



THE 2022 TECHMED EVENT



Mimicking the stroma-induced vasculature compression in pancreatic tumors

Marcel A. Heinrich

University of Twente, Advanced Organ bioengineering & Therapeutics (AOT)



**THE 2022
TECH-MED
EVENT**

ABOUT ME

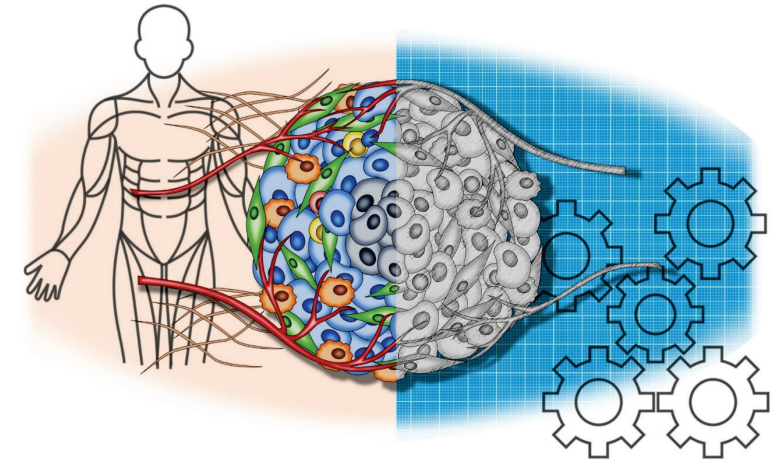
Postdoctoral Researcher at the Advanced Organ bioengineering & Therapeutics (AOT) department

2014 B.Sc. in Biomedical Technologies, University of Twente

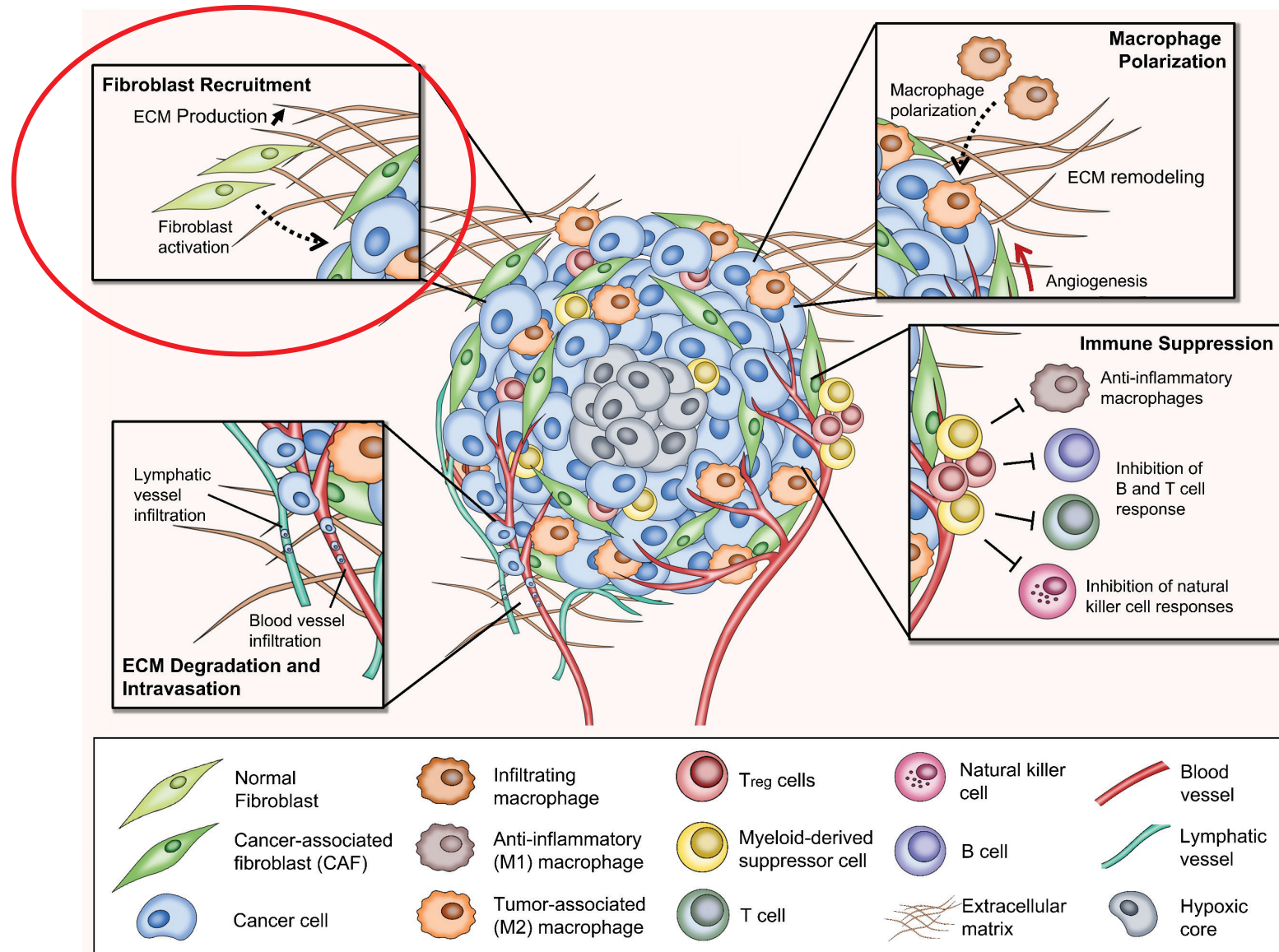
2016 **M.Sc. cum laude** in Biomedical Engineering,
University of Twente
Therapies targeting the tumor microenvironment

2015/2016 Research Fellow at **Harvard Medical School/** Brigham
and Women's Hospital, Boston, MA
Khademhosseini Lab/ Zhang lab - 3D bioprinted tissues / in vitro models

2022 **Ph.D. cum laude**, University of Twente
Engineering the tumor microenvironment - Novel 3D in vitro models to study cellular interactions & therapeutics



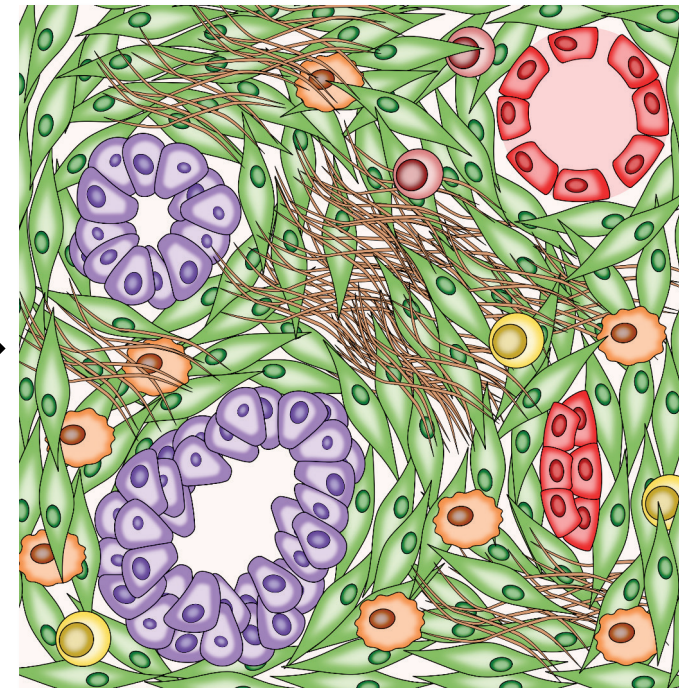
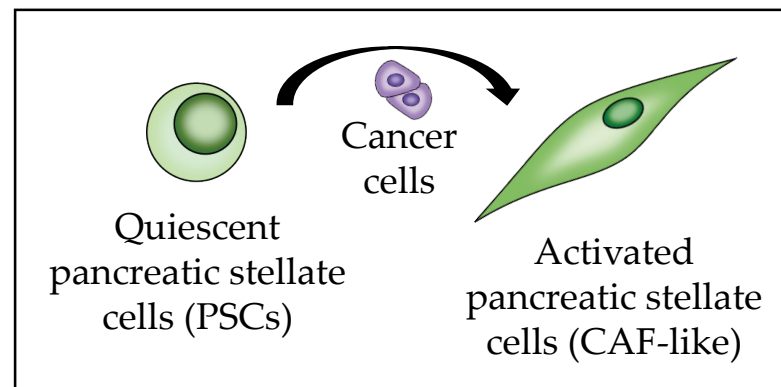
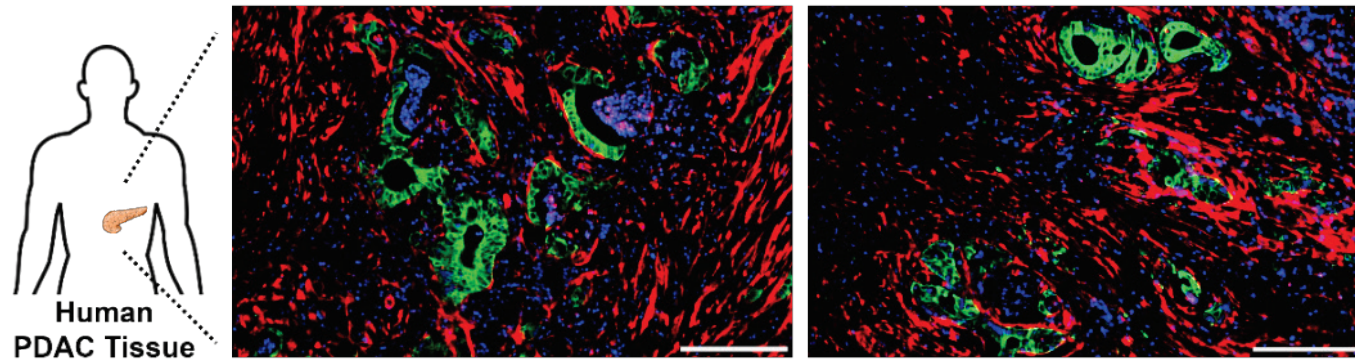
TUMOR MICROENVIRONMENT



Rodriguez, Heinrich et al.,
Trends Cancer 2021,
7(3):249-264

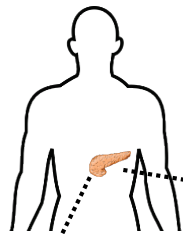
CANCER-ASSOC. FIBROBLASTS

Underlying process in fibrotic tumors (e.g. **pancreatic cancer**, liver cancer etc.)

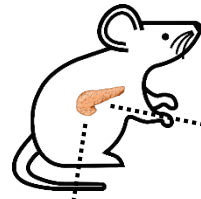
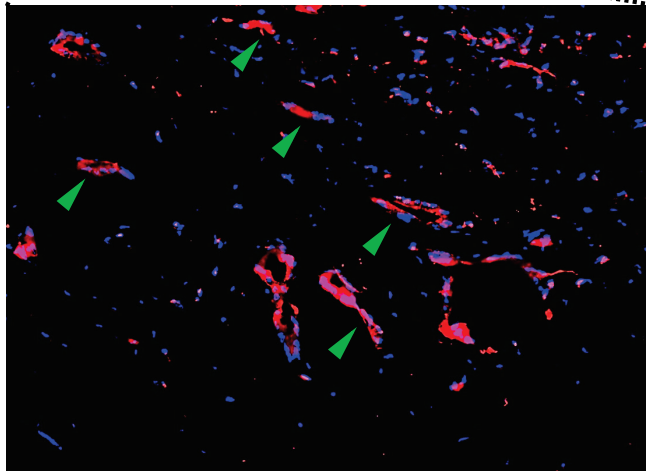


Heinrich et al., Adv. Drug Deliv. Rev. 2021, 174:265-293
Pednekar, Heinrich et al., Cancers 2021, 13(19):5006

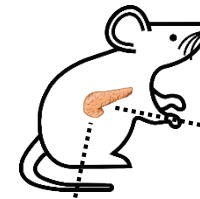
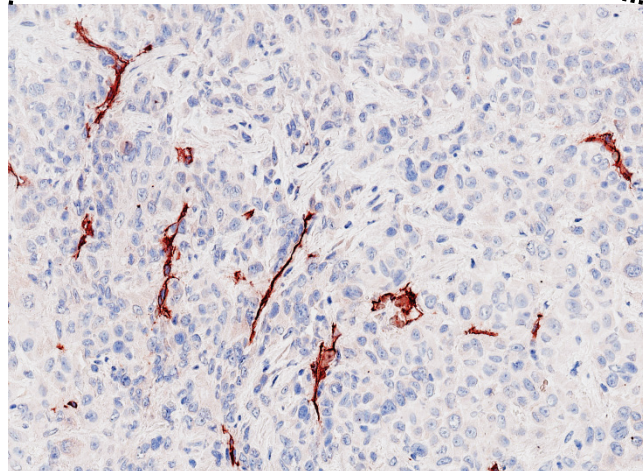
BLOOD VESSEL COMPRESSION



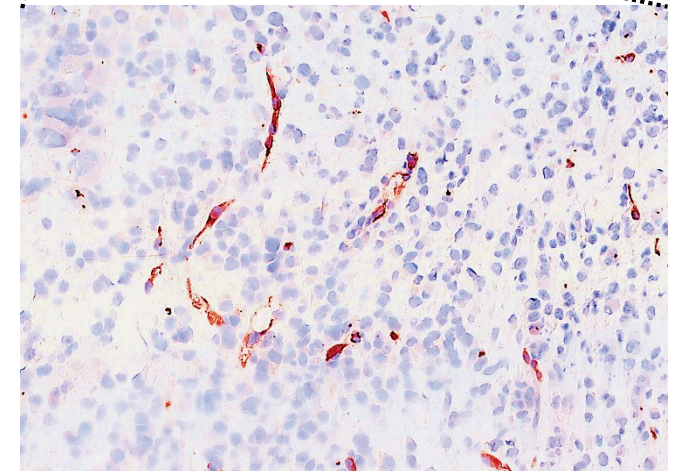
**Human PDAC
Tissue**



**Panc-1/PSC
Injection Model**

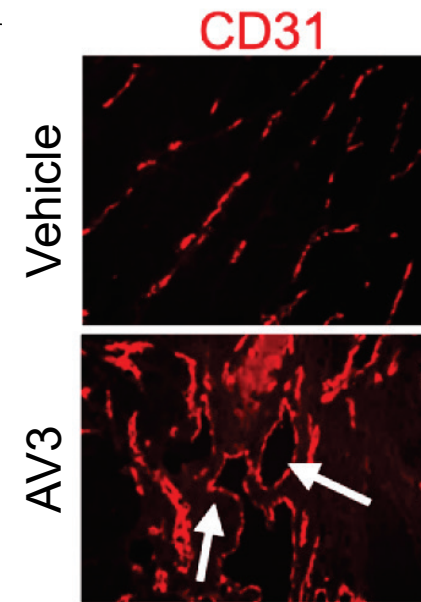


**MiaPaCa-2/PSC
Injection Model**

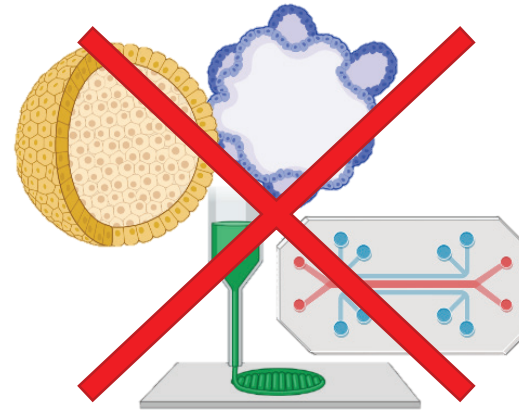
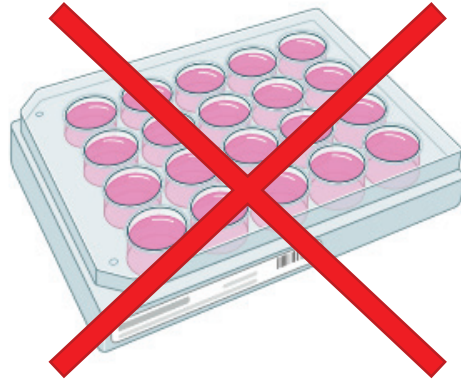


Kuninty et al., AV3

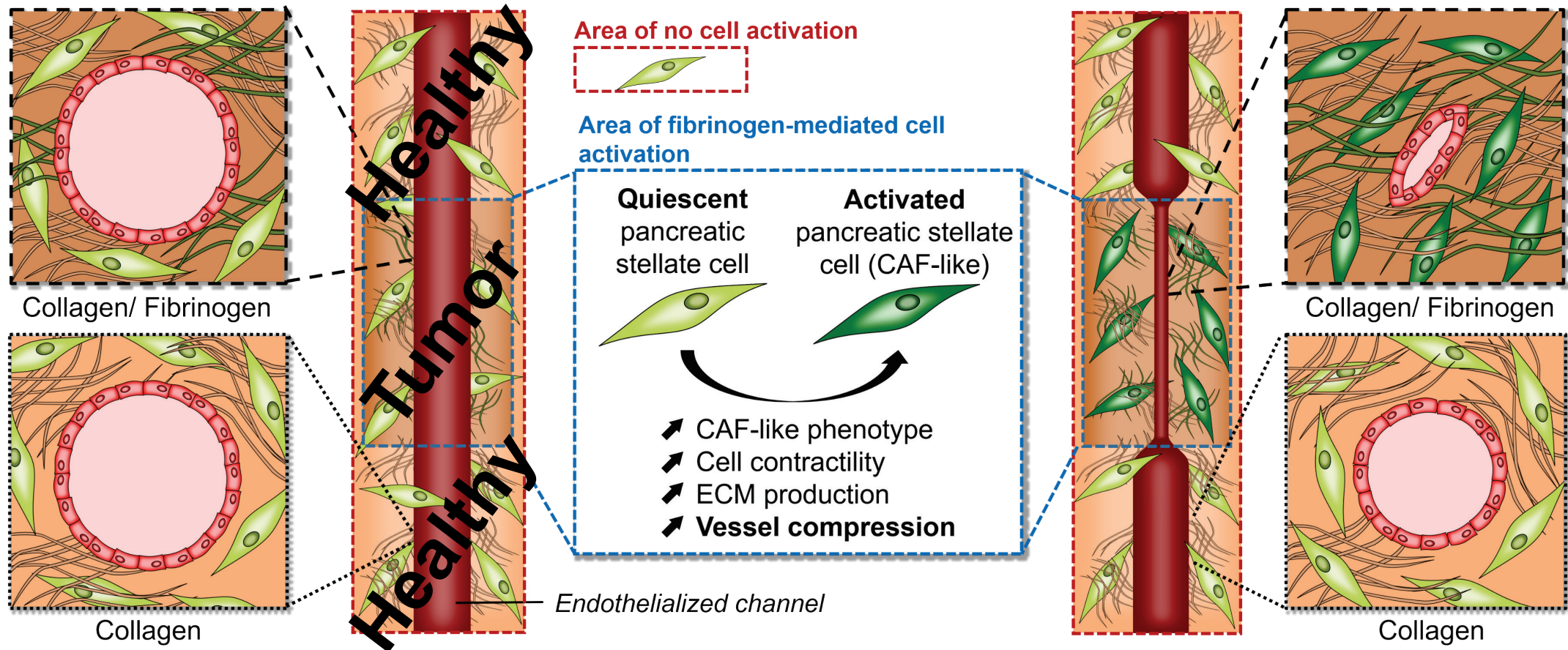
- Inhibit the tumor-promoting function of CAFs (tumor reduction in combination with chemotherapy)
- Drastic increase in the efficacy of chemotherapy
- Reduce the excessive amounts of ECM
- Re-opening of blood vessels



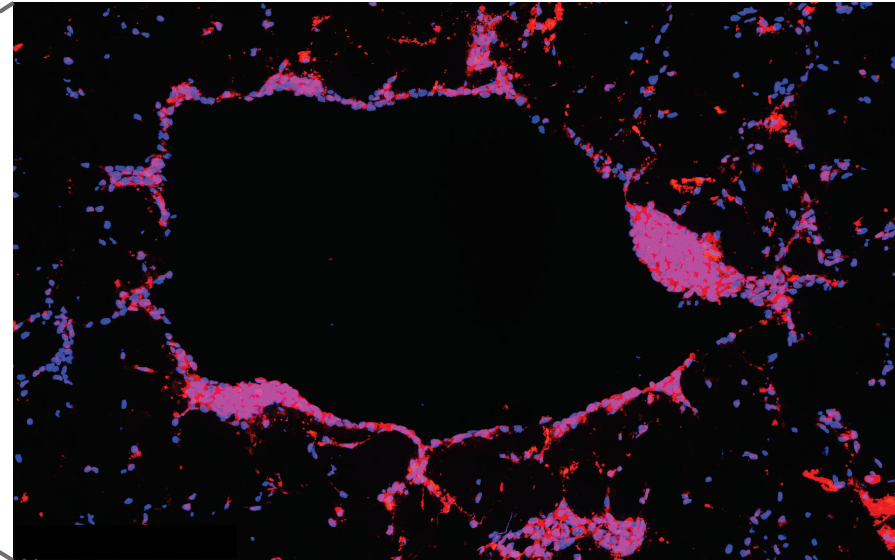
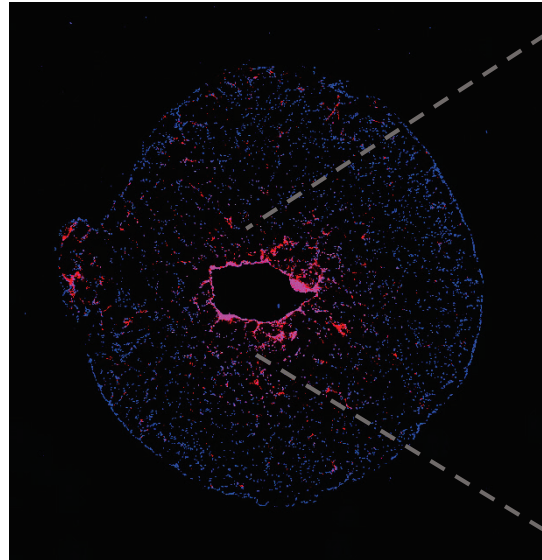
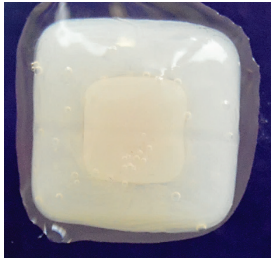
Can we model vascular compression?



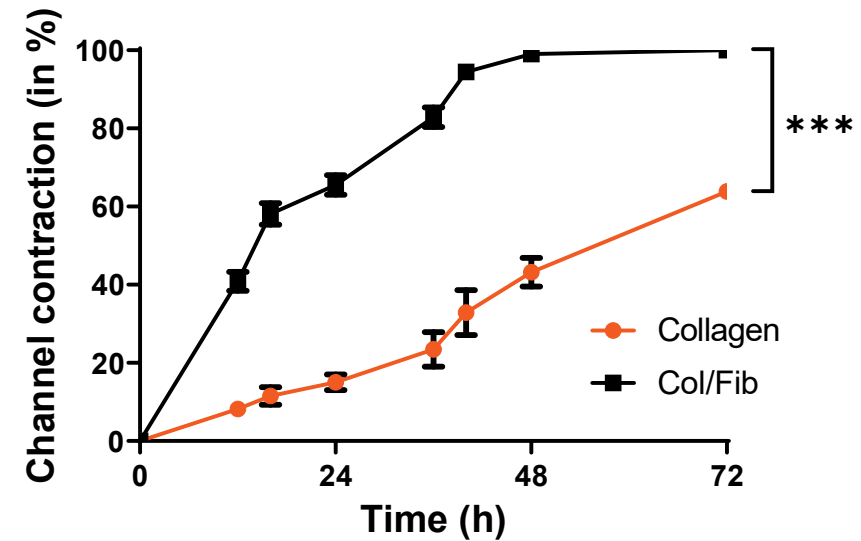
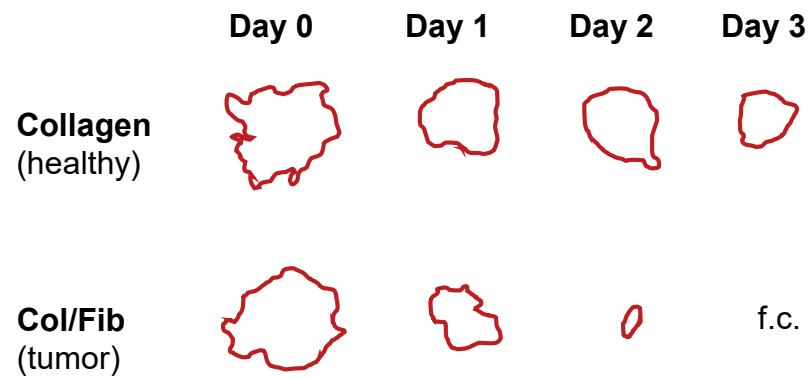
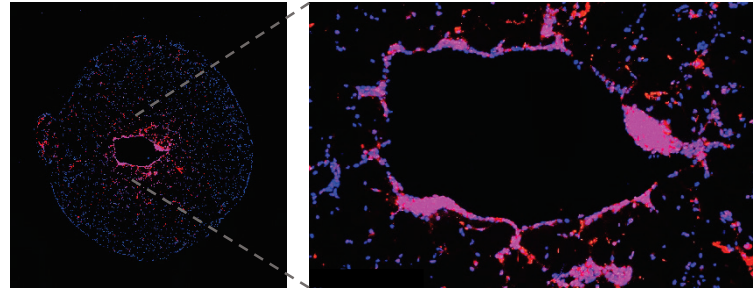
→ Let us develop a model then!



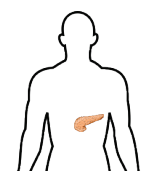
THE MODEL IN PRACTICE



THE MODEL IN PRACTICE



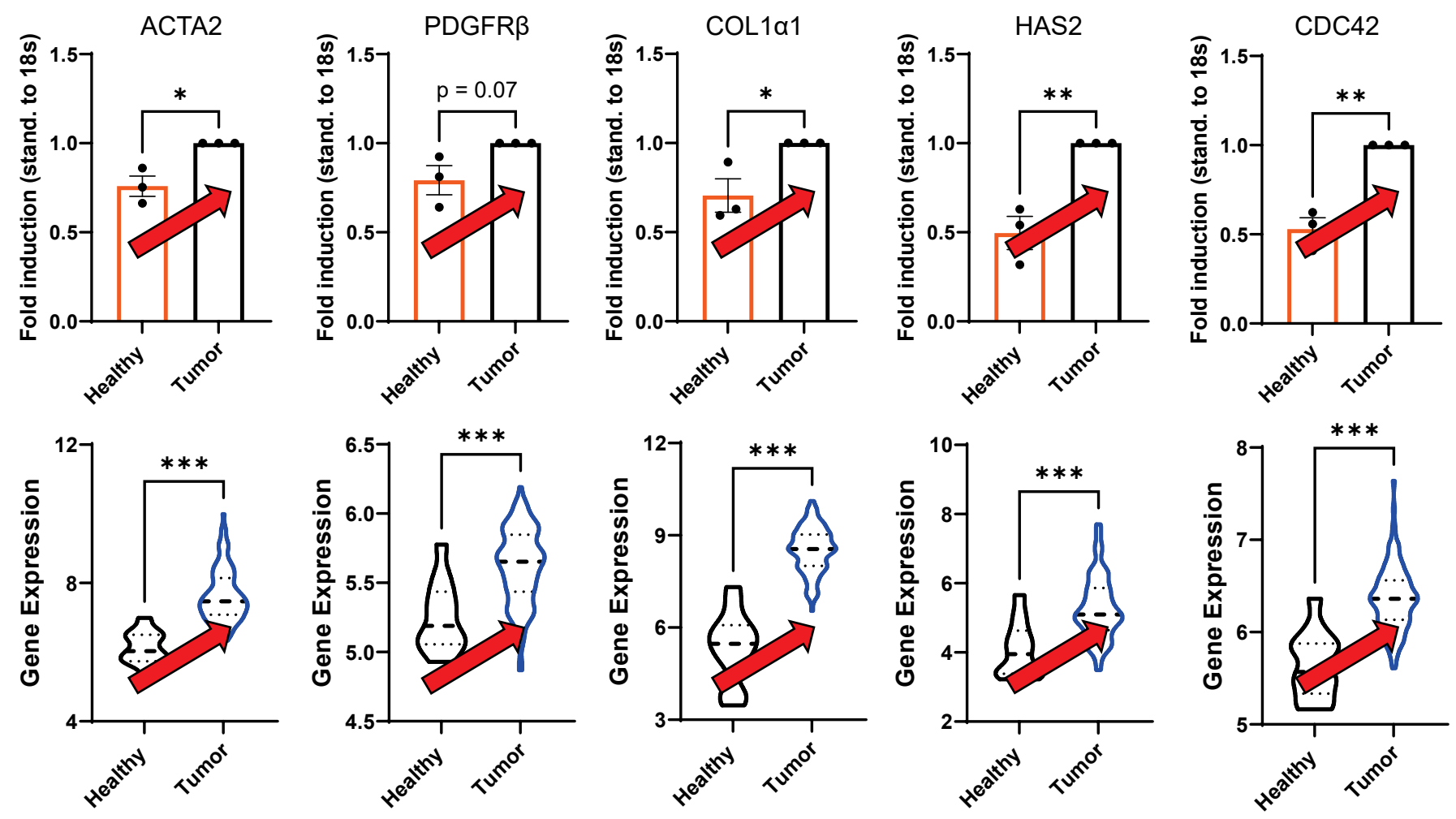
MODEL VS. HUMAN



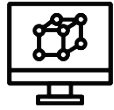
Cell Activation

Matrix proteins

Cell contraction



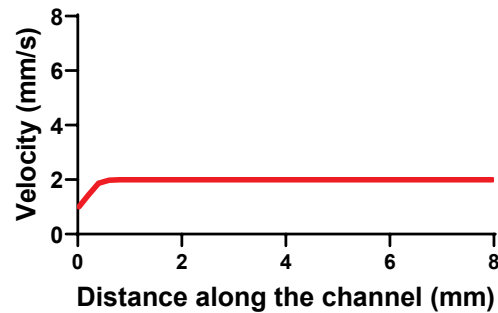
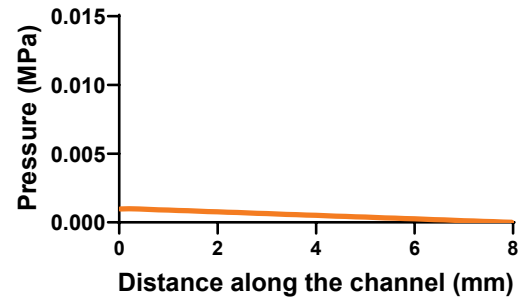
WHAT ABOUT FLOW?



Computational Simulation

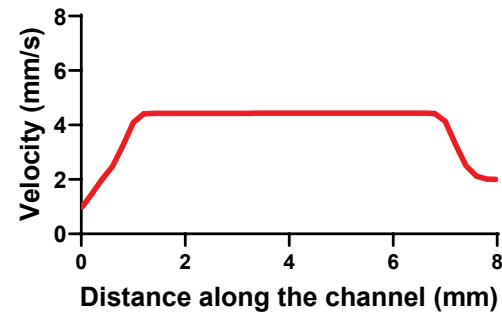
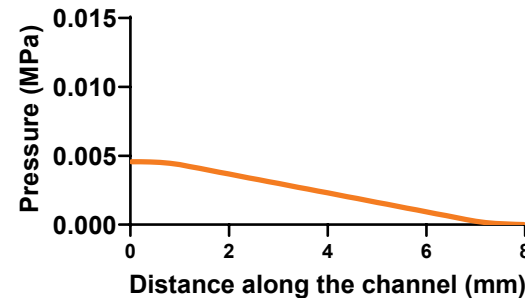
0% Compression

Day 0



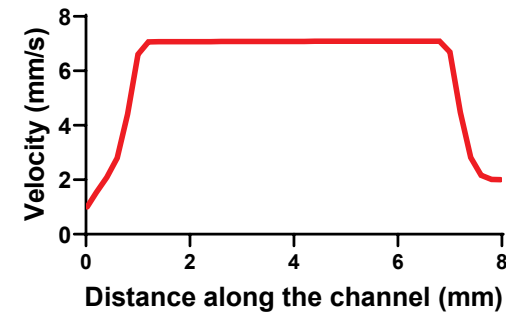
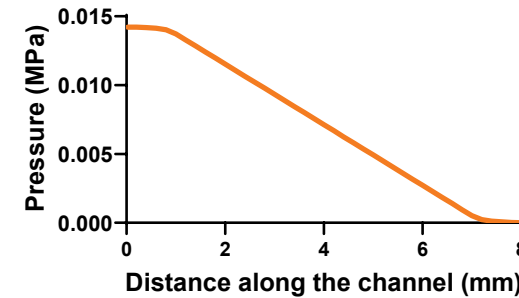
36% Compression

Day 1



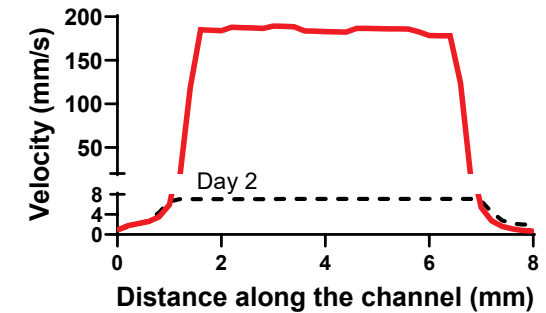
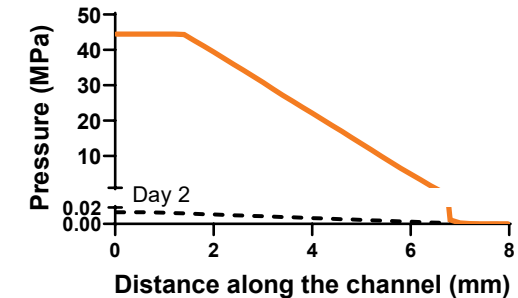
54% Compression

Day 2

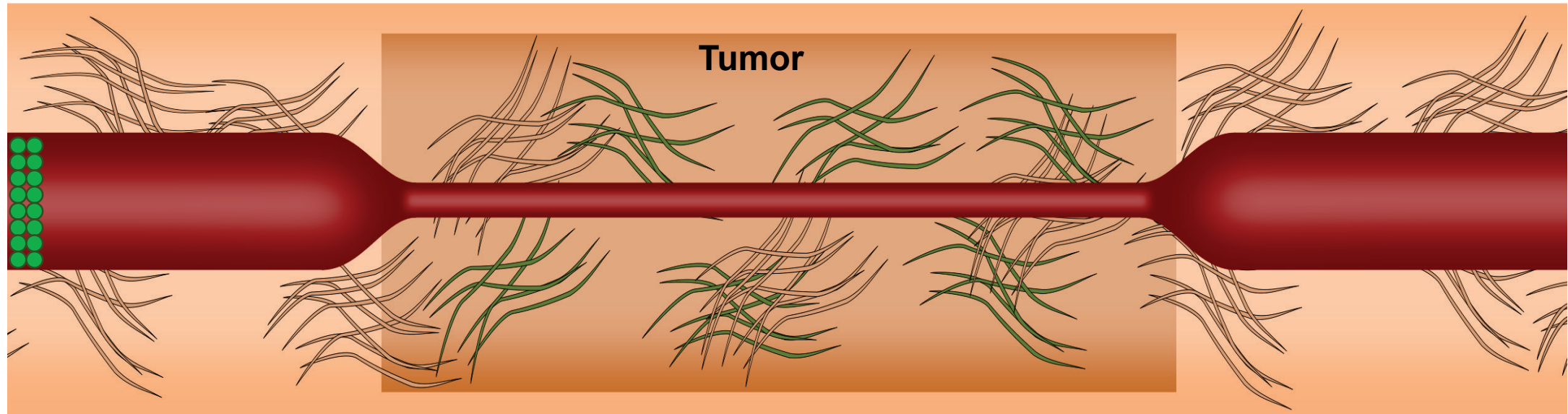
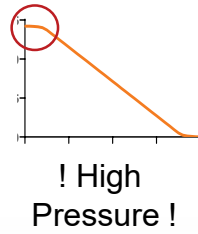


96% Compression

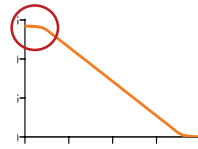
Day 3



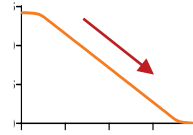
TOO FAST, TOO LESS



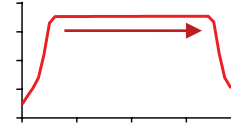
TOO FAST, TOO LESS



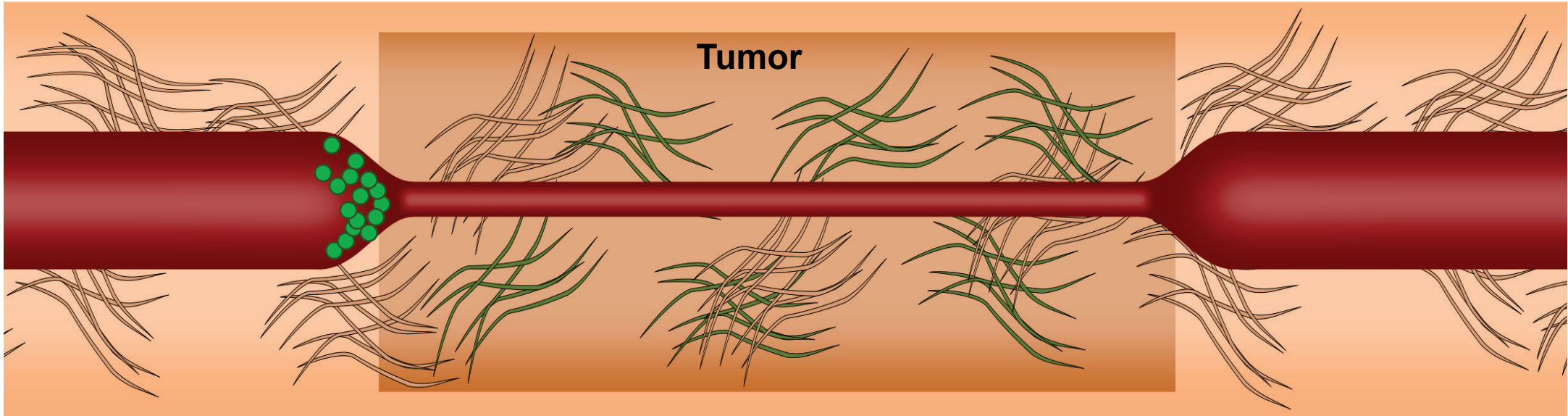
! High
Pressure !



! High
Pressure Drop !

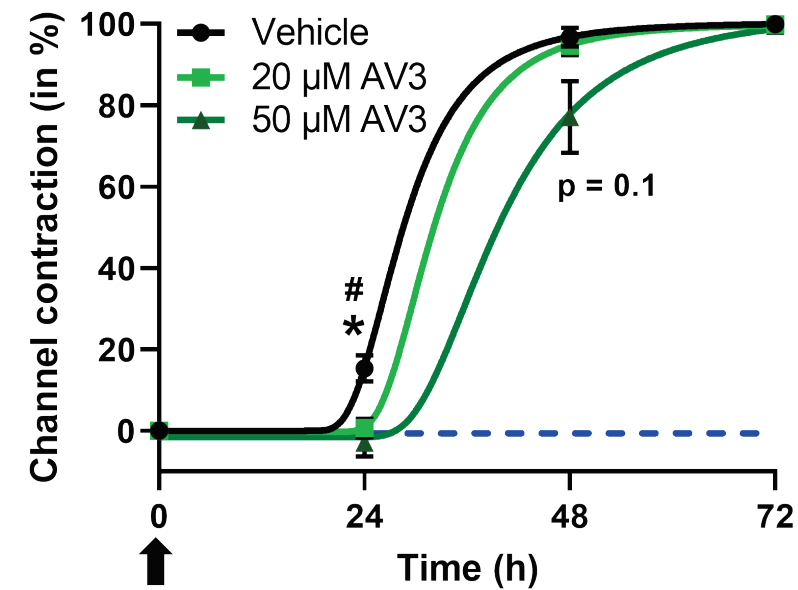
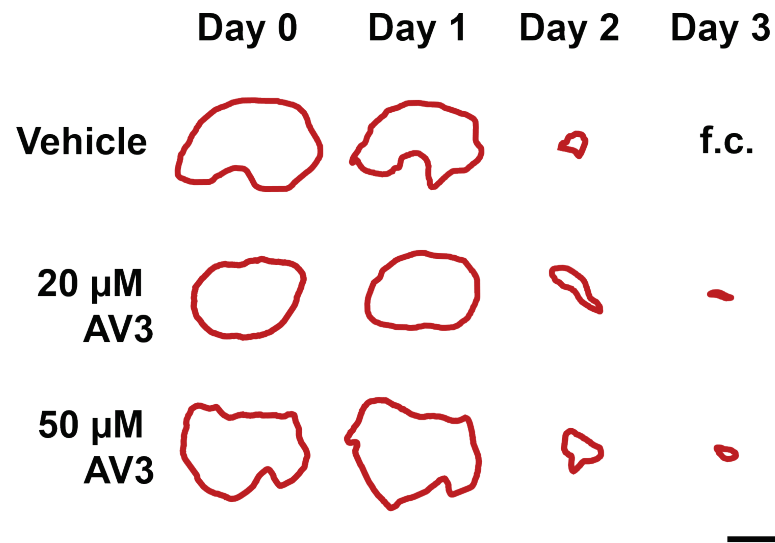
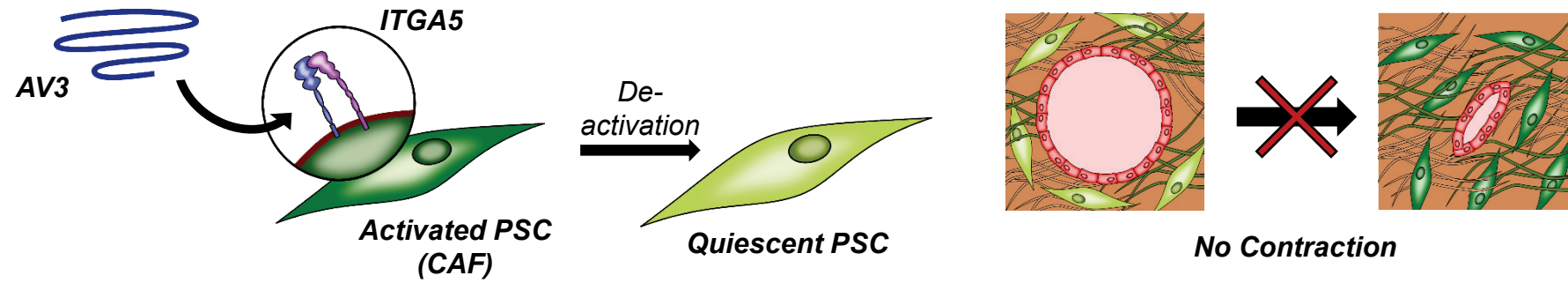


! High
Flow Velocity !

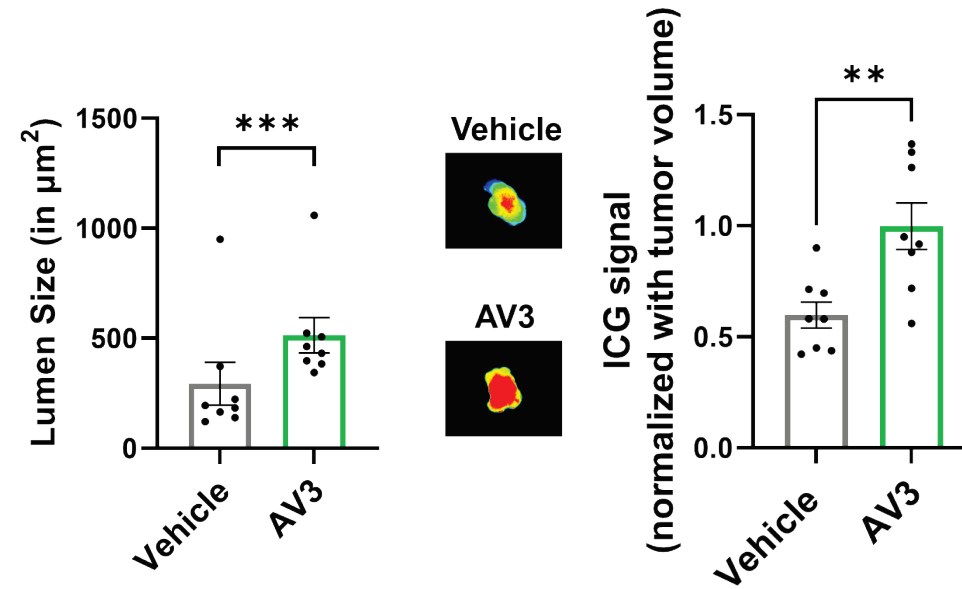
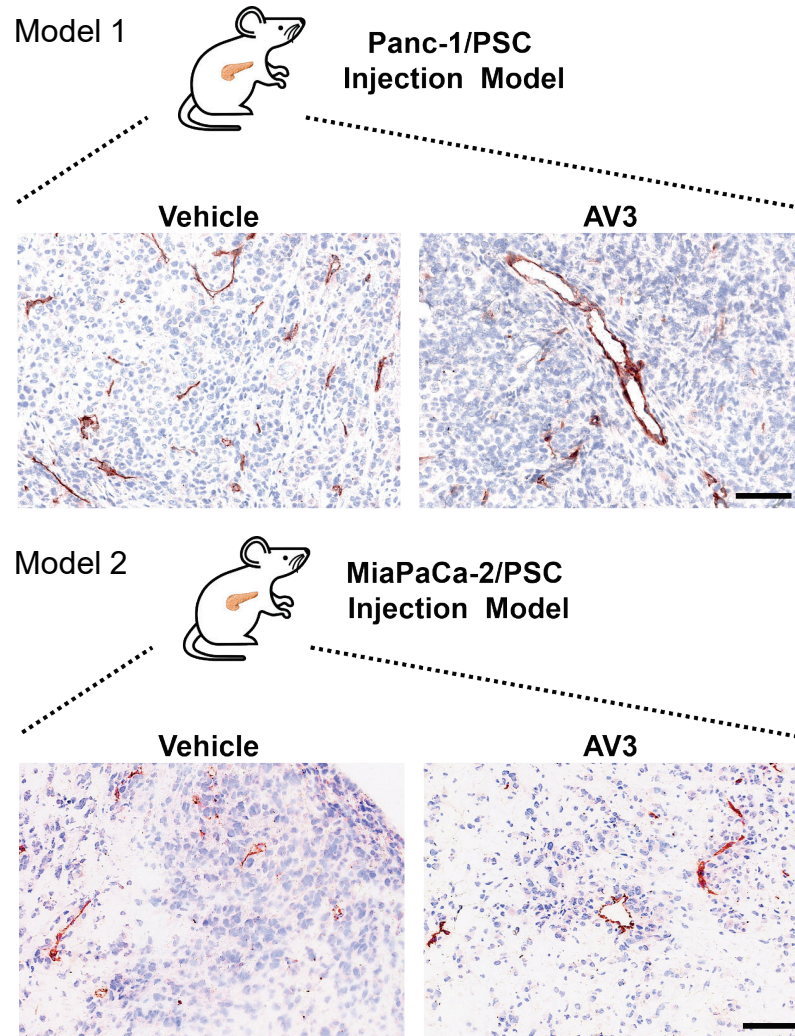


- Might leak out early
- Flow too fast to enter the tumor site

CAN WE STOP IT?




VALIDATION IN MICE



We successfully mimicked the compression of vasculature in a controlled laboratory environment


Bioactive Materials 22 (2023) 18–33

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Microarchitectural mimicking of stroma-induced vasculature compression in pancreatic tumors using a 3D engineered model



Marcel Alexander Heinrich ^{a,1}, Irene Uboldi ^{a,1}, Praneeth Reddy Kuninty ^a, Marc J.K. Ankone ^a, Joop van Baarlen ^b, Yu Shrike Zhang ^c, Kartik Jain ^d, Jai Prakash ^{a,*}

^a Department of Advanced Organ Bioengineering and Therapeutics, Engineered Therapeutics Section, Technical Medical Centre, University of Twente, 7500AE, Enschede, the Netherlands

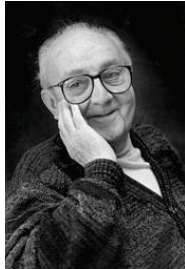
^b Laboratorium Pathologie Oost-Nederland (LabPON), 7550 AM, Hengelo, the Netherlands

^c Division of Engineering in Medicine, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, 65 Landsdowne St, Cambridge, MA, 02139, USA

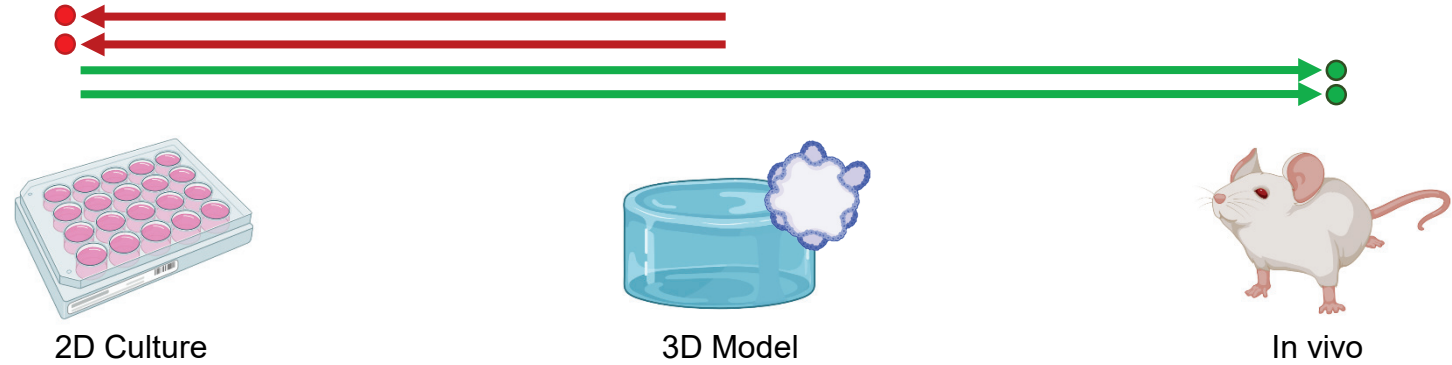
^d Department of Thermal and Fluid Engineering, Biofluid Dynamics Section, University of Twente, 7500 AE Enschede, the Netherlands

Heinrich, Uboldi et al., Bioact. Mater. 2022, 22:18-33

TAKE-HOME MESSAGE



"Essentially, all models are wrong, but some are useful"
(George E.P. Box)



→ More efficient, sustainable and affordable drug development

THANK YOU!



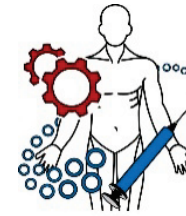
Prof. Jai Prakash



Irene Uboldi, MSc

University of Twente
Dr. Kartik Jain
Dr. Praneeth Kuninty
Marc Ankone

LabPON
Joop van Baarlen



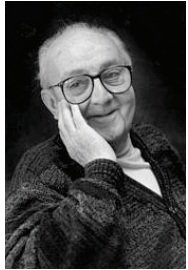
Advanced
Organ bioengineering &
Therapeutics

**UNIVERSITY
OF TWENTE.**

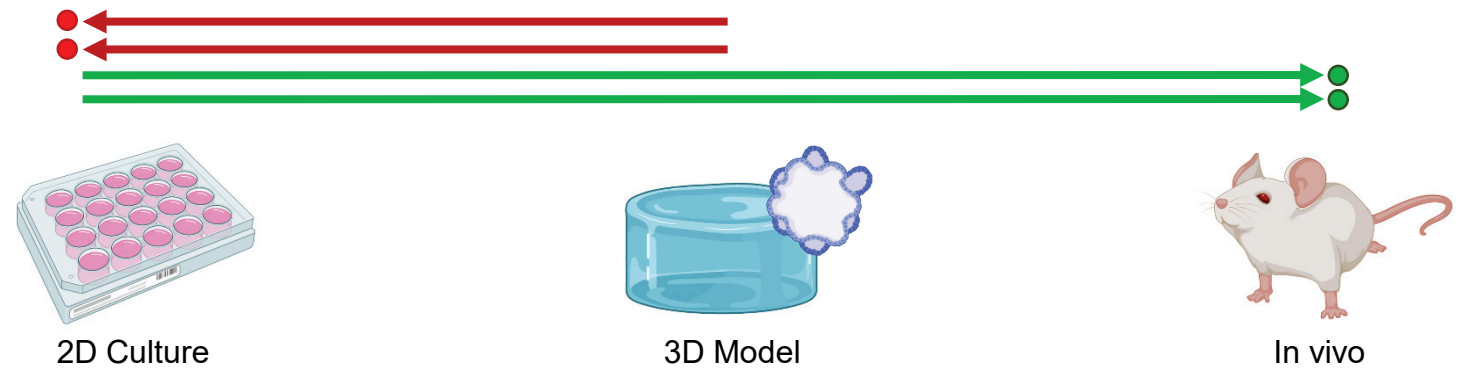
**TECHMED
CENTRE**



THANK YOU!



"Essentially, all models are wrong, but some are useful"
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