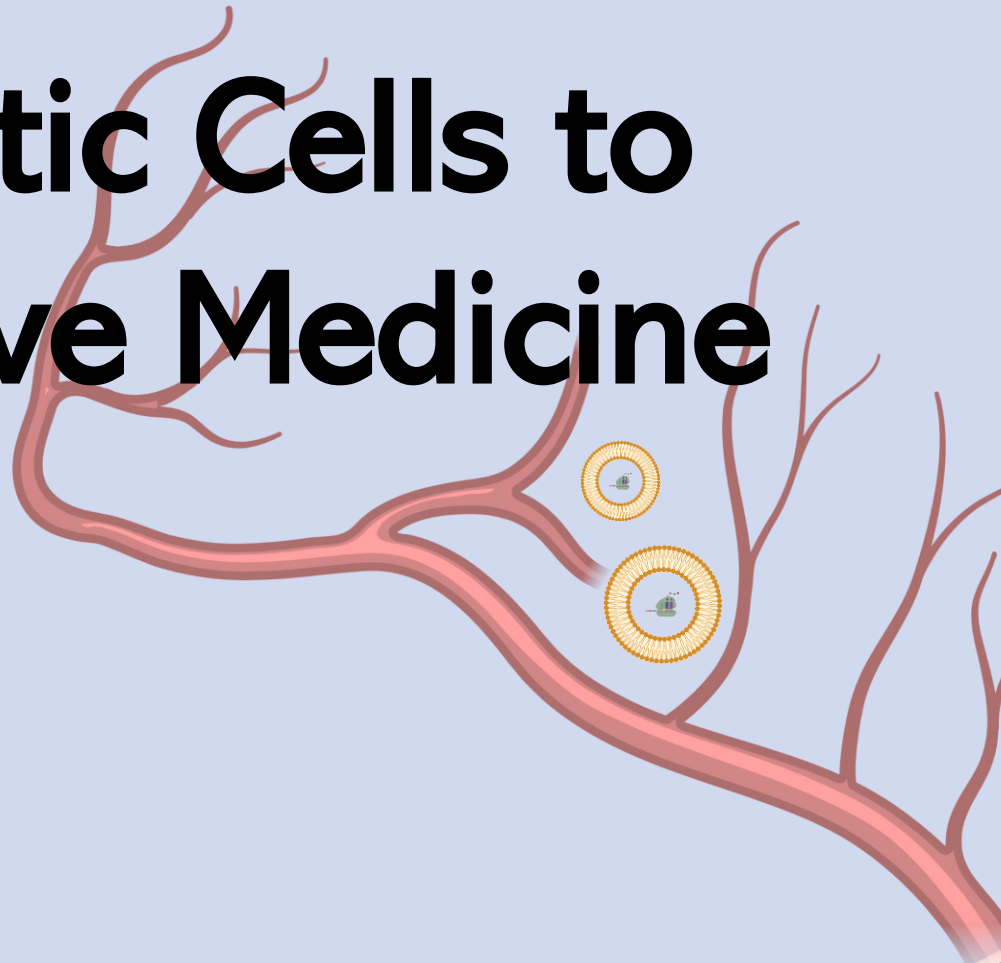
Harnessing Synthetic Cells to Support Regenerative Medicine



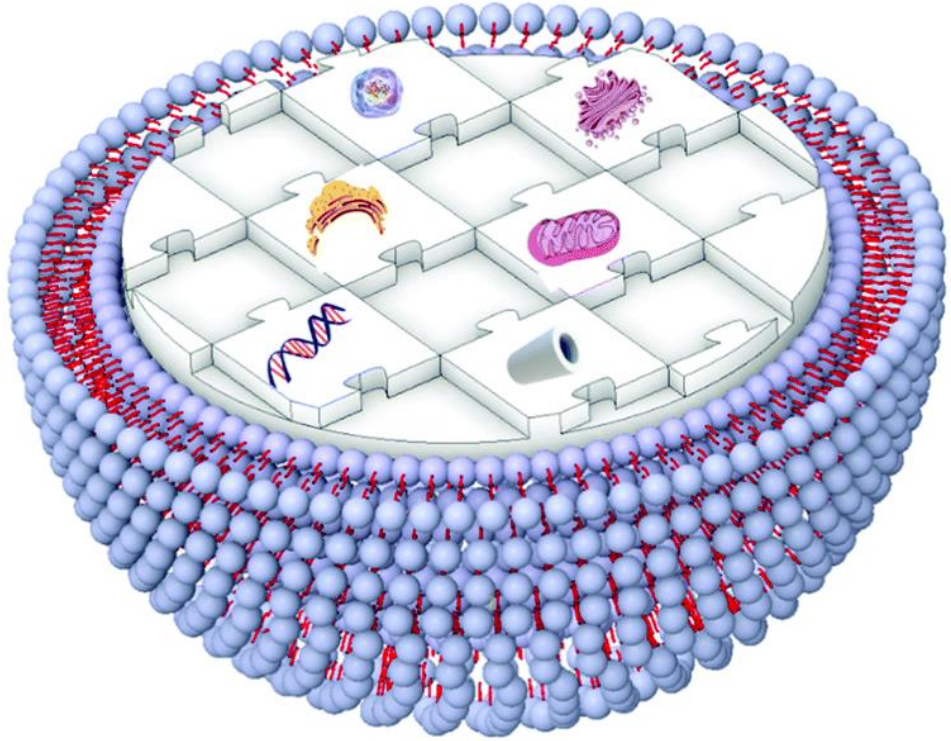
Gal Chen
Schroeder lab

TECHNION
Israel Institute
of Technology

CRS 2022 Annual Meeting & Expo
July 11 – 15, 2022 | Montreal Congress Center, Montreal Canada
Advanced Delivery Science

Applying Synthetic Biology to Drug Delivery

Natural Cell



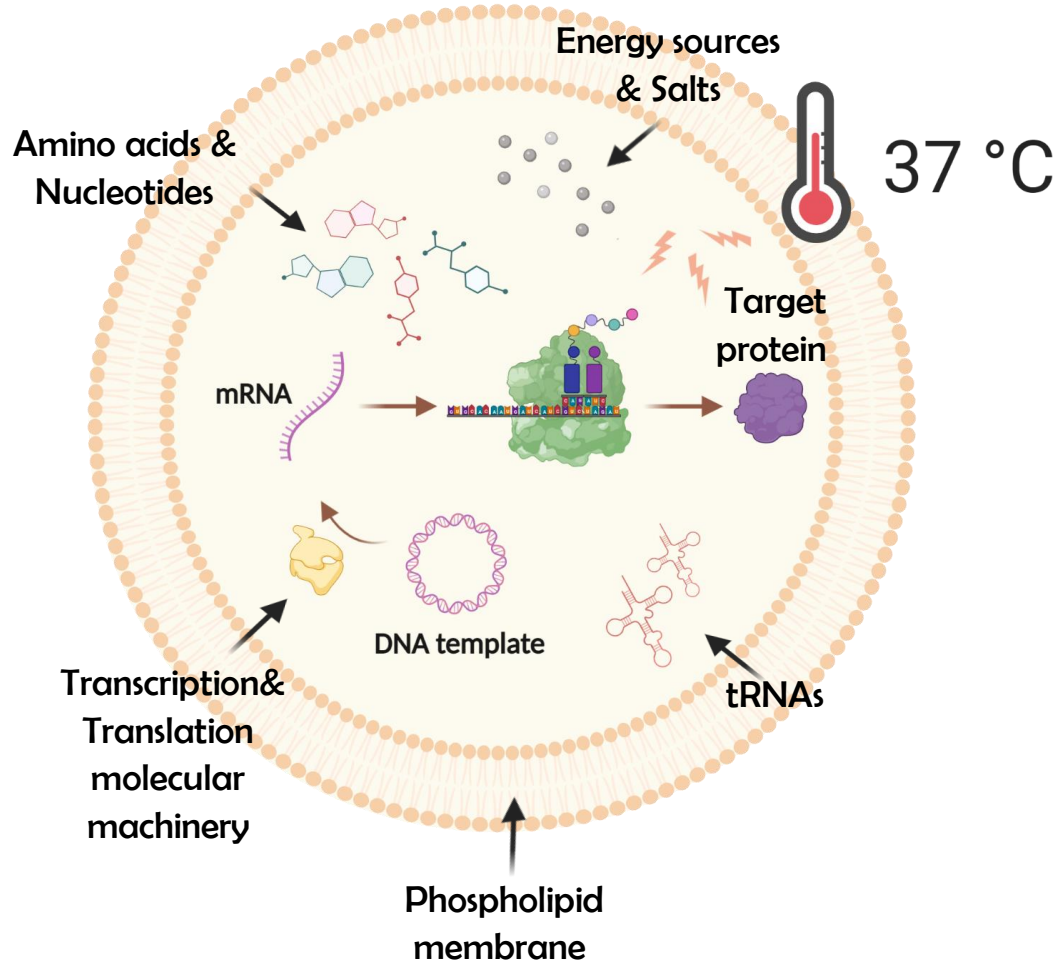
Synthetic Cell

Diltemiz, S.E., et al. Cell (2021).

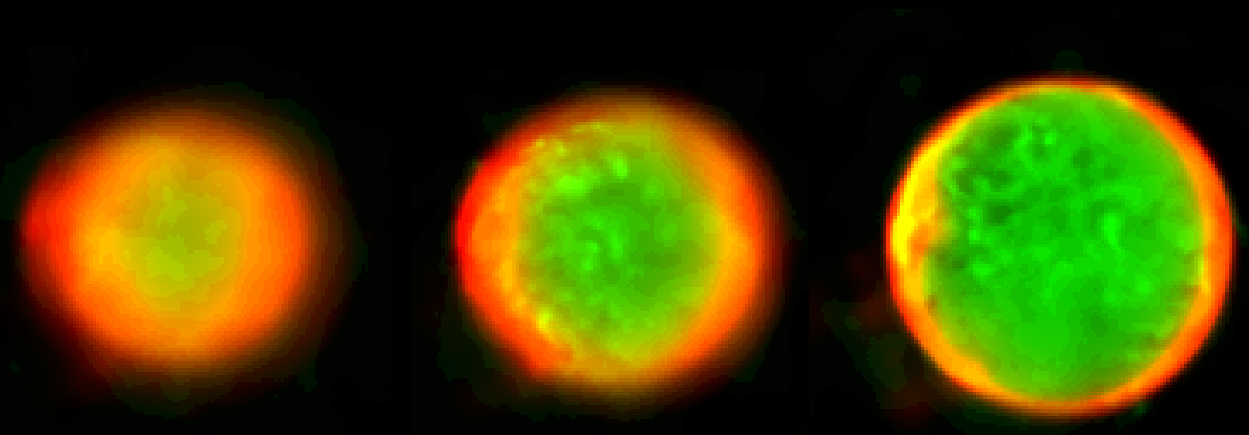
Synthetic Cells (SCs) Architecture

Gene-expressing synthetic cell

Cell-Free Protein Synthesis (CFPS) system encapsulated in a lipid bilayer envelop

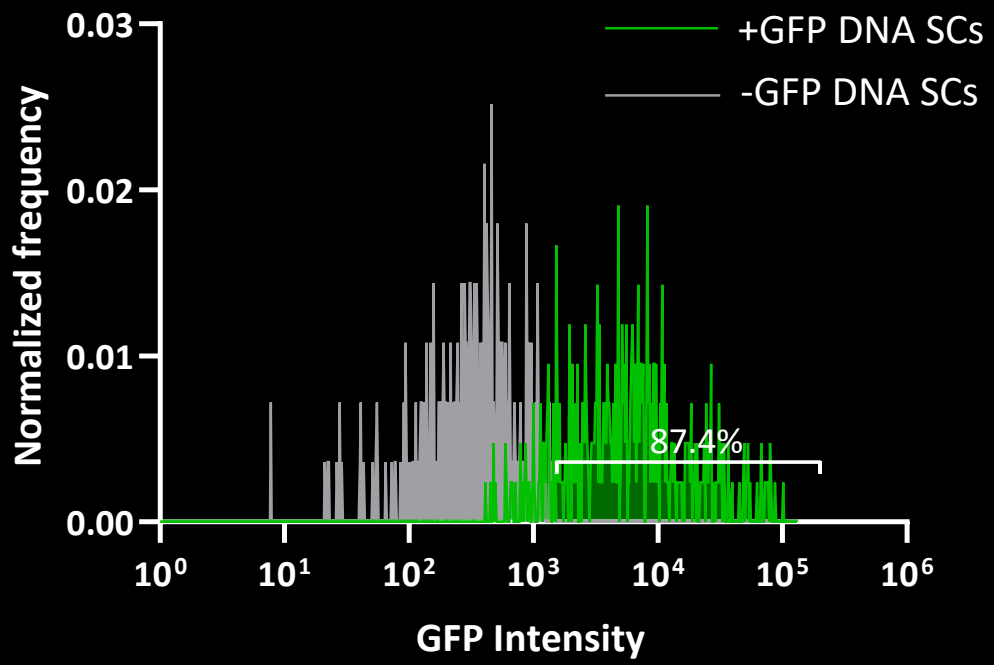


Gene Expression in SCs



30µm

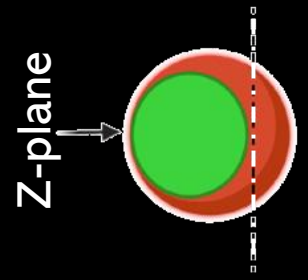
Representative images of GFP producing SC in 2µm z-steps



Imaging flow cytometry analysis

Produced green fluorescent protein (GFP) - Green

Cy-5 labeled membrane - Red



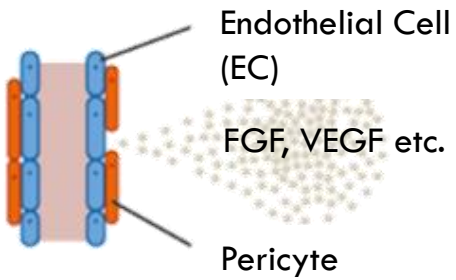
Chen, G. et al. (2022) Submitted, unpublished data.

Interfacing SCs with Living Tissue

Stages of Angiogenesis

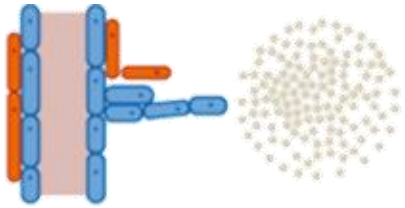
Proangiogenic stimuli

→ Cytokine gradient built-up



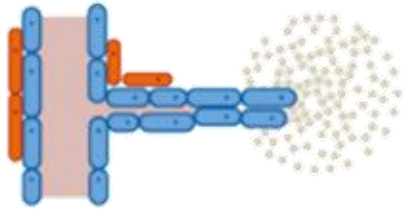
Sprouting → Proliferation

→ Migration of Endothelial Cells

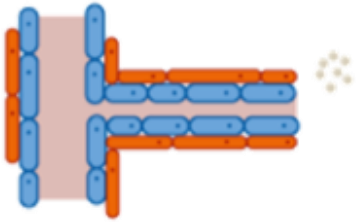


Endothelial Cells

Tube Formation



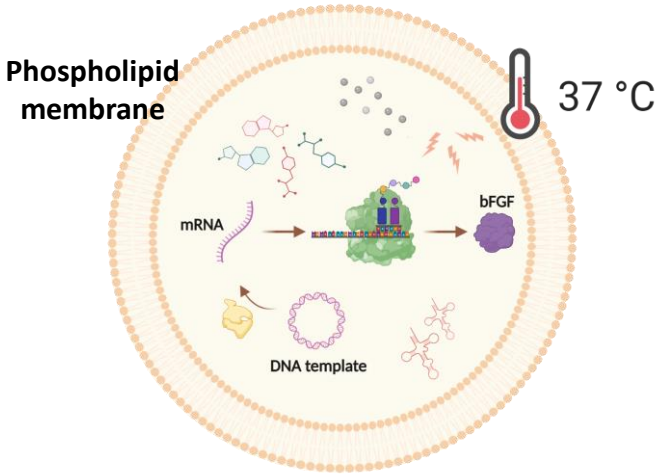
Vessel Maturation



Can protein-producing synthetic cells be integrated into living tissue to promote the multi-stage physiological process of forming new blood vessels?

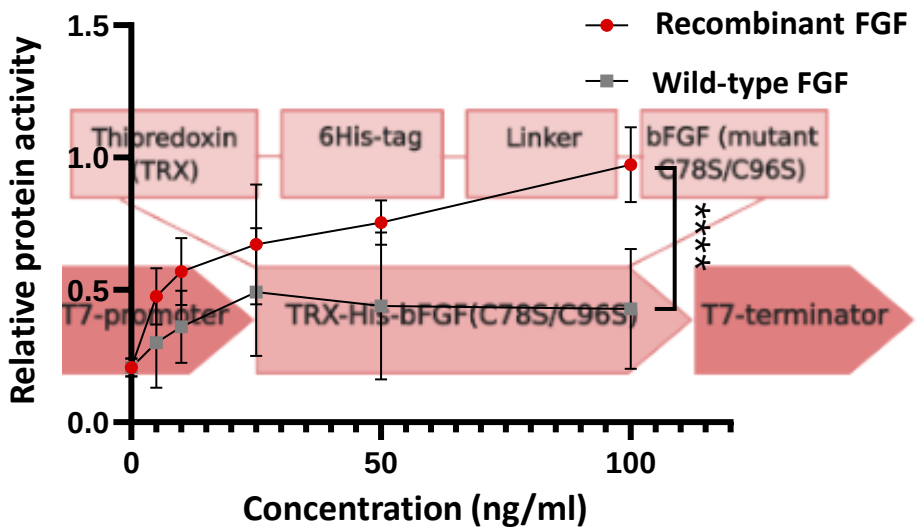
Figures obtained from: www.sigmaaldrich.com/technical-documents/protocols/biology/cell-culture/endothelial-angiogenesis-assay

Engineering Proangiogenic SCs

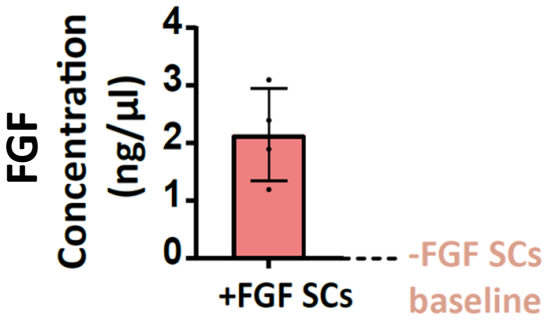


Fibroblast Growth Factor (FGF)-producing SC

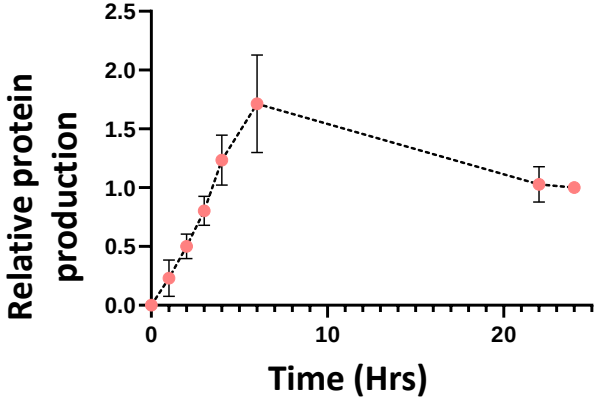
Design Recombinant vs. wild-type FGF for production in SCs



Verification and quantification of FGF production in SCs



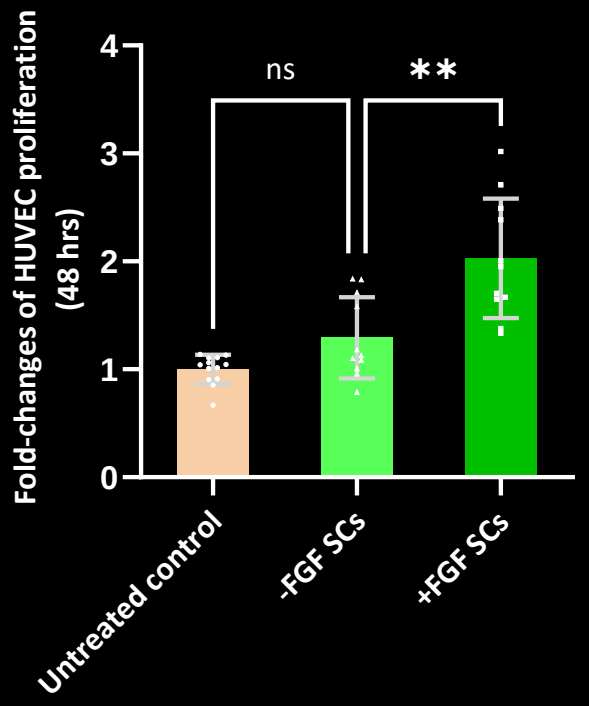
FGF production kinetics in SCs

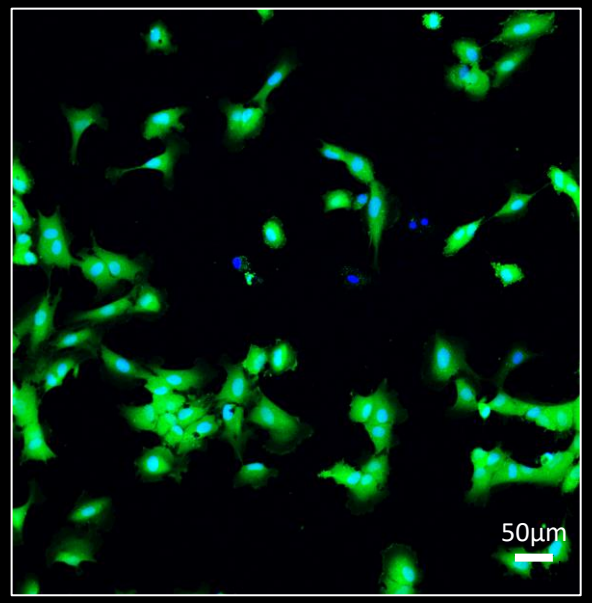


Chen, G. et al. (2022) Submitted, unpublished data.

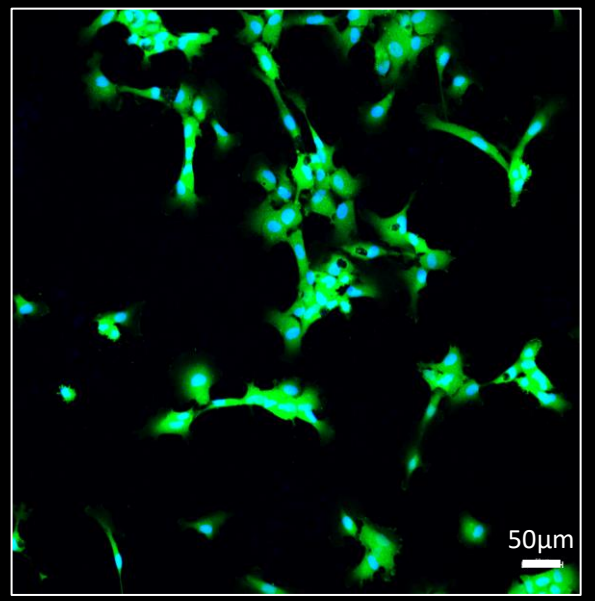
Proangiogenic SCs Stimulate Endothelial Cells Proliferation

Metabolic and microscopic-based proliferation assays after 48 hours of treatment with SCs

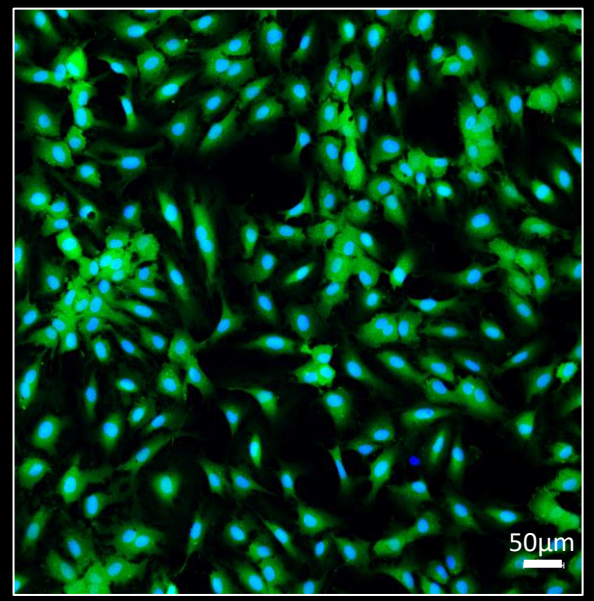




Untreated Control



Non producing SCs



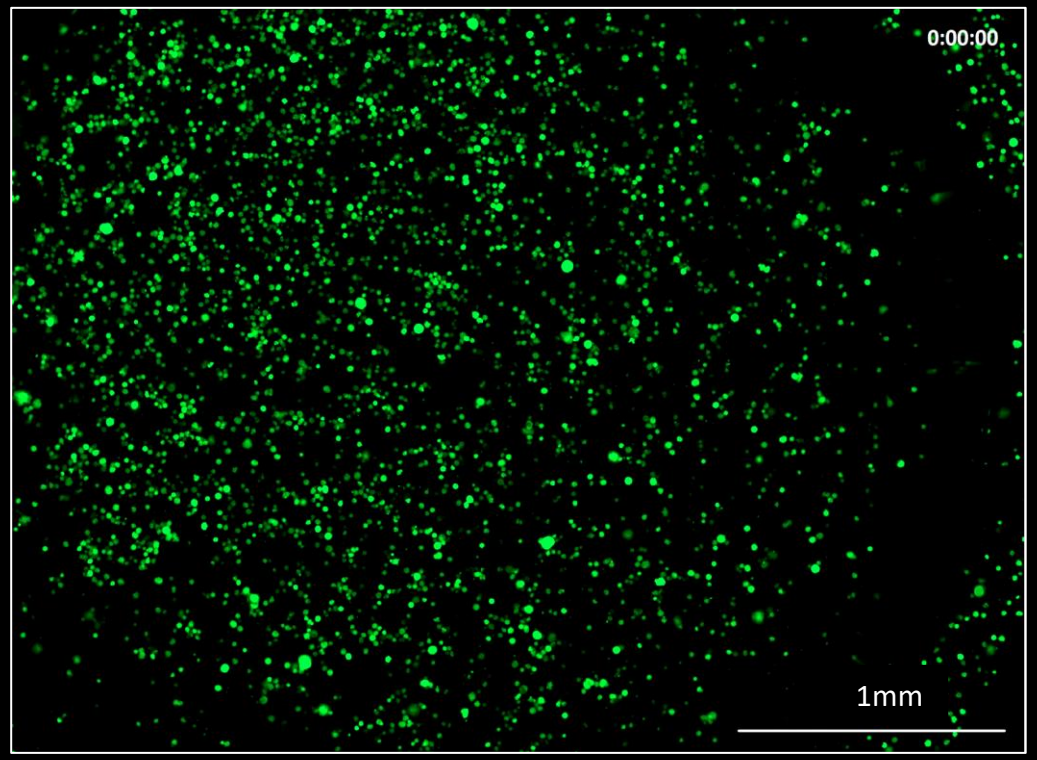
FGF producing SCs

Live HUVECs
Cell nuclei

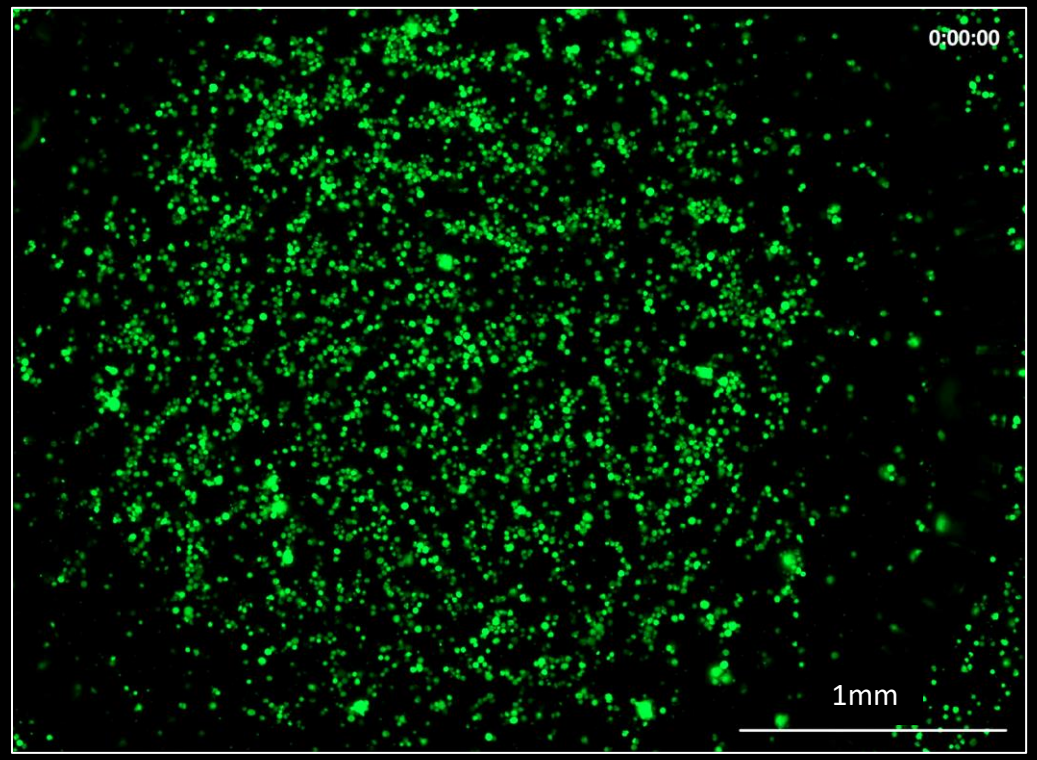
Chen, G. et al. (2022) Submitted, unpublished data.

Proangiogenic SCs Guide the Formation of Endothelial Cell Capillaries

Untreated control



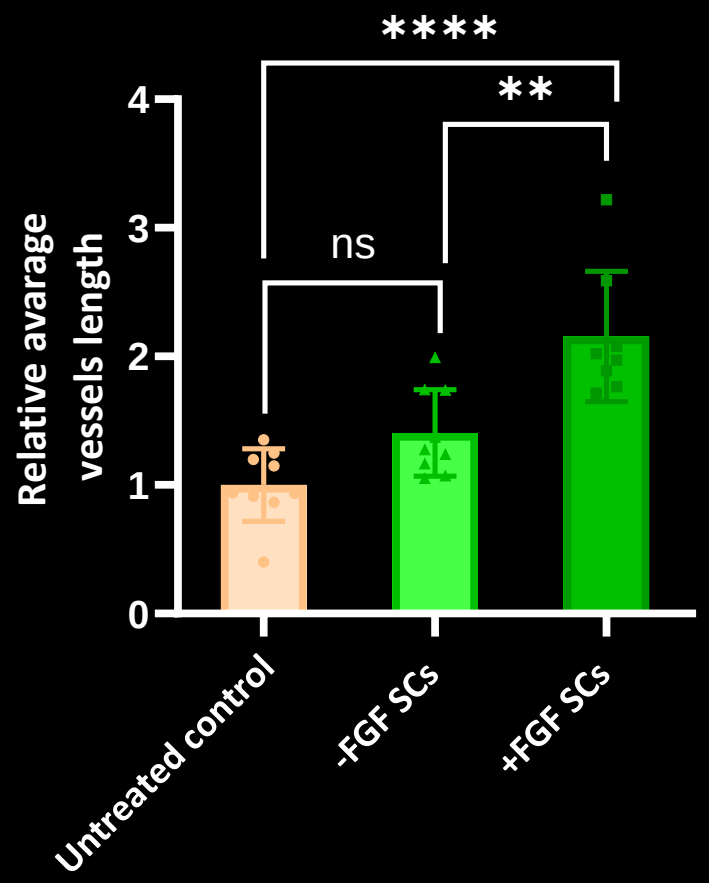
FGF-producing synthetic cells

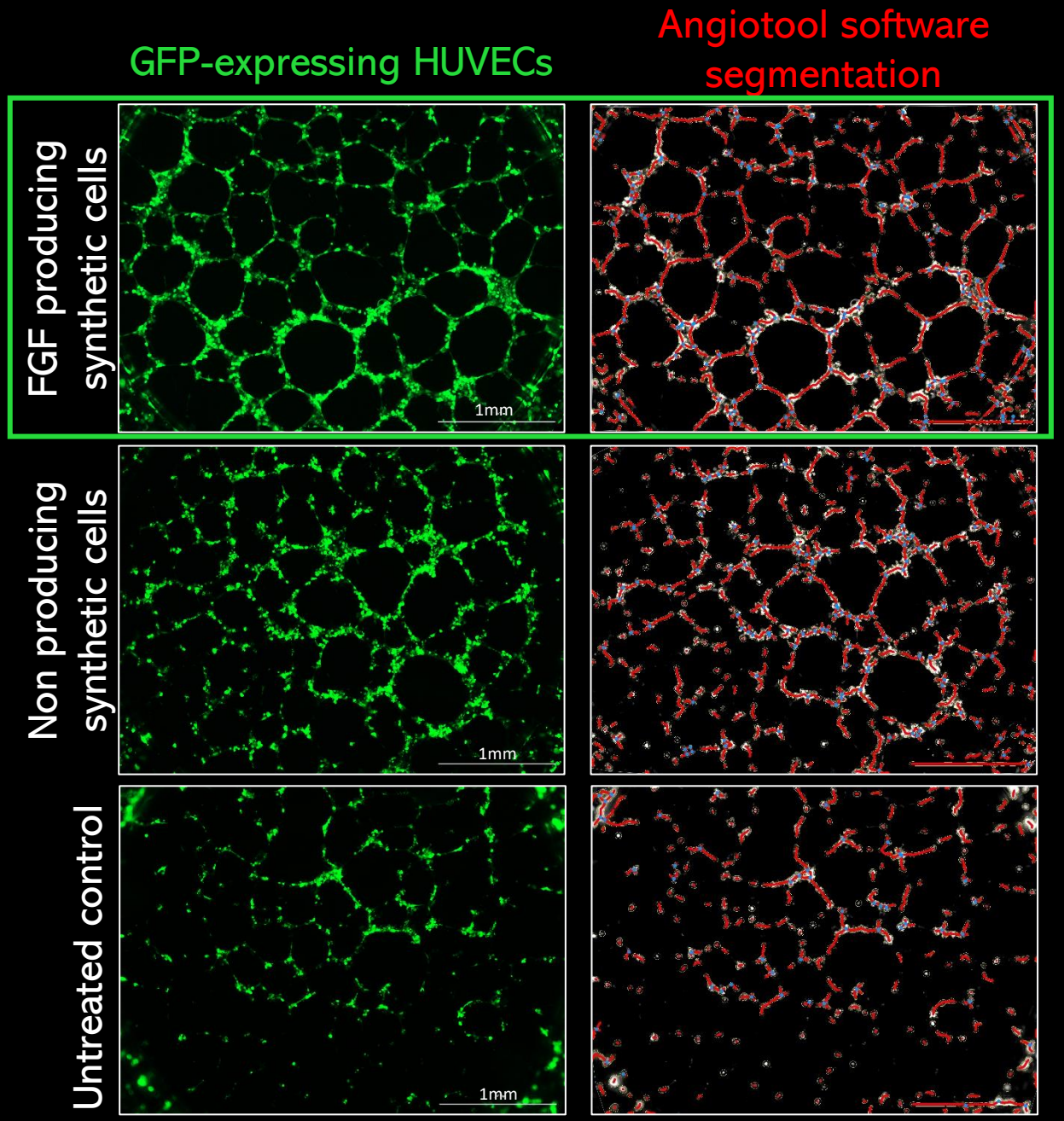


GFP-expressing HUVECs

Chen, G. et al. (2022) Submitted, unpublished data.

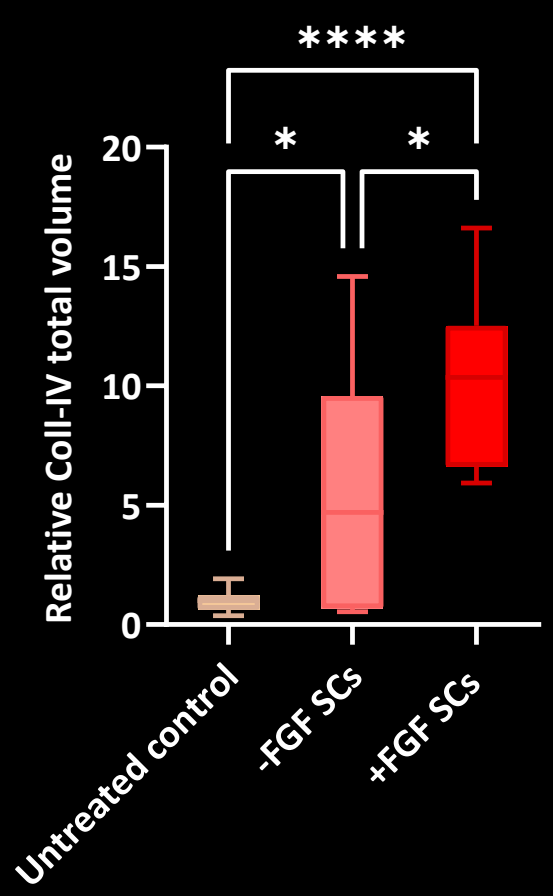
Proangiogenic SCs Guide the Formation of Endothelial Cell Capillaries

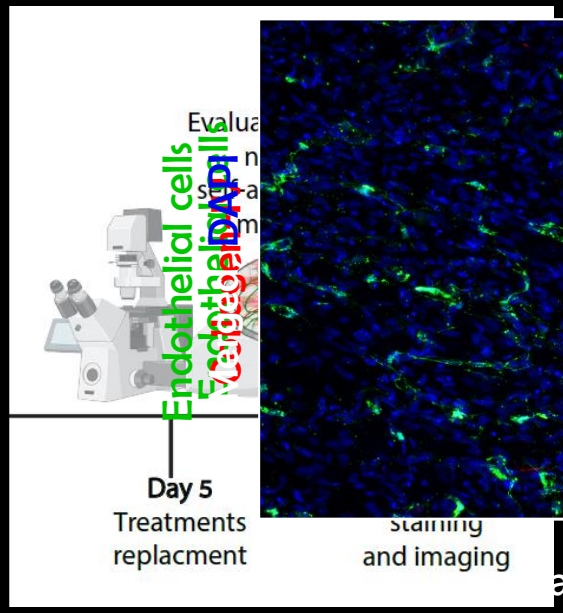




Chen, G. et al. (2022) Submitted, unpublished data.

SCs Enhance the Formation of Stabilized Vascular Networks in Engineered Scaffolds

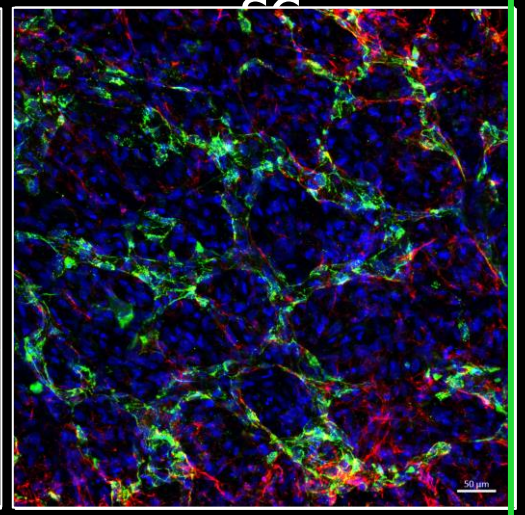


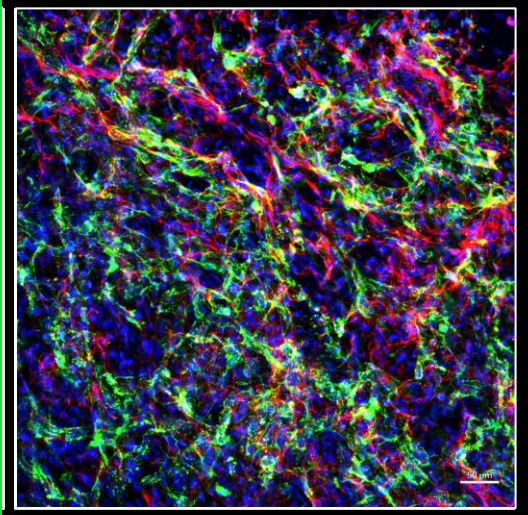


Untreated control

Non producing

FGF producing SCs





ative maximum intensity projection confocal images show fixed and immuno-stained scaffolds 7-days post-seeding

Forming vessel markers (HUVEC-GFP, VE-Cadherin)
Vessel maturation marker (Collagen-IV)
Cell nuclei

In collaboration with **Prof. Shulamit Levenberg** and **Dr. Shira Landau**

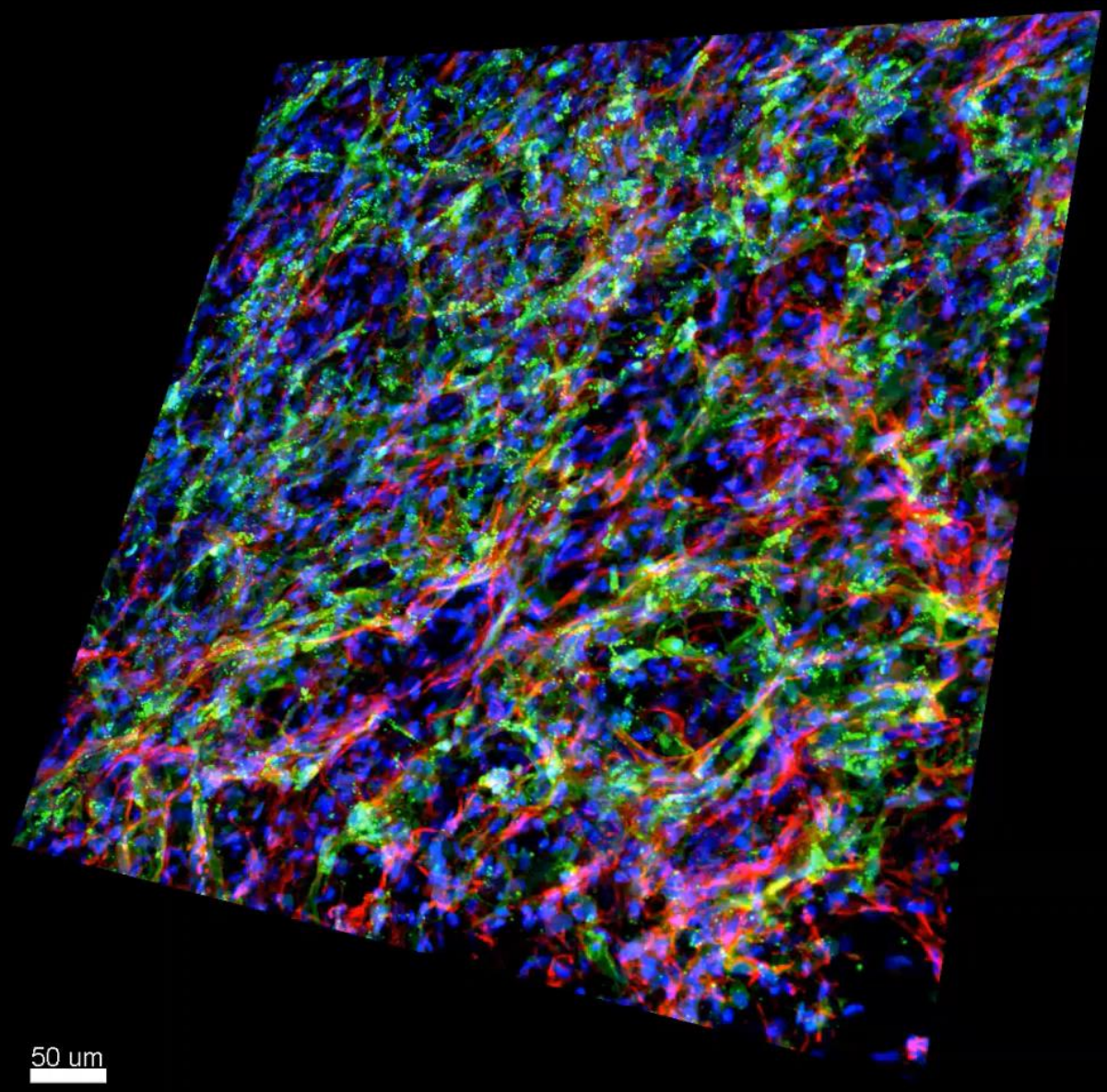
Chen, G. et al. (2022) Submitted, unpublished data.

Vascular Network Formation and Maturation on Engineered Construct Induced by SCs

Forming vessels markers
(HUVEC-GFP, VE-Cadherin)

Vessel maturation marker
(Collagen-IV)

Cell nuclei



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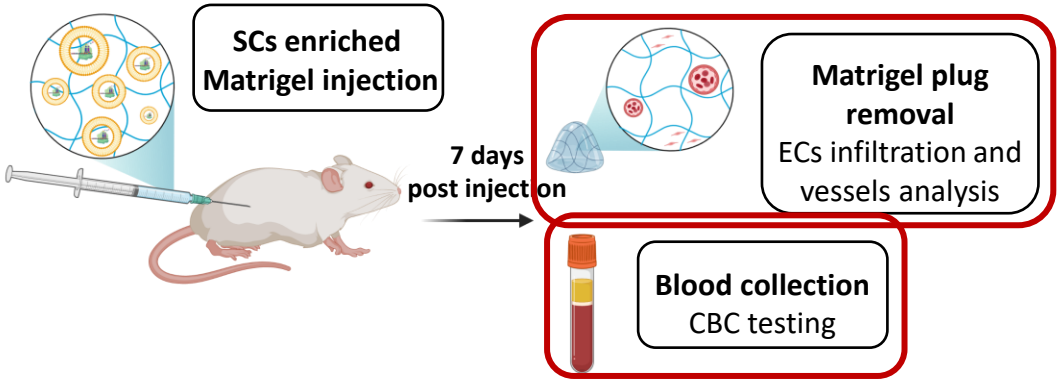
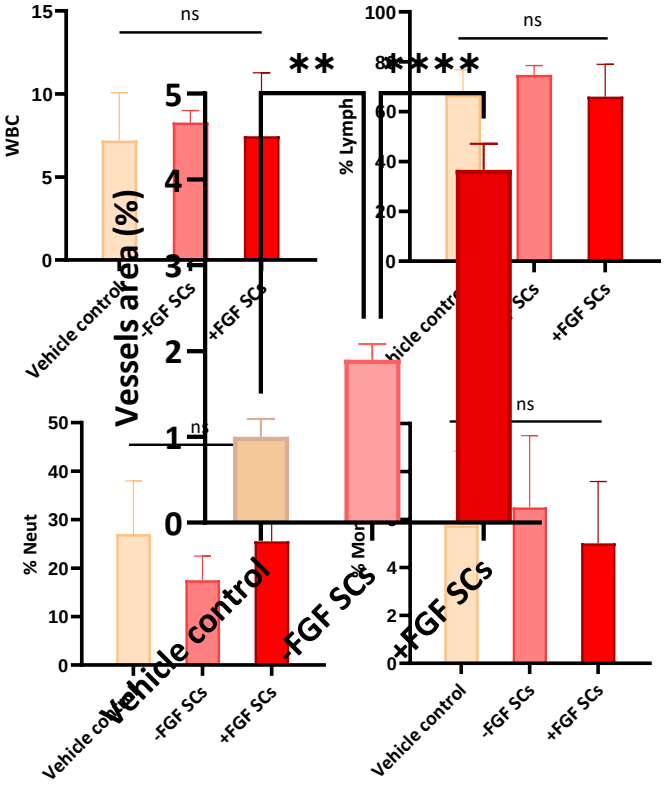
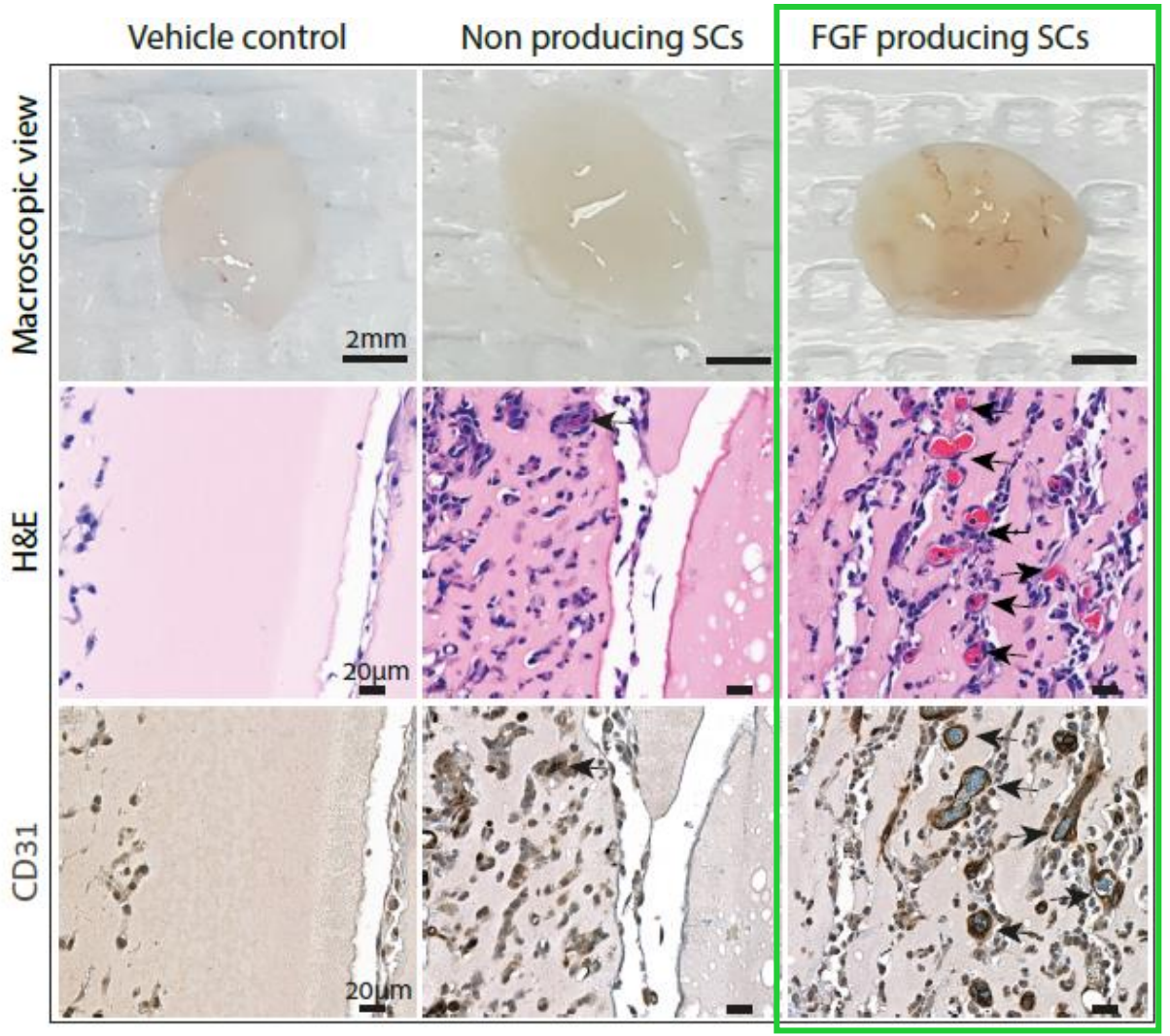
Chen, G. et al. (2022) Submitted, unpublished data.

In-Situ Production of FGF by SCs Promotes In-Vivo Angiogenesis







Chen, G. et al. (2022) Submitted, unpublished data.

Summary

Engineering and assembly of proangiogenic synthetic cells that autonomously synthesize biologically relevant concentrations of recombinant human FGF

Proangiogenic synthetic cells were demonstrated to stimulate different angiogenic-related cellular processes

Implanted synthetic cells triggered the recruitment of new blood vessels by *in-situ* production of the recombinant growth factor

An early-stage demonstration of the possible capabilities of synthetic cells to serve as dynamic biomimetic supporters of different physiological processes

Thank You!

Prof. Avi Schroeder

Rotem Levin

Dr. Omer Adir

Maya Kaduri

Ofri Doppelt

Dr. Jeny Shklover

Dr. Janna Shainsky

Our Collaborators

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TECHNION Israel Institute of Technology

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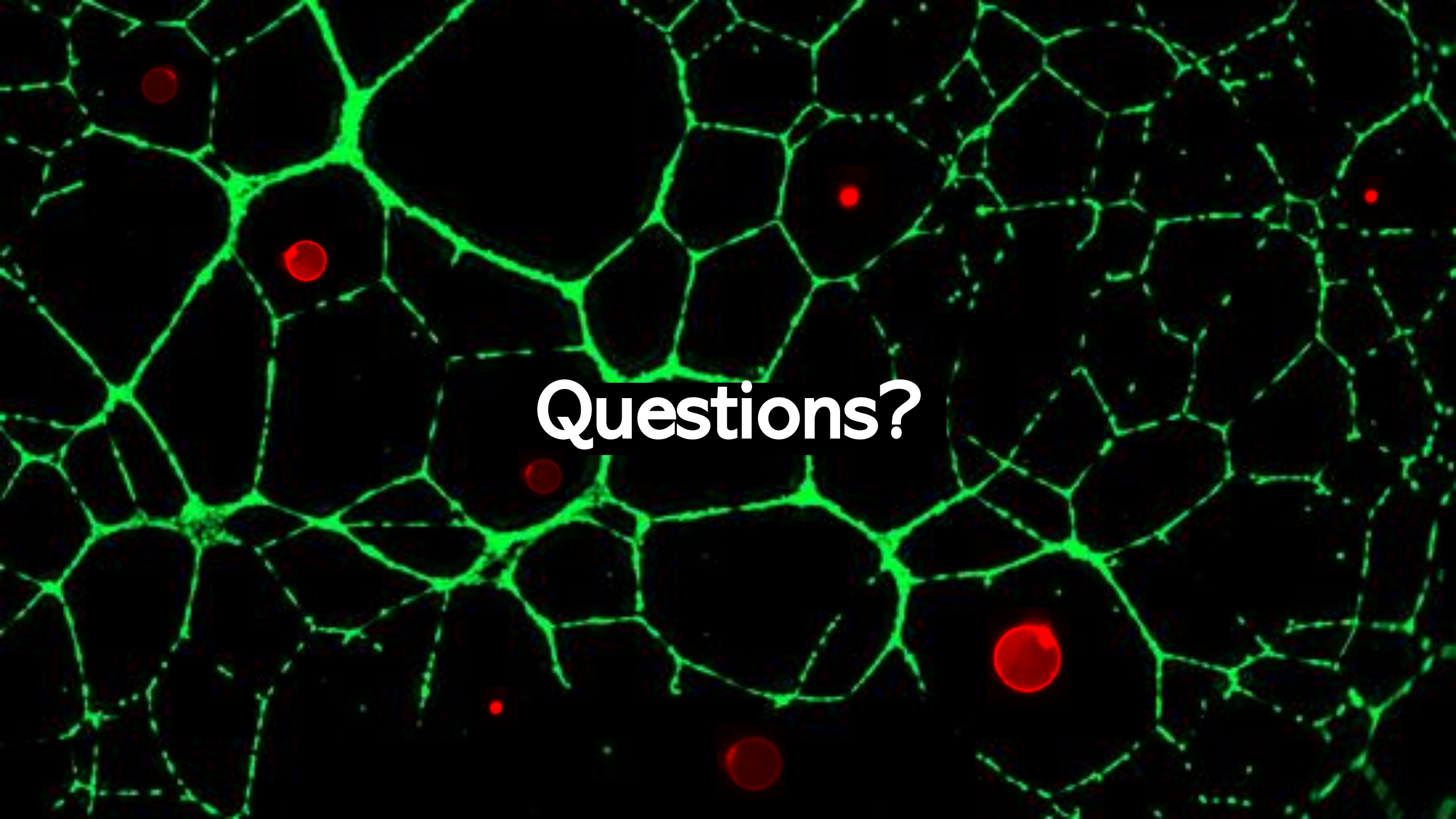
THE ROTHSCHILD CAESAREA FOUNDATION

teva


Questions?