Recapitulating the Native Tendon Environment in a Synthetic 3D Anisotropic Hydrogel as an Engineered Extracellular Matrix

Tayler Hebner, Destina Genc, Danielle Benoit, University of Oregon

What was achieved?:
A synthetic 3D hydrogel scaffold was engineered to replicate the structural and biochemical features of native tendon tissue. Using a two-stage polymerization strategy, the researchers created anisotropic poly(ethylene glycol)-based hydrogels with aligned polymer networks and enzymatically degradable crosslinks. This design enabled encapsulated tenocytes to adopt aligned morphologies and actively remodel their environment. The materials supported sustained cell viability and promoted deposition of an organized extracellular matrix primarily composed of type I collagen, characteristic of regenerative tendon tissue.

Why is it important?:
Tendon injuries often heal through the formation of disorganized scar tissue, leading to reduced mechanical performance and high rates of reinjury. A major challenge in regenerative medicine is recreating the anisotropic structure and dynamic remodeling behavior of native tendon. This work demonstrates that combining structural alignment with cell-responsive degradability in a synthetic scaffold can guide cell organization and promote regenerative outcomes. By enabling cells to both align and replace the scaffold with native matrix, this approach provides a pathway toward improved therapies for tendon repair and other load-bearing soft tissues.

How did BioPACIFIC MIP enable this?
BioPACIFIC MIP enabled this work by providing access to WAXS and expert support from facility staff, enabling characterization of hydrogel anisotropy and its role in guiding cellular organization and matrix formation.

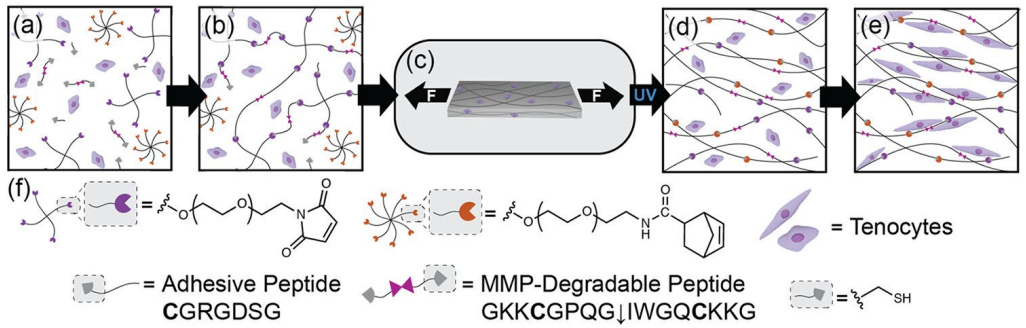


Figure 1. *Anisotropic hydrogels were synthesized as 3D scaffolds for encapsulated tenocytes by a process in which (a) all starting materials were mixed in solution before (a to b) a lightly crosslinked network was formed via thiol-Michael addition, followed by (c) mechanical stretching of the hydrogel and (c to d) a secondary photoinitiated thiol–ene crosslinking step to retain applied strain and orientation of the network. The anisotropic polymer network provides a template for (e) alignment of tenocytes in a pro-regenerative environment. (f) Shows representative starting materials.*

Publication: *ACS Appl. Bio Mater. 2026, 9, 4, 2282–2293*
https://doi.org/10.1021/acsabm.5c02408