Tendon-derived ECM enables percutaneous delivery of iMSC^{SCX+} for tendon defect healing

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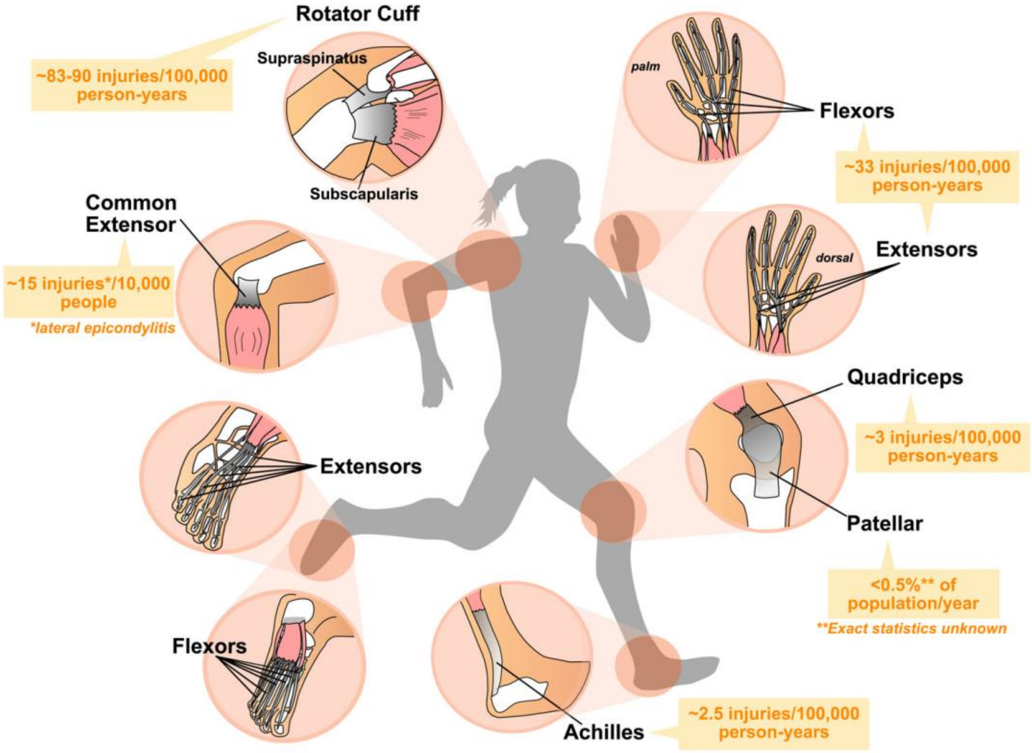
NEXT-GENERATION DELIVERY INNOVATIONS

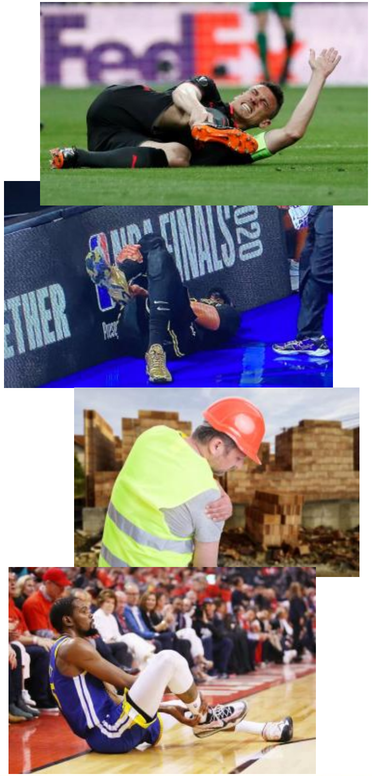
How common is the tendon injury?



Chun et al., 2022 (10.1038/s41598-021-04656-z)

Tendon injuries and chronic disorders

Cedars Sinai



Tendon injuries

Prevalence:

- Between 30-50 years old > 1%
- Lifetime risk of elite athletes > 53%
- Risk of young athletes > 18%

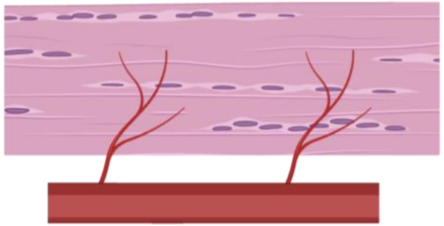
Tendinopathy → inflammation

Prevalence:

- Sports > 23%
- Physical work > 19%

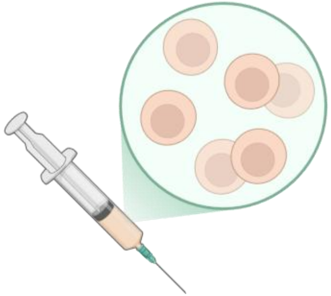
Why tendon fails to regenerate?

Hypocellularity



Hypovascularity

Triggering tendon regeneration



- ✔ Dynamically immunomodulatory
- ✔ Differentiation to tenocytes
- ✘ Phenotypic Drift over passages
- ✘ Dedifferentiation / Transdifferentiatic
- ✘ May promotes fibrosis

Triggering tendon regeneration

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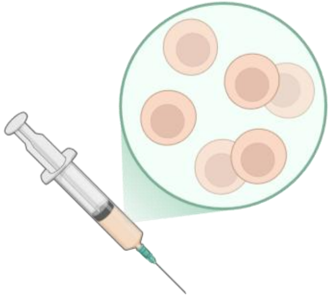
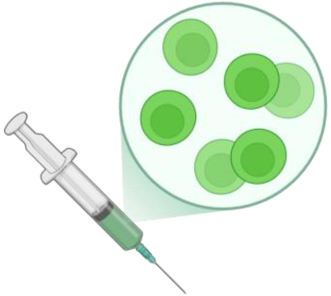
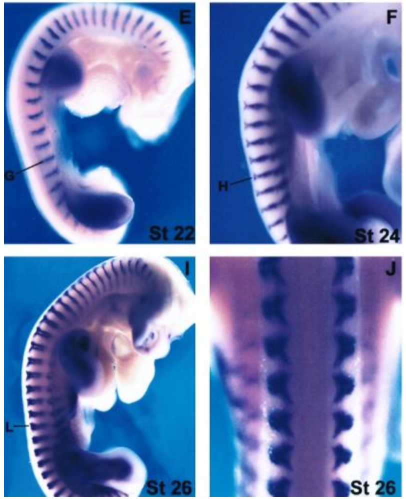
Mesenchymal stem cells (BM-MSCs, AD-MSCs)	iPSC-derived mesenchymal stem cells
	
✔ Dynamically immunomodulatory	✔ Dynamically immunomodulatory
✔ Differentiation to tenocytes	✔ Differentiation to tenocytes
✘ Phenotypic Drift over passages	✔ Resistant to phenotypic drift
✘ Dedifferentiation / Transdifferentiation	✔ Homogeneity
✘ May promotes fibrosis	✔ Unlimited source

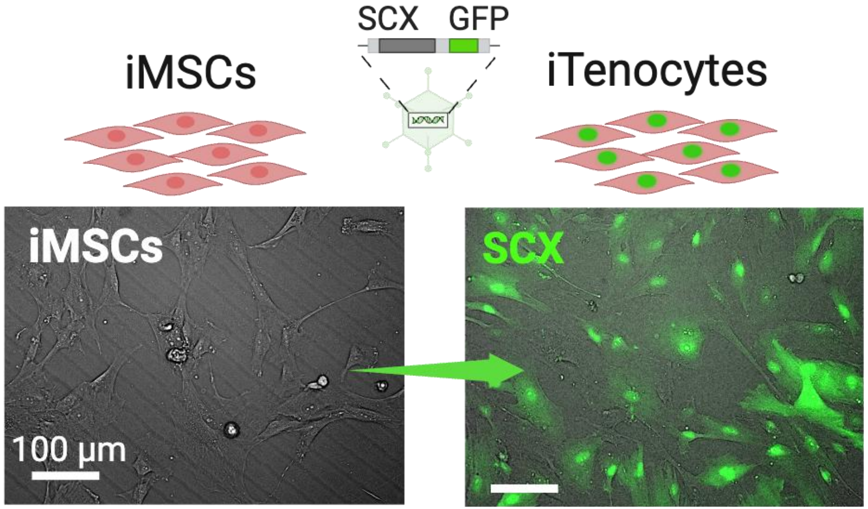
iMSCs can be genetically modified for tenogenic induction

Scleraxis (SCX) identified in tendon cells (tenocytes)



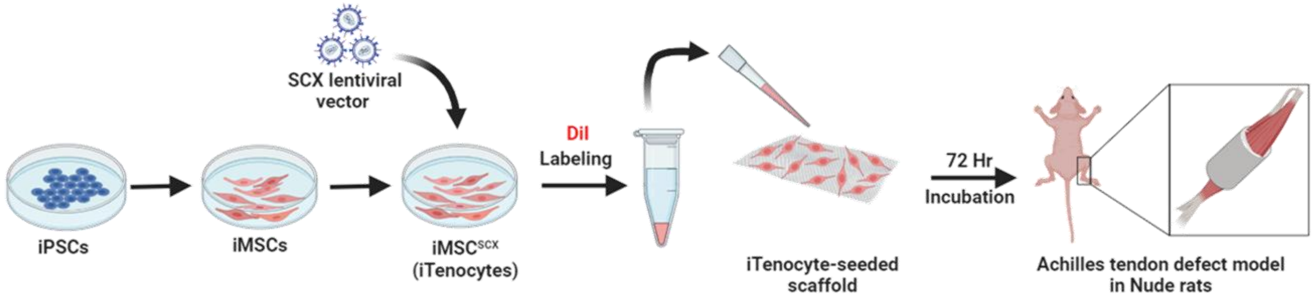
Brent et al., 2003

SCX-lentiviral vector



Sheyn et al., 2016

iTenocytes induced tendon regeneration



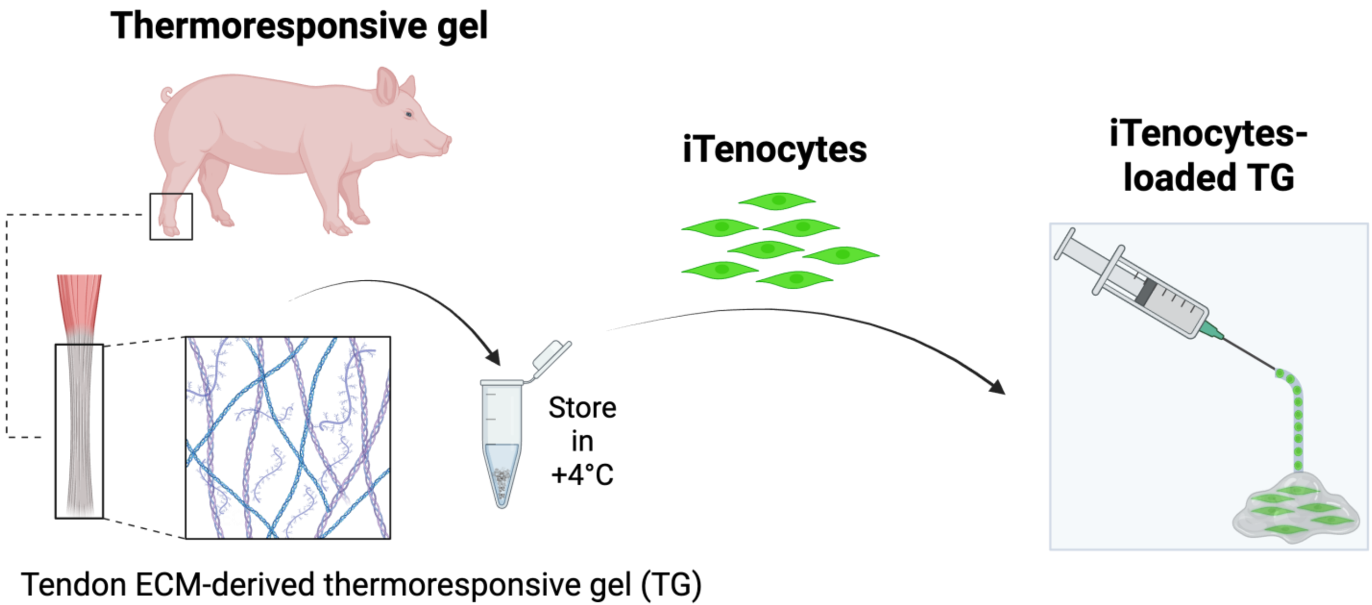
Adhesive gap-filling structure for better cell implantation

Bioresorbable cell carrier to replace growing tissue

Thomas Spaeter, PhD
Postdoc in Sheyn Lab

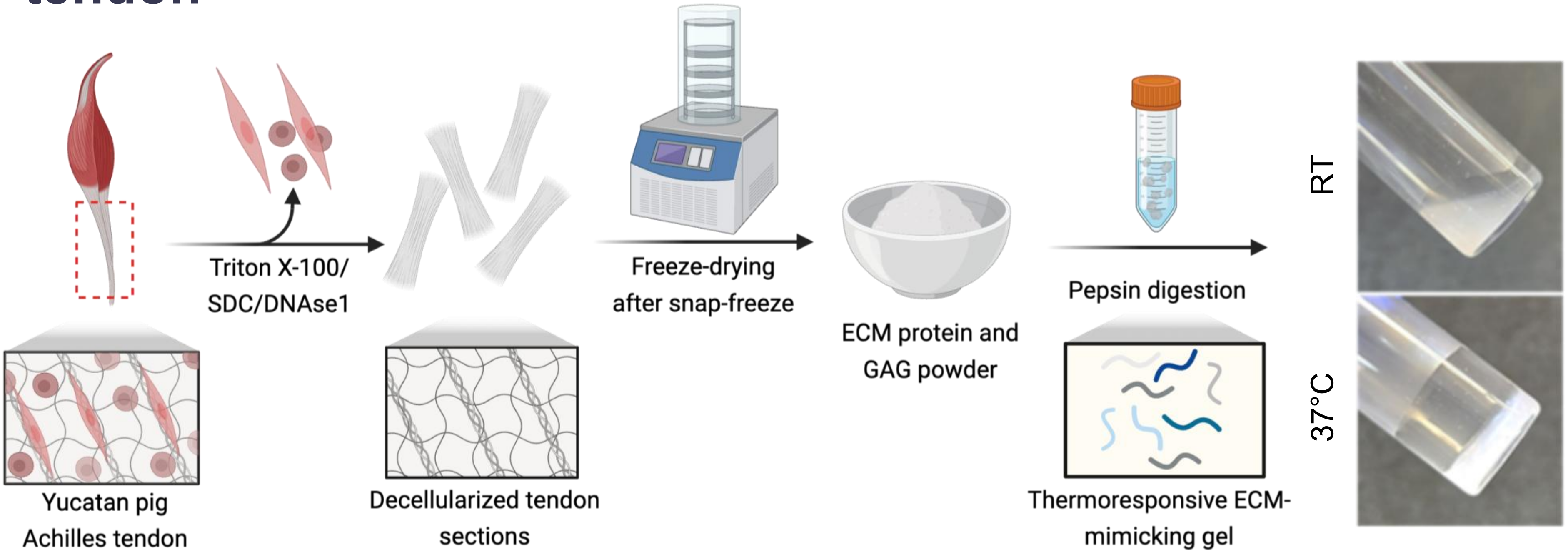
Patricia Del Rio
RA 2 in Sheyn Lab

Hypothesis



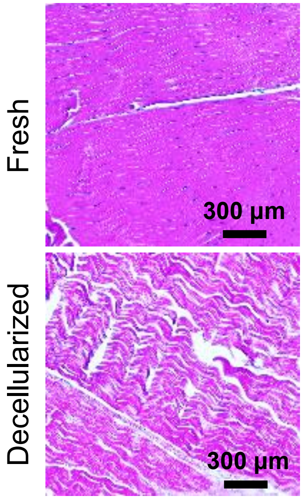
Tendon regeneration can be achieved by bioresorbable and pro-tenogenic iTenocyte-loaded TG transplanted in defected tendon

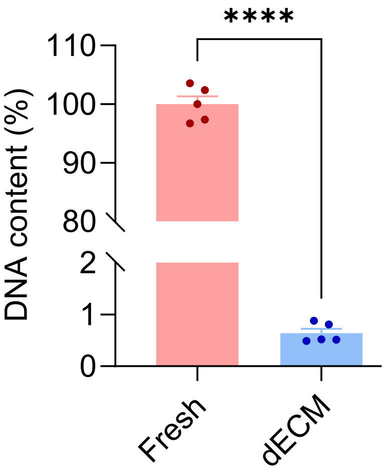
TG is produced by decellularization of porcine tendon



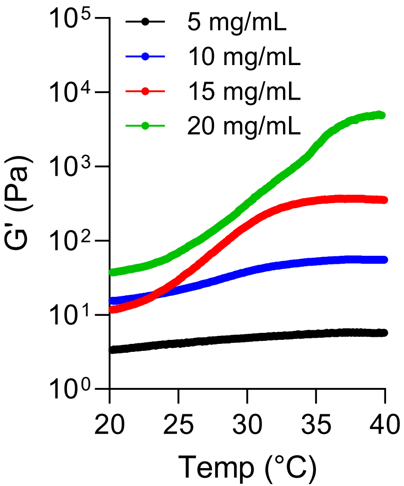
TG quality control

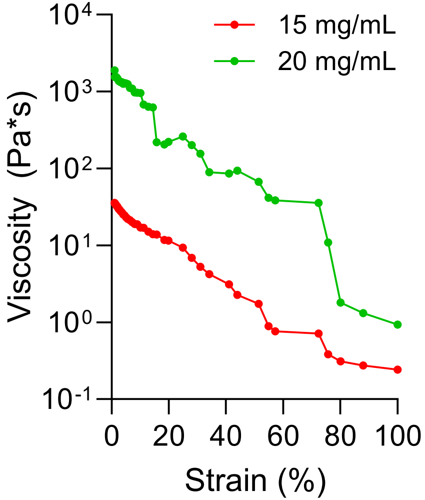
Porcine Achilles Tendon was successfully decellularized





Thermoresponsive strain-thinning material = Injectable gel





TG has favorable mechanical and biochemical features

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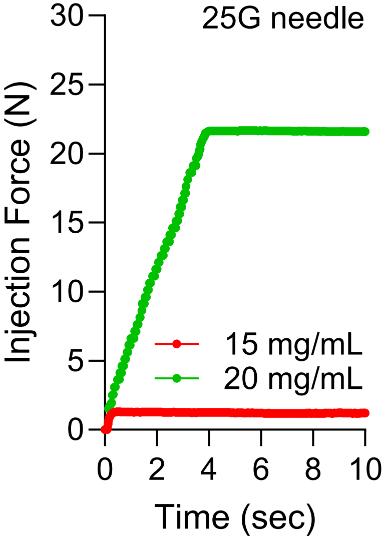

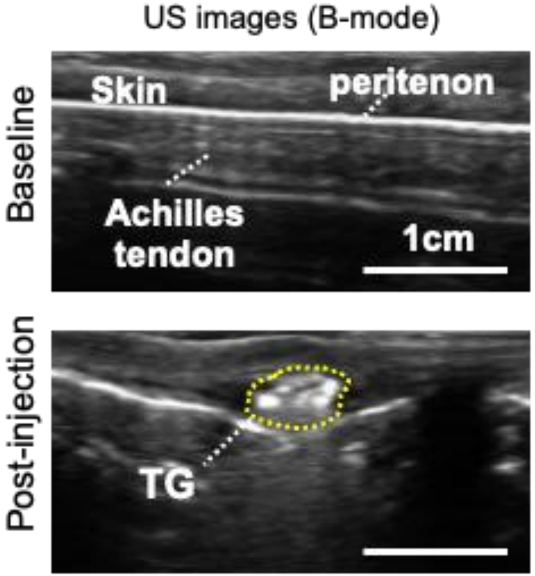

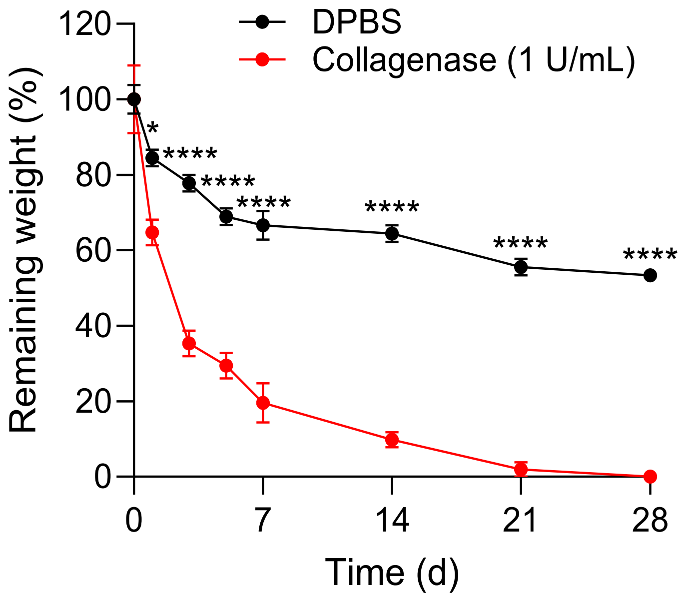

TG and PureCol® (PC) are different at protein-level

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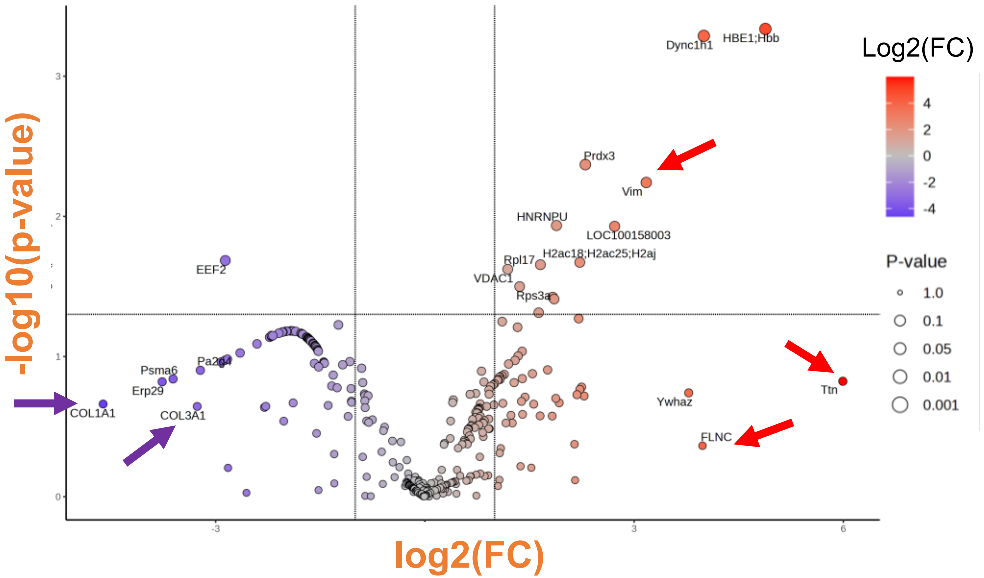
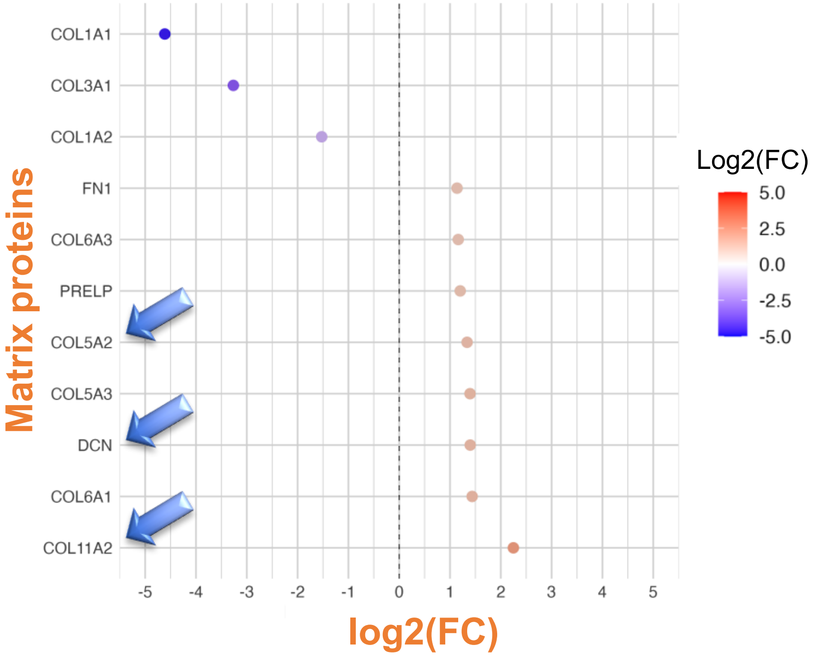
Comparison of proteins (PC as control)





Movement of the iTenocytes out of TG into the plate

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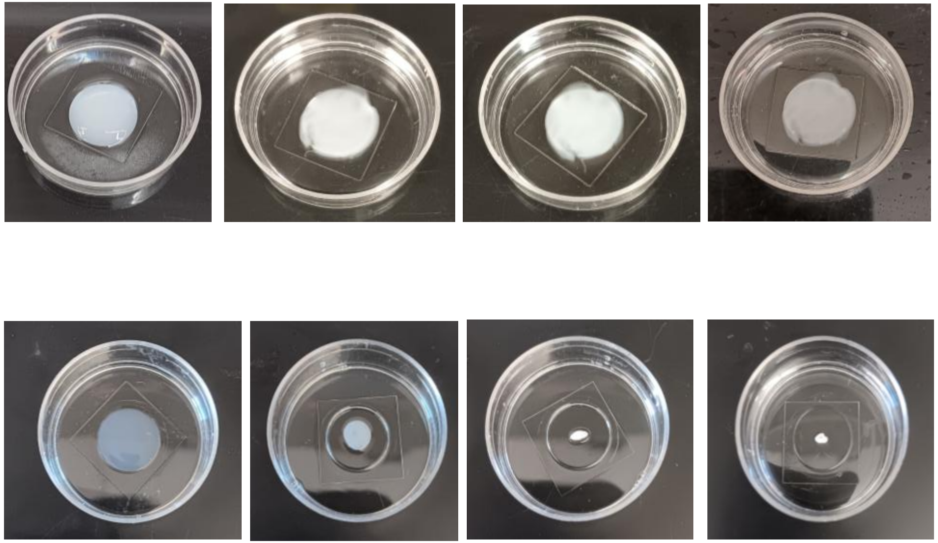
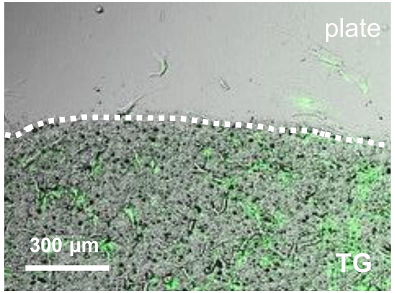
2 h post gelation | Day 1 | Day 3 | Day 7

- iTenocytes

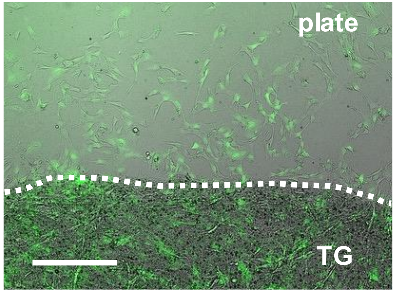
+ iTenocytes



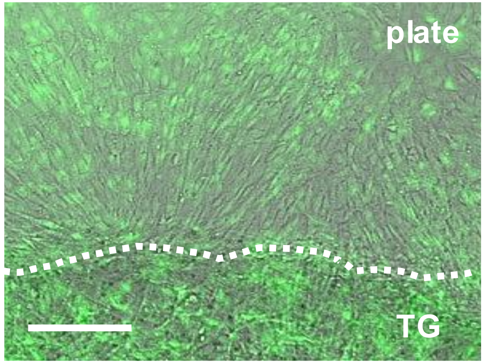
Day 1



Day 3



Day 7



iTenocytes colonized TG completely

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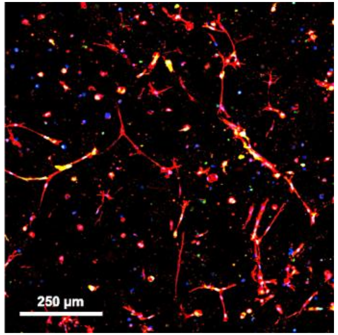
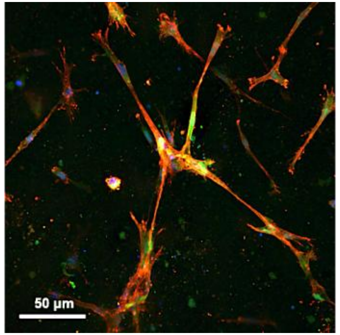
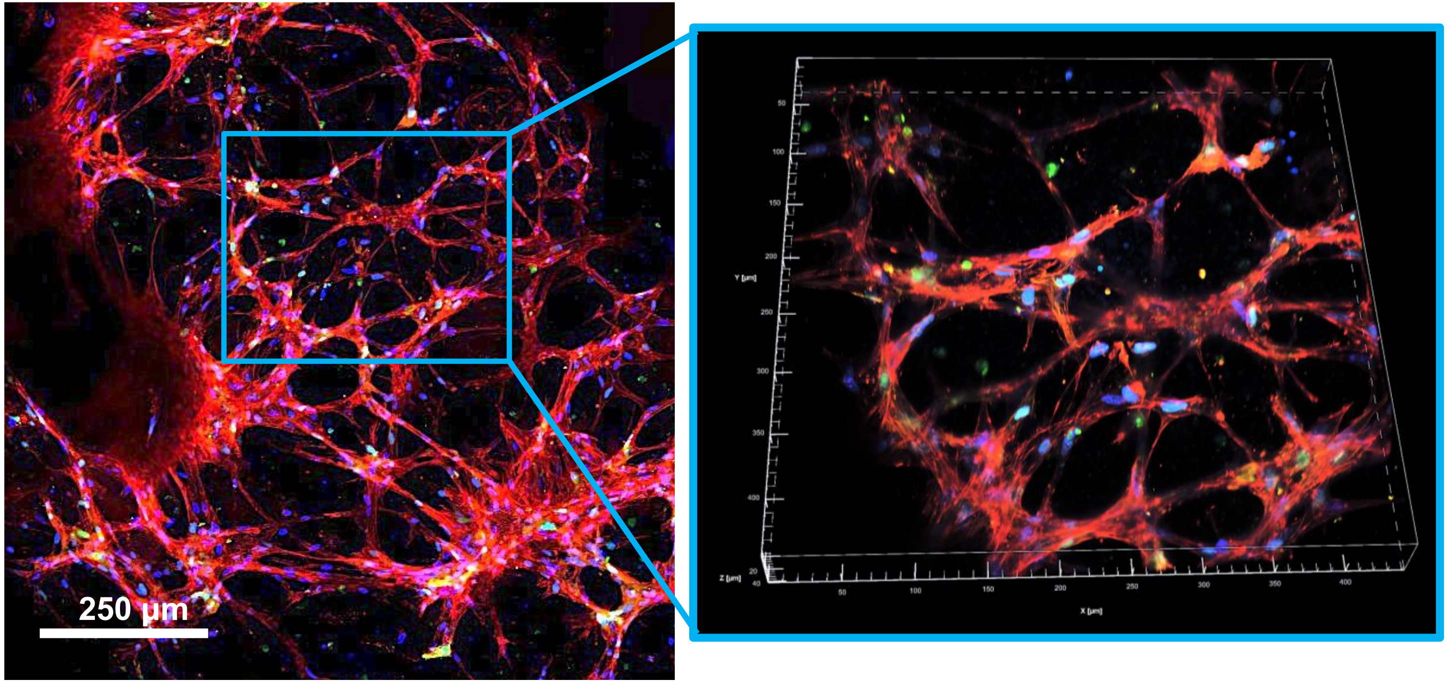
Day 3

Nuclei F-actin SCX





Day 7



TG led to faster maturation of iTenocytes than PC

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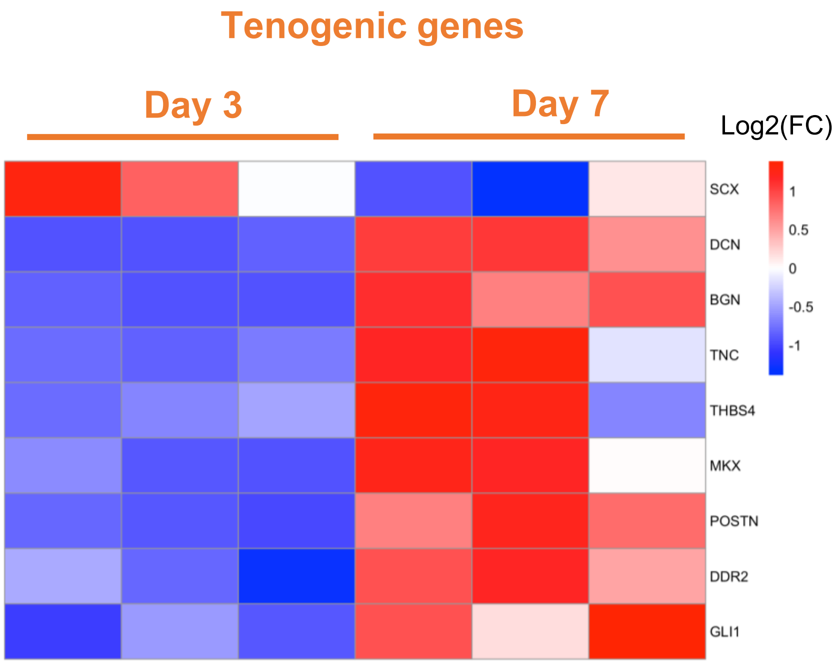
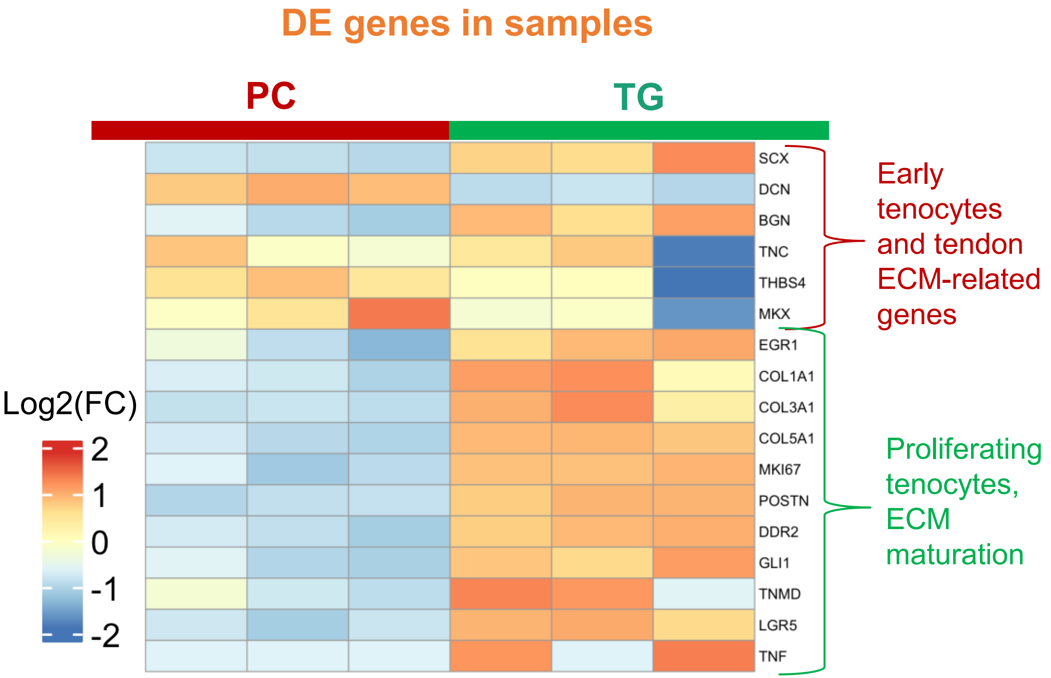
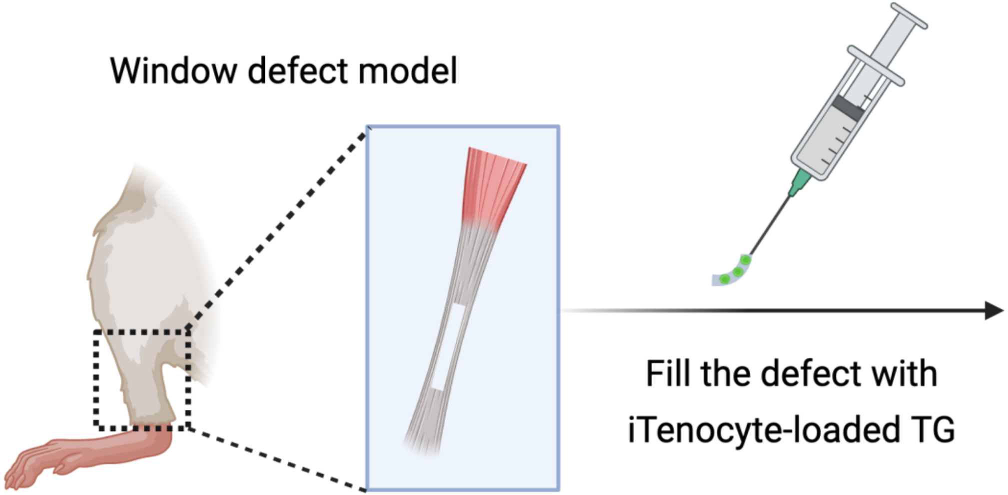


iTenocyte-loaded TG over time



In vivo work

Window defect model



Fill the defect with
iTenocyte-loaded TG

Proof-of-concept study:

1. Are cells alive in acute phase and survived to proliferative phase?
2. Can TG and/or iTenocyte-loaded TG combination improve neo-tendon deposition?

Acknowledgements

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