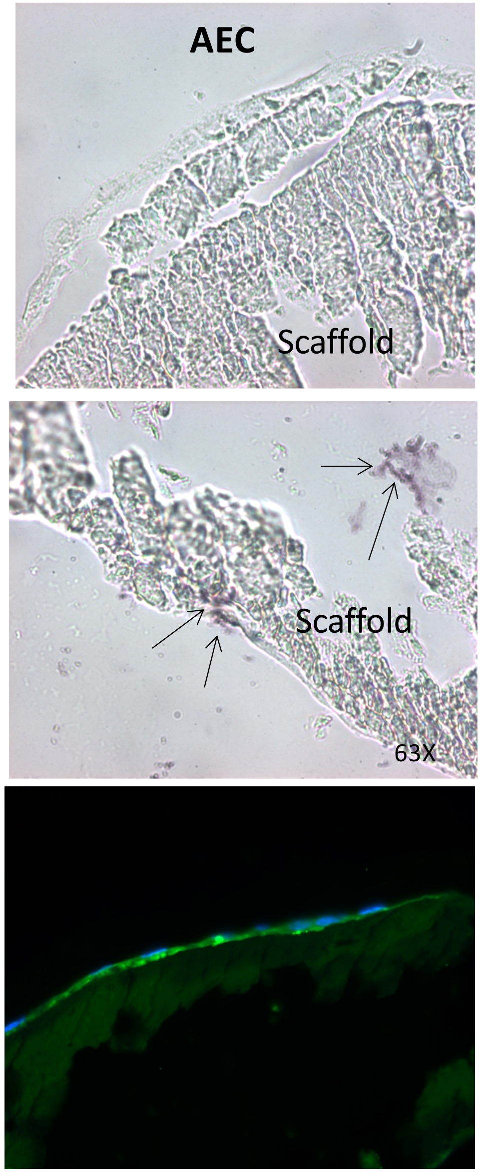
Calcein AM = alive cells
Propidium iodide = dead cells

Cell viability (% live/total cells)	
AEC	88%

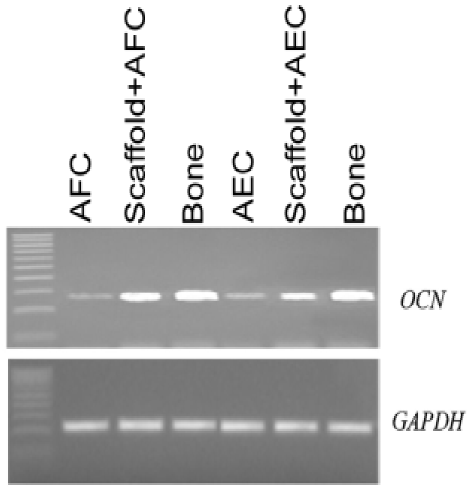
CTR neg (GM)

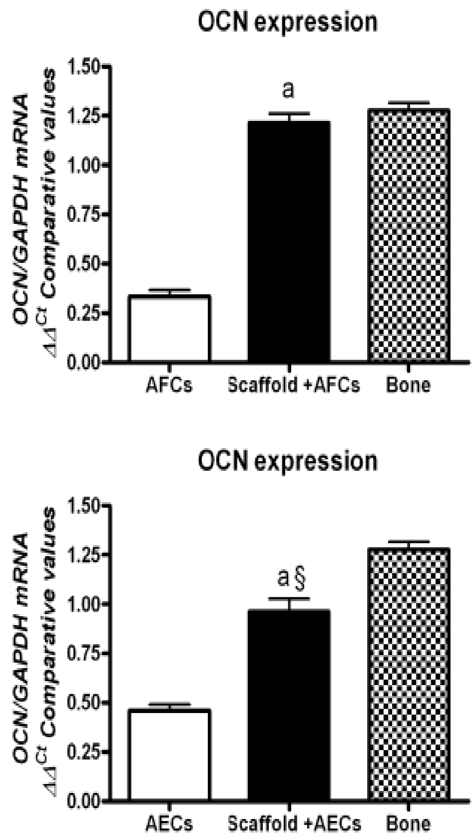
ALP positività
(DM)

OCN positività
(DM)



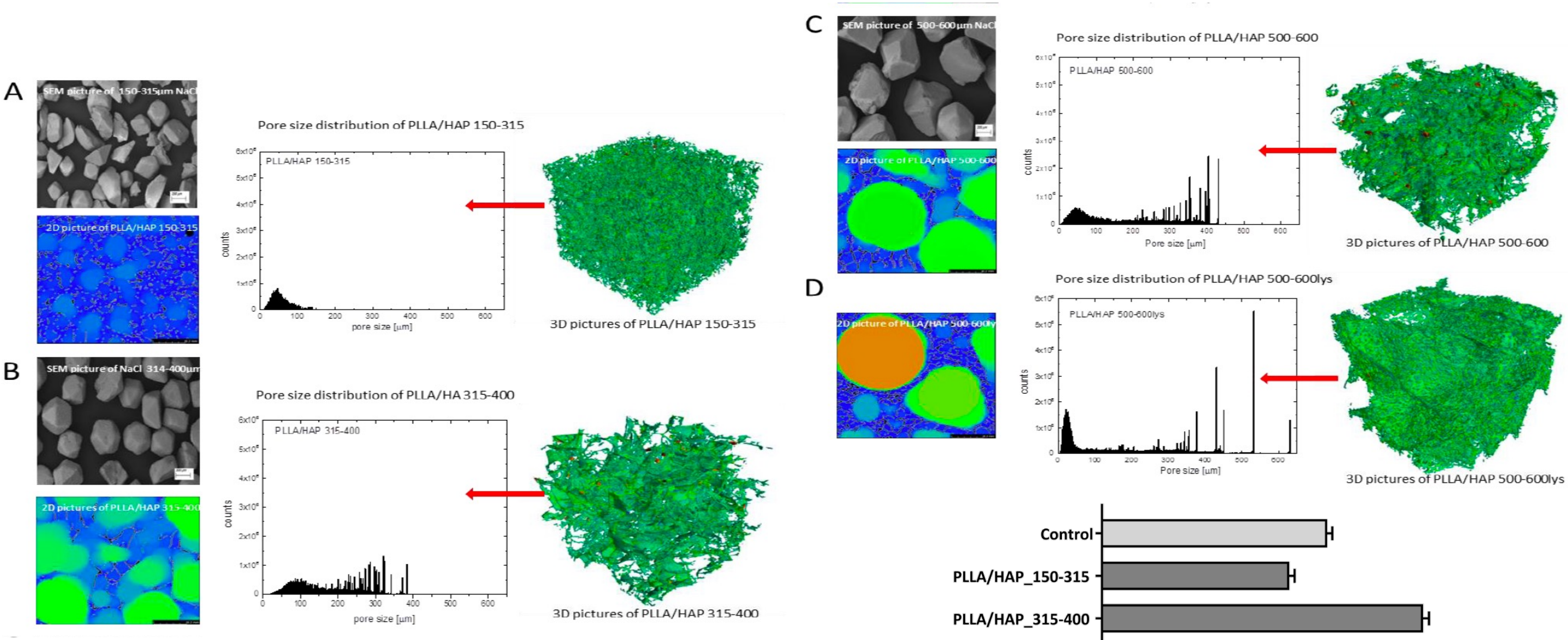
DIFFERENZIAMENTO OSTEOGENICO

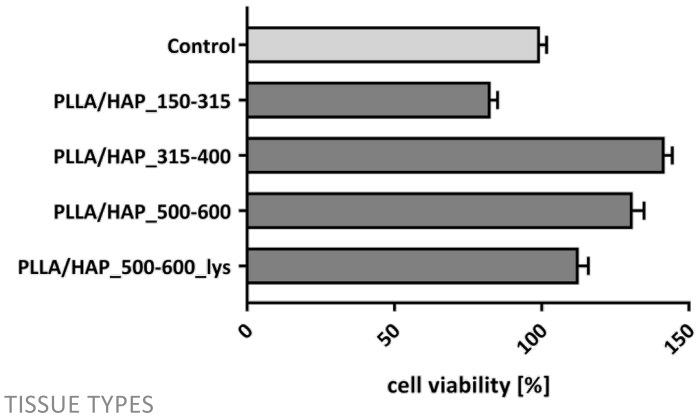




a $p<0.05$
§ $p<0.05$

Bone Tissue Engineering

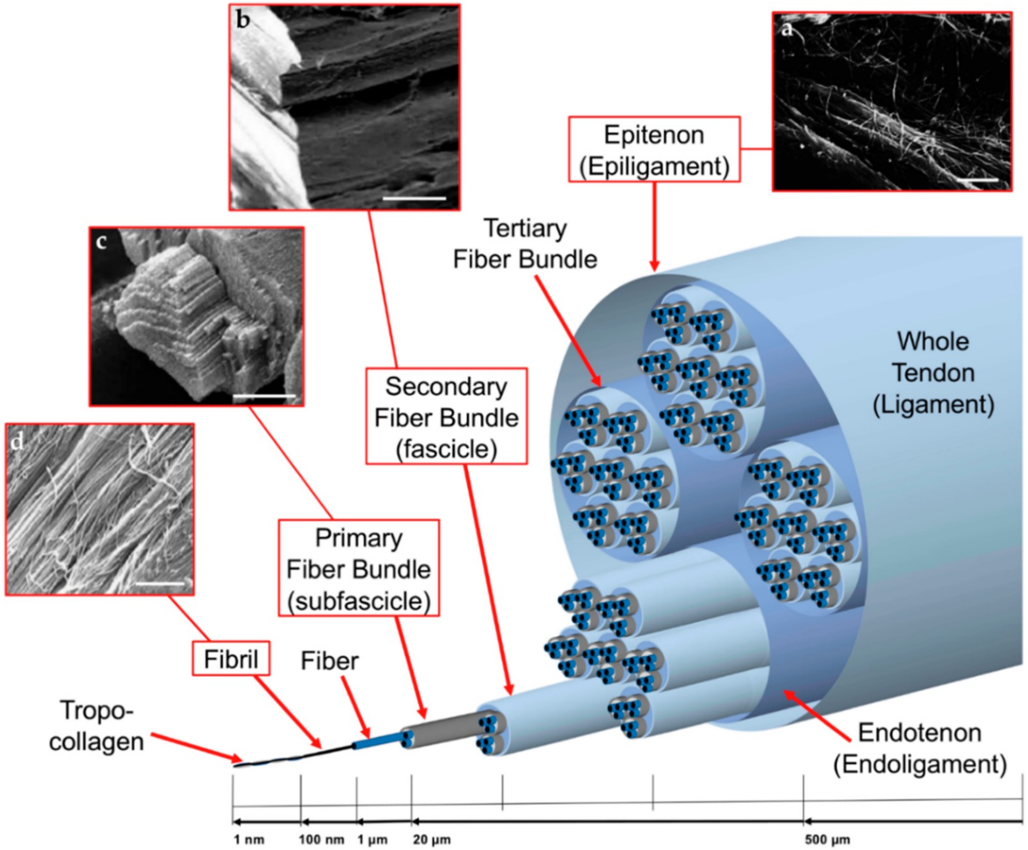




Szustakiewicz et al., Int. J. Mol. Sci. 2021, 22, 3607

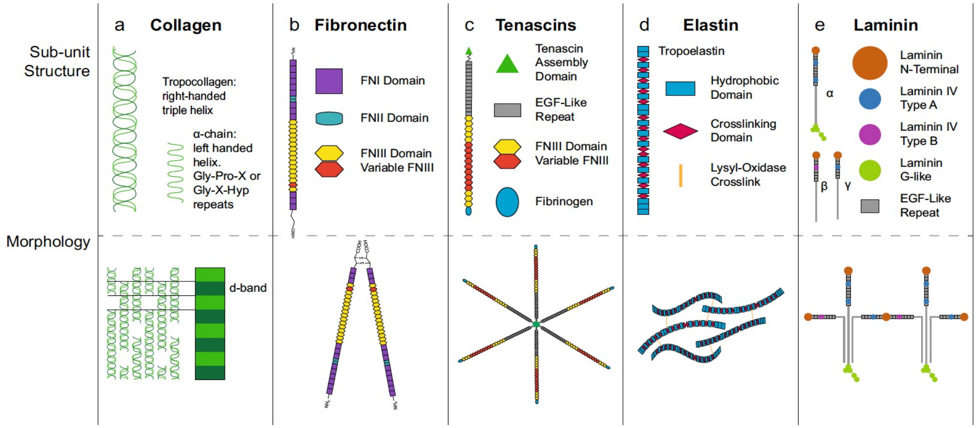
Tendon Tissue Engineering

- Tendons are fibro-elastic structures that connect muscles to bones or other insertion structures.
- The structure of tendons is organized to provide resistance against longitudinal stresses generated by muscles. Microscopically, healthy tendons are dense connective tissues predominantly composed of parallel, closely packed collagen fibers and cells within a well-ordered extracellular matrix (ECM).
- Tendons are surrounded by a bed of loose areolar tissue called epitenon, or they may reside within a tunnel of dense fibrous tissue, the tendon sheath.
- They have a high resistance to mechanical loads, and allow the conduction, distribution, and modulation of the force exerted by the muscles to the structures to which they are connected.

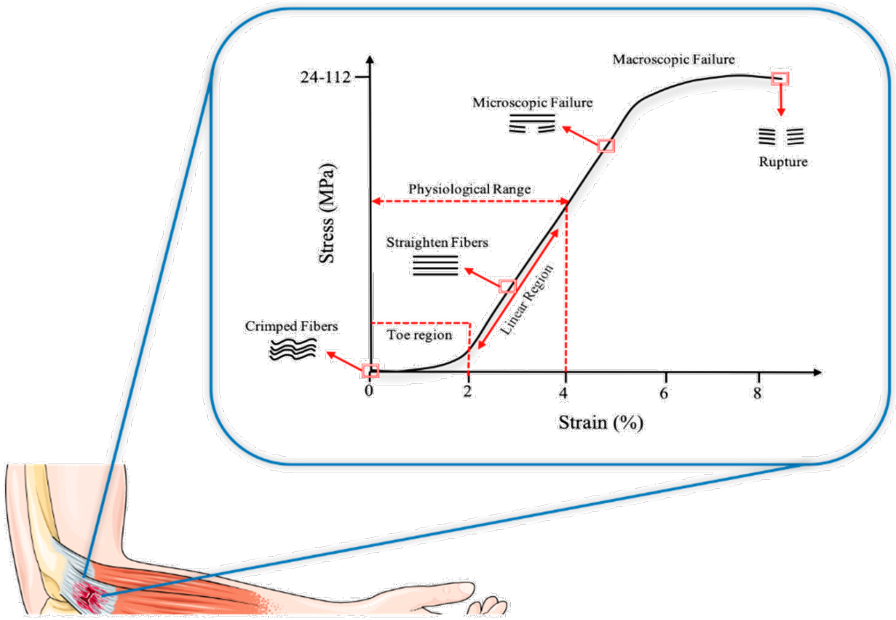


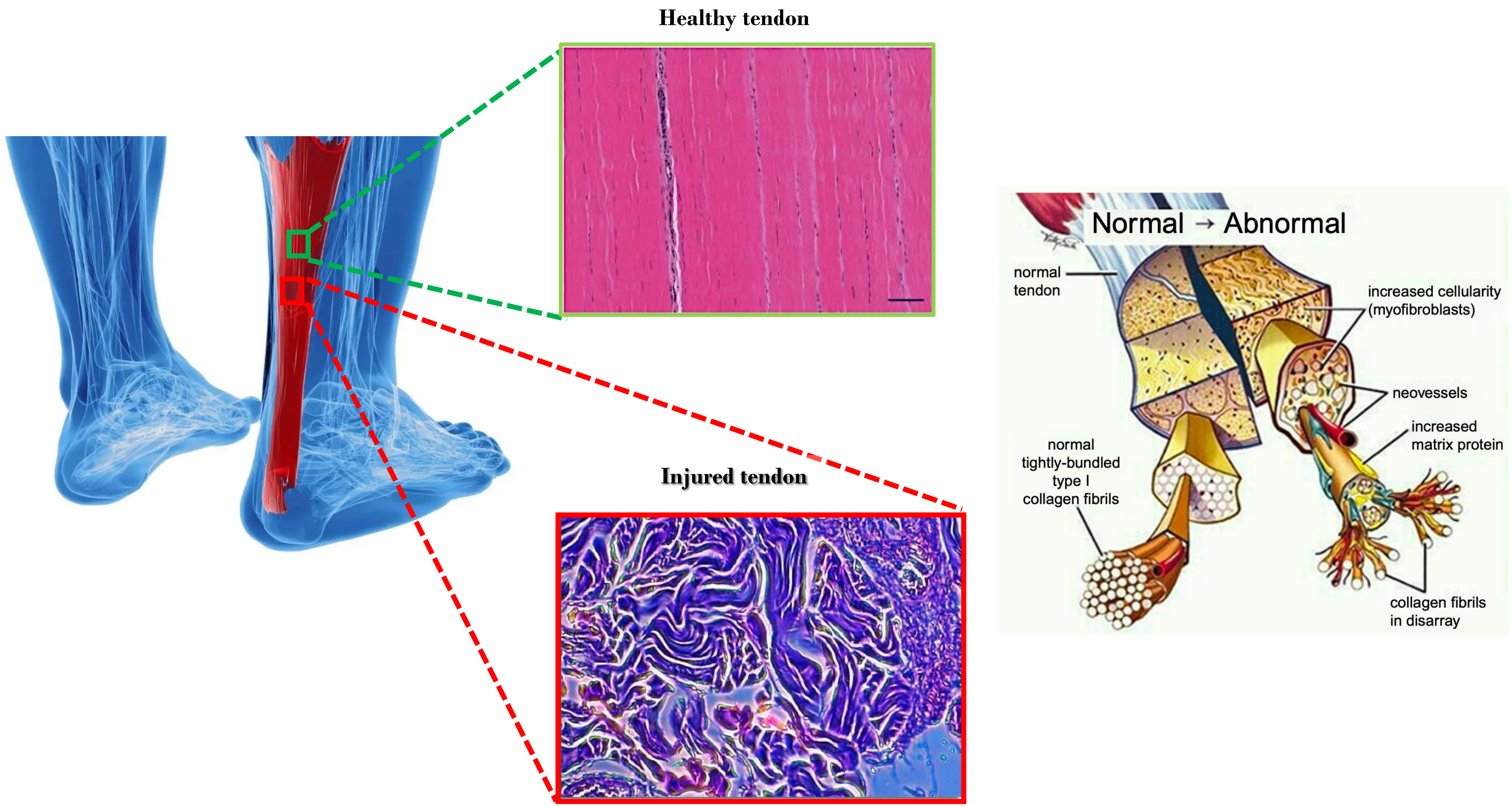
Tendon Tissue Engineering

- Tendons are a fibrous connective tissue formed mainly by collagen fibers, which determine mechanical and physiological properties, and elastin fibers that give it elasticity. Collagen and elastin are immersed in a matrix of proteoglycans and water, where the collagen is 60% to 85% of the dry mass of the tendon, while the elastin is just 2%. Collagen type I is the predominant protein, with small amounts (about 5%) of collagen type III and type V.



- Healthy tendons have high strength and minimal elasticity to resist mechanical loads. Human tendons rupture happens at 8% strain, while 4% strain produces plastic deformation.

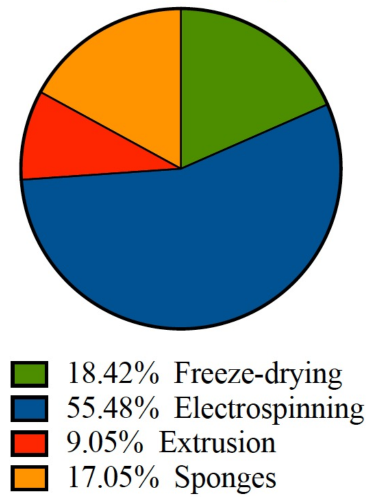


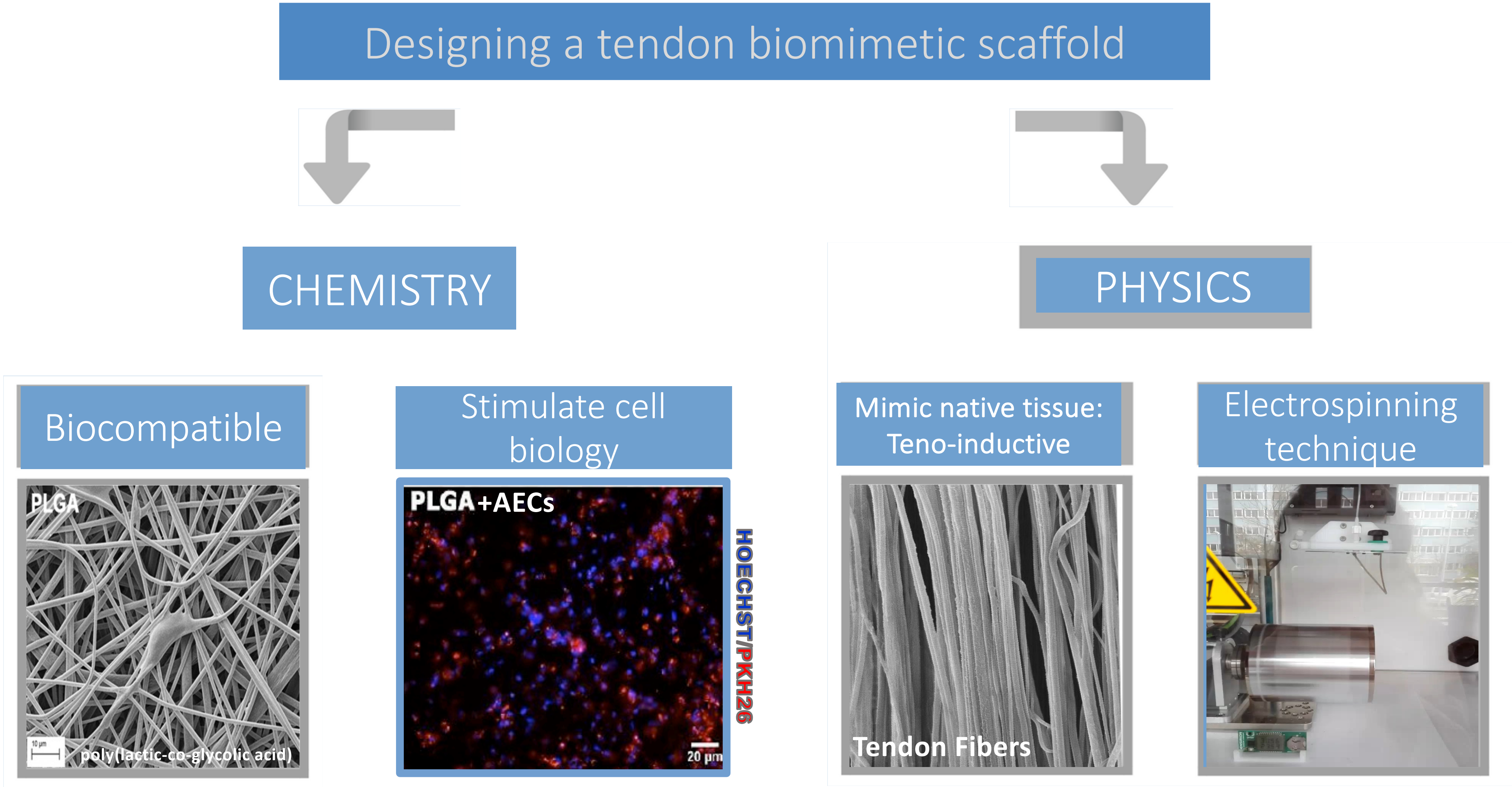

Healthy tendon
Injured tendon
Normal → Abnormal
normal tendon
increased cellularity (myofibroblasts)
neovessels
increased matrix protein
normal tightly-bundled type I collagen fibrils
collagen fibrils in disarray

Tendon Tissue Engineering

Acronym	Extended Name	Application
P(LLA-CL)	Poly(L-lactide-co-ε-caprolactone)	Tendon/Ligament Ligament Tendon
PDLLA	Poly(D,L-lactic acid)	Ligament
PLDLA	Poly(L-lactide-co-D,L-lactic acid)	Ligament
PLLA	Poly(L-lactic acid)	Tendon/Ligament Ligament Tendon Ligament-to-Bone Interface Tendon-to-Muscle Interface Tendon Anti-Adhesion
PELA	Poly(L-lactic acid)-poly(ethylene glycol)	Tendon Anti-Adhesion
PDLLGA	Poly(D,L-lactide-co-glycolic acid)	Ligament Tendon
PLGA	Poly(lactic-co-glycolic acid)	Tendon/Ligament Ligament Tendon Tendon-to-Bone Interface
PLLGA	Poly(L-lactic-co-glycolic acid)	Tendon/Ligament Tendon-to-Bone Interface Bone-Ligament-Bone
PCL	Poly(ε-caprolactone)	Tendon/Ligament Ligament Tendon Tendon/Ligament-to-Bone Interface Ligament-to-Bone Interface Tendon-to-Bone Interface Tendon-to-Muscle Interface Tendon Anti-Adhesion Bone-Ligament-Bone
PCLDLLA	Poly(ε-caprolactone-co-D,L-lactic acid)	Ligament
PU	Poly(urethane)	Ligament Tendon
PEUR	Poly(ester urethane)	Ligament
PEUUR	Poly(ester urethane urea)	Tendon/Ligament Ligament Ligament-to-Bone Interface
PEUUR2000	Poly(ester urethane urea) elastomer	Ligament-to-Bone Interface
BPUR10	Biodegradable Poly(urethane urea) 10	Tendon-to-Bone Interface
BPUR50	Biodegradable Poly(urethane urea) 50	Tendon-to-Bone Interface
PEO	Poly(ethylene oxide)	Tendon/Ligament Tendon
PEGDA	Poly(ethylene glycol diacrylate)	Ligament
PEDOT	Poly(3,4-ethylenedioxythiophene)	Ligament
PDO	Poly(dioxanone)	Tendon
PAN	Poly(acrylonitrile)	Tendon
PVDF-TrFe	Poly(vinylidene fluoride-trifluoro ethylene)	Tendon
DP	Biodegradable Poly(ester urethane) block copolymer (DegraPol®)	Tendon Anti-Adhesion
P3HB	Poly(3-hydroxybutyrate)	Tendon/Ligament
Nylon6.6	Nylon 6.6	Tendon/Ligament
SE	Silk	Ligament Tendon Tendon-to-Bone Interface
SF	Silk Fibroin	Tendon
Fibrinogen	Fibrinogen	Tendon/Ligament
Coll	Collagen	Tendon/Ligament Tendon Tendon-to-Muscle Interface
CTS	Chitosan	Tendon/Ligament-to-Bone Interface Tendon Tendon Anti-Adhesion
GT	Gelatin	Tendon
HA	Hyaluronic acid	Tendon Anti-Adhesion
mGLT	Methacrylated Gelatin	Tendon
Carbothane™ 3575A	Poly(carbonate)-based thermoplastic poly(urethane)	Tendon/Ligament
MWCNTs	Multi Wallen Carbon Nanotubes	Tendon/Ligament

Number of publications on the techniques used for tissue engineering since 1990




Designing a tendon biomimetic scaffold
CHEMISTRY
PHYSICS
Biocompatible
Stimulate cell biology
Mimic native tissue: Teno-inductive
Electrospinning technique
PLGA
poly(lactic-co-glycolic acid)
PLGA+AECs
20 µm
HOECHST/PKH26
Tendon Fibers