

Microscale tissue engineering for organ-on-chip models

03.09.2025

David Barata, Ph.D.

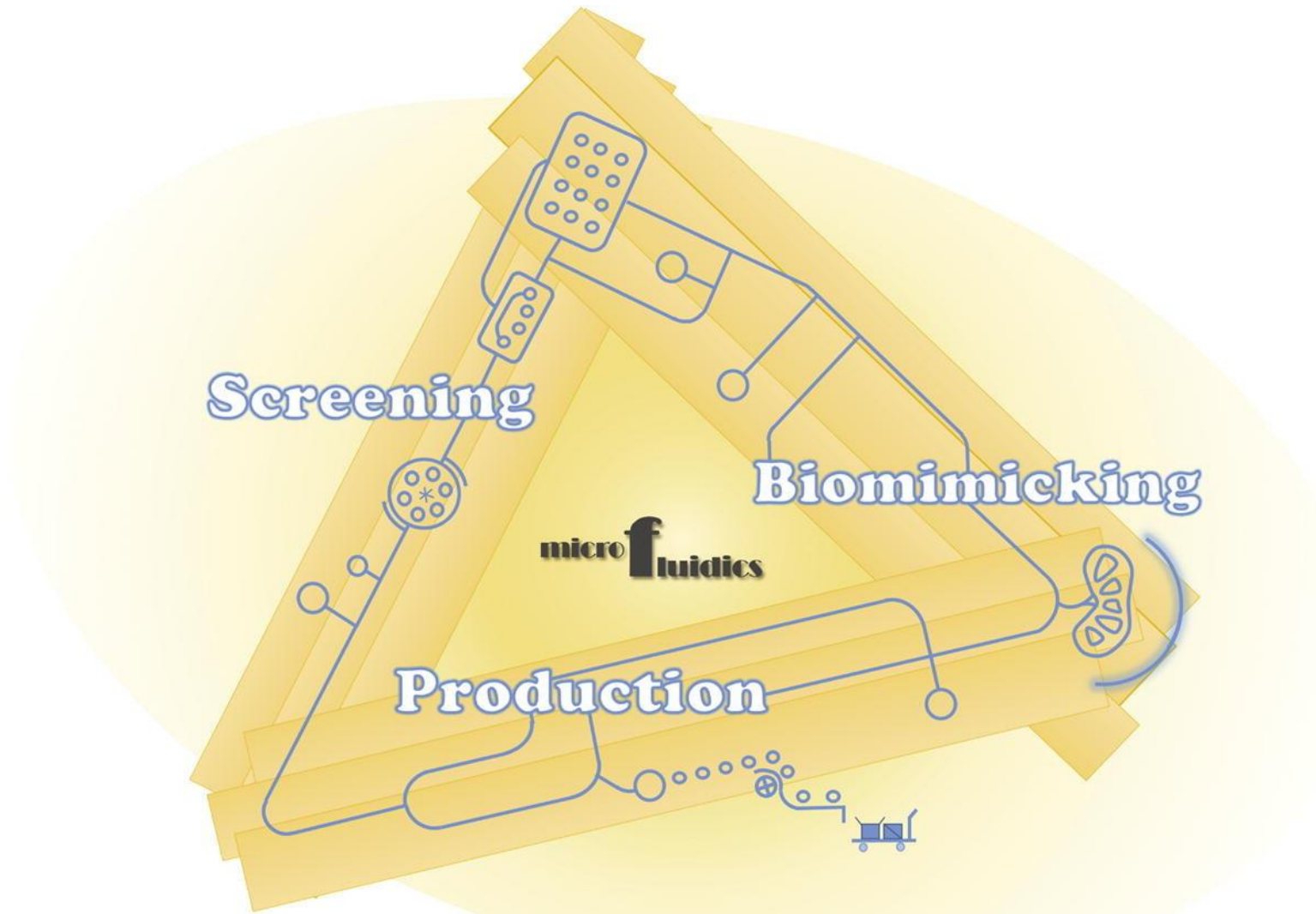
MERLN / NUTRIM
Maastricht University, Maastricht, The Netherlands

Chemnitz Seminar

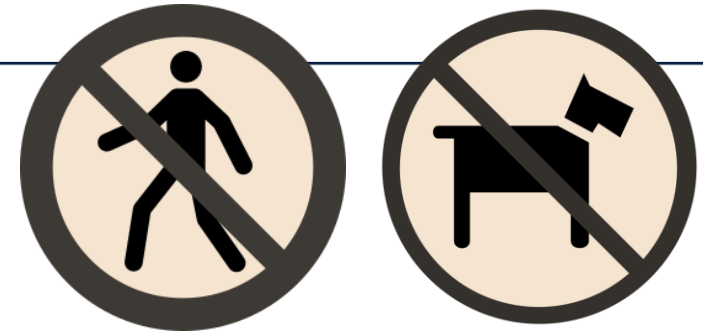
» **Sensor Systems
for One Health** «

 **Fraunhofer**
ENAS

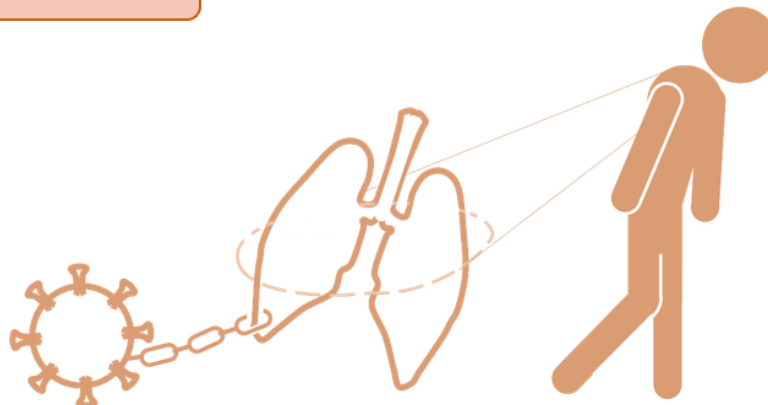




Why do we need *in vitro* assays?

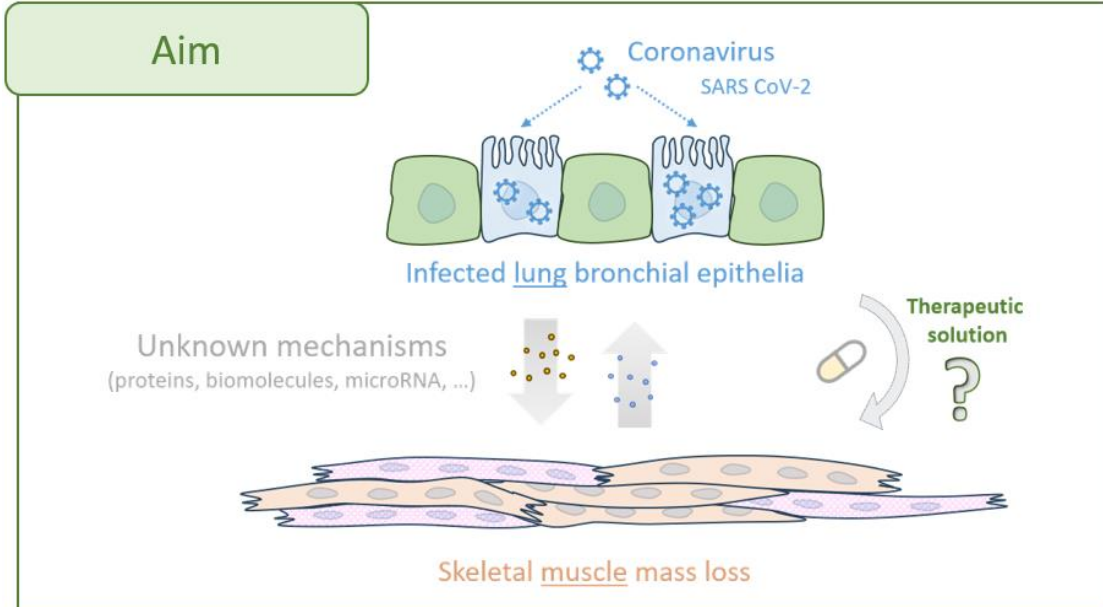


Problem



Covid-19 post-infection brings fatigue, muscle wasting

Aim



Coronavirus SARS CoV-2

Infected lung bronchial epithelia

Unknown mechanisms
(proteins, biomolecules, microRNA, ...)

Skeletal muscle mass loss

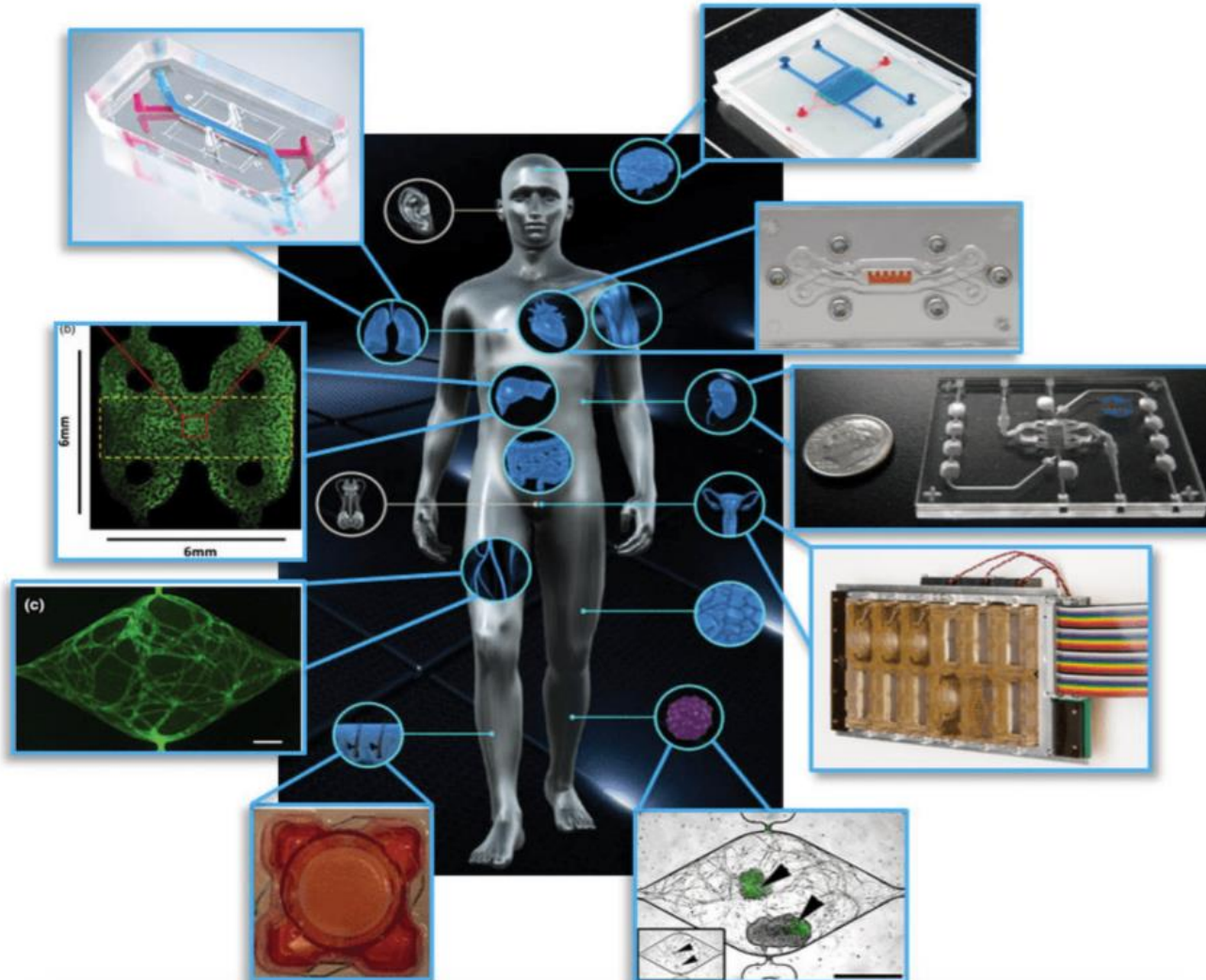
Therapeutic solution ?

Bioengineering physiologically relevant microenvironments

Bone-on-chip

Lung-on-chip

Cancer-on-chip



Bone-on-chip

Bone regeneration: from "in vivo" to "microfluidics" scale

Osteoinductive ceramics as a synthetic alternative to autologous bone grafting

pore space) followed by BCP1150 ($17.7 \pm 5\%$). Significantly less bone was observed in BCP1300 ($11 \pm 7.5\%$) indicating that both chemistry and structural properties can influence the in vivo osteoinductive potential of the ceramics (Fig. 4B).

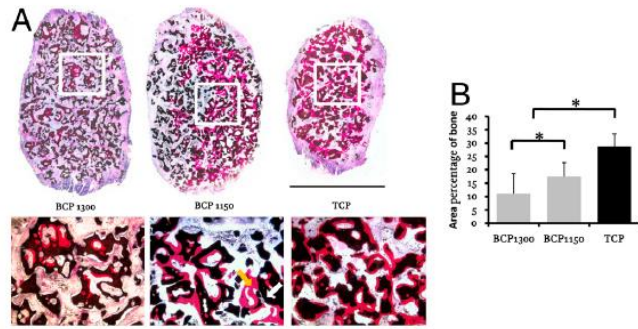


Fig. 4. Osteoinductive potential of different calcium phosphate ceramics implanted intramuscularly in sheep. (A) Histological sections showing the newly formed bone (orange arrow) and the calcium phosphate ceramic (white arrow) upon 12 weeks implantation. Basic Fuchsin stains the newly formed bone red, methylene blue stains fibrous tissue blue, and the scaffold is shown in black. (B) Quantification of newly formed bone. The error bars represent standard deviations. An asterisk (*) denotes statistical difference (one-way Anova and Tukey's test, $P < 0.05$). (Top, Scale bar: 10 mm.) (Bottom, Scale bar: 200 μm .)

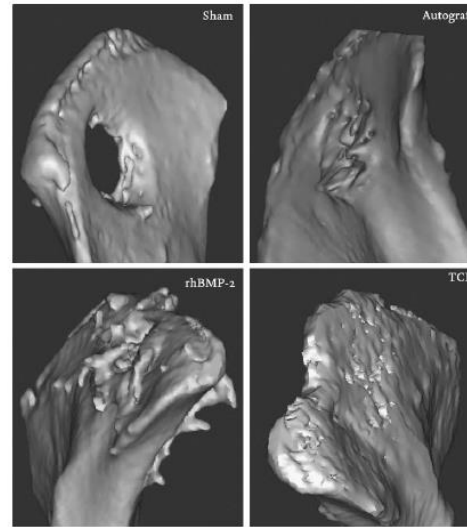
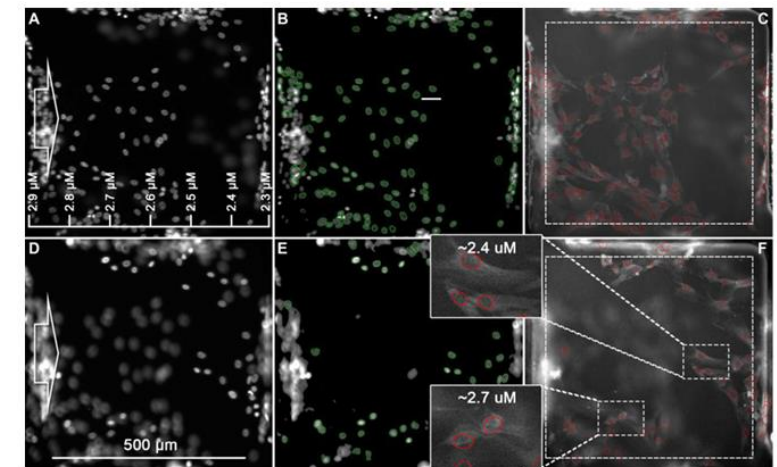
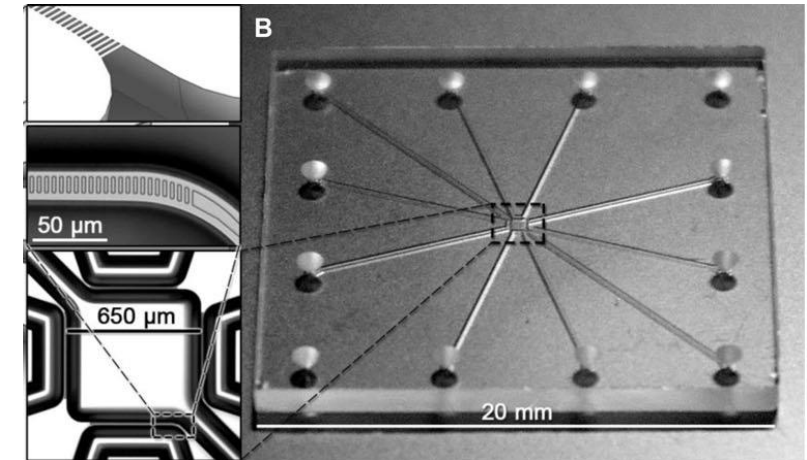


Fig. 5. Ilium defect. Figure presents three-dimensional models of the os ilium after 12 weeks implantation. Bone formation outside the margins of the defect was found in the rhBMP-2 group, whereas in the TCP group, the material remained within the defect with new bone formation and implant resorption observed at 12 weeks.

Glass-glass microfluidic chip



Harink et al. (Electrophoresis, 2015)

Using biomaterials to make cell-friendly microenvironments

BIOMIMETIC

Cargo aircraft

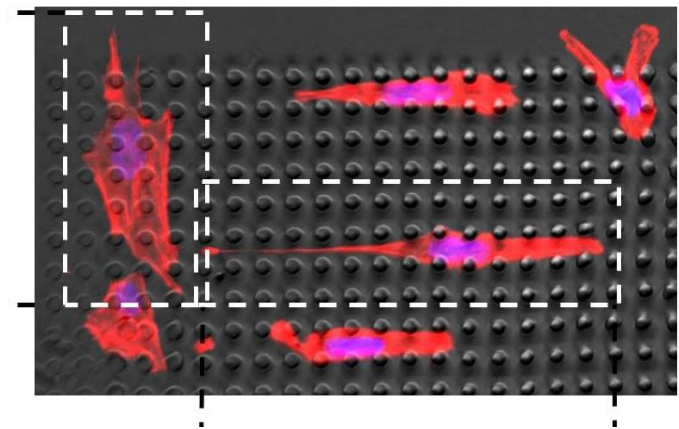
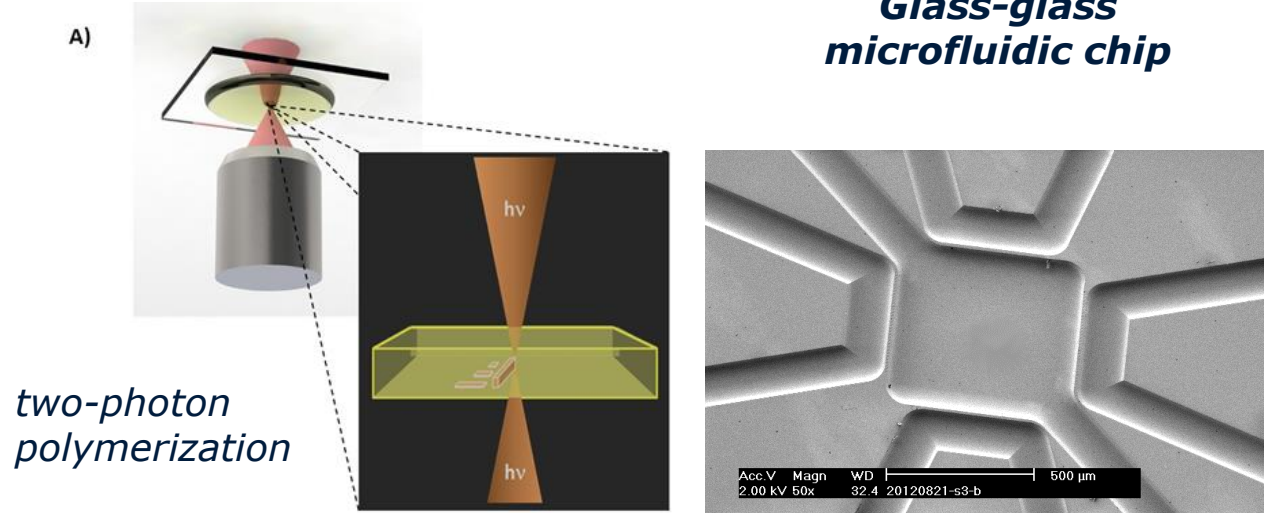
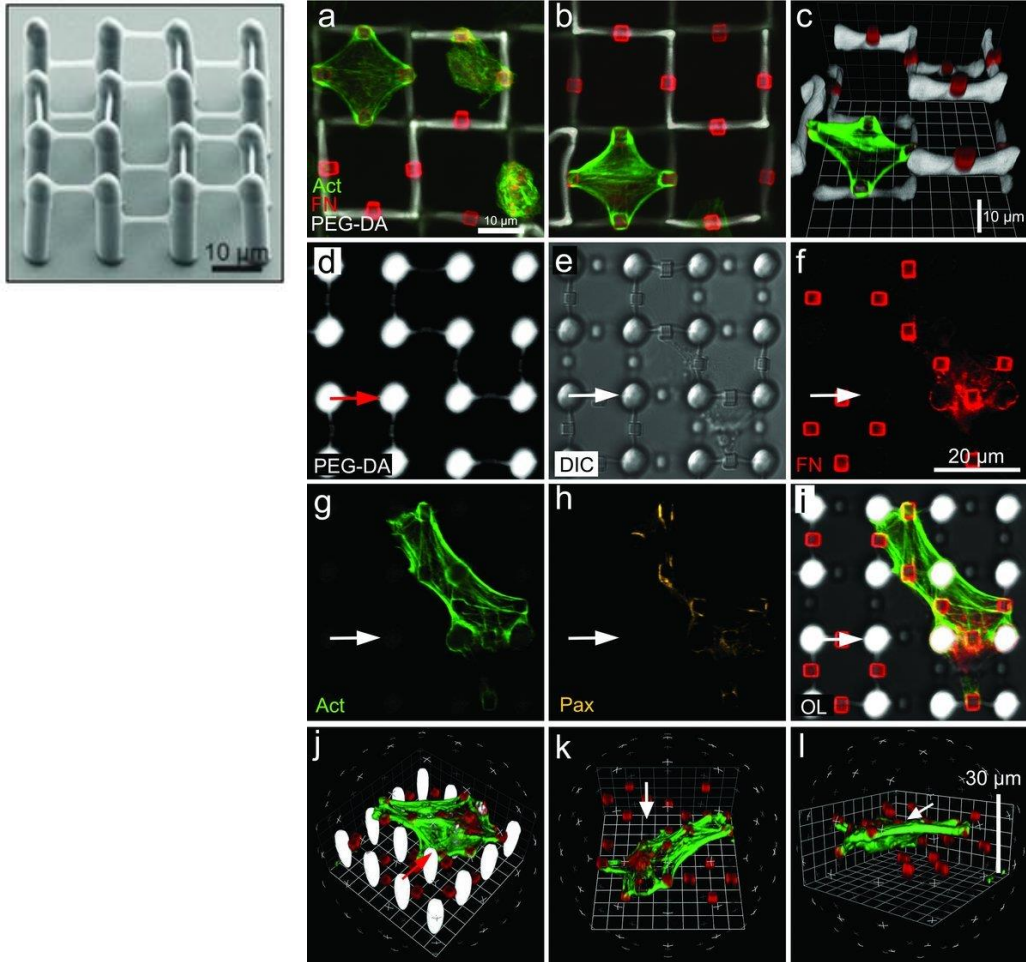


Passenger aircraft



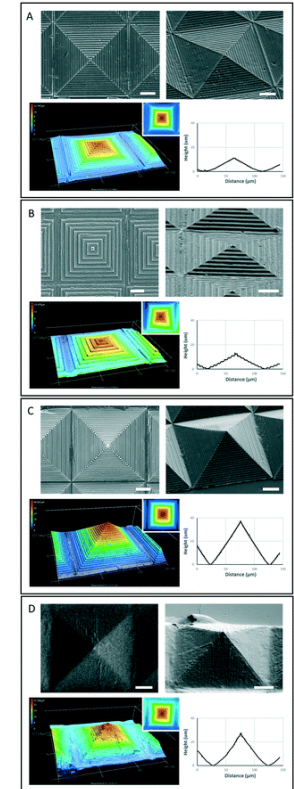
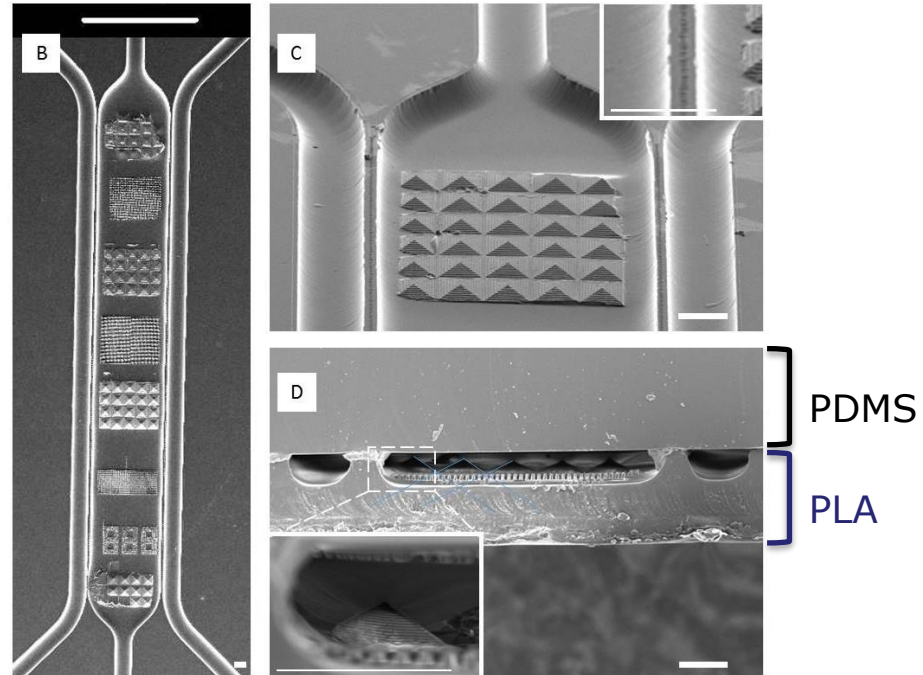
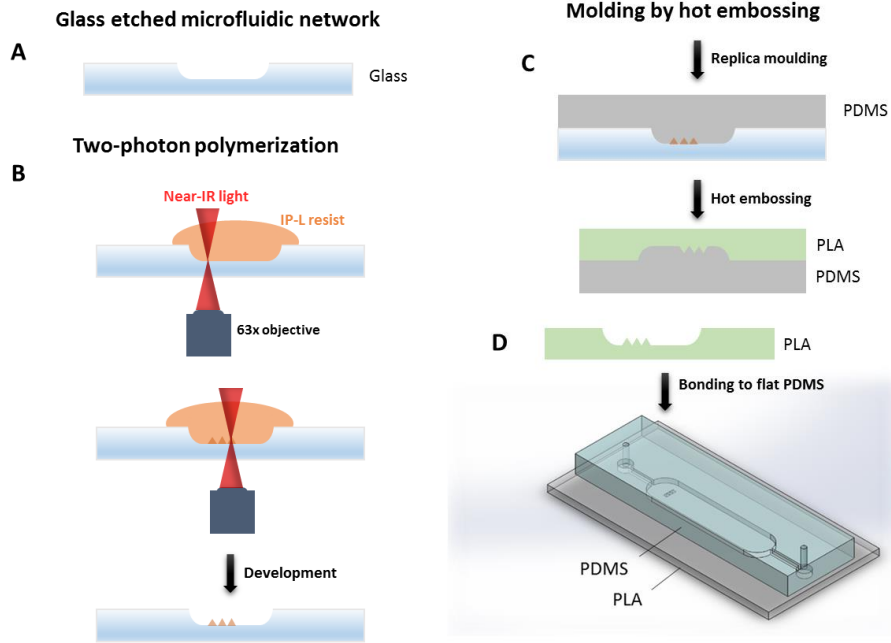
<https://www.youtube.com/watch?v=ZjXKzhdHtHe0>

Introducing 3D micro polymeric materials with sub-micron resolution

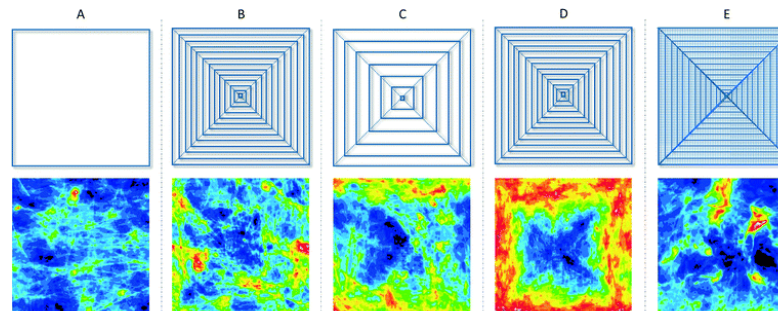


3D micropatterning of biomaterials based microfluidic devices

3D Topography

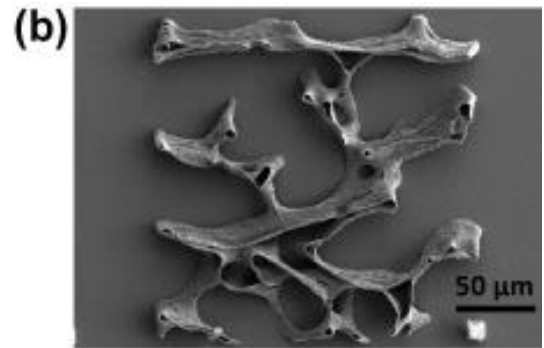
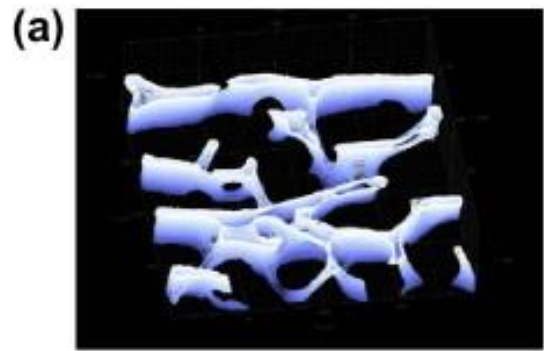


*Osteoblast
distribution*



Introducing 3D microanatomical object on-chip

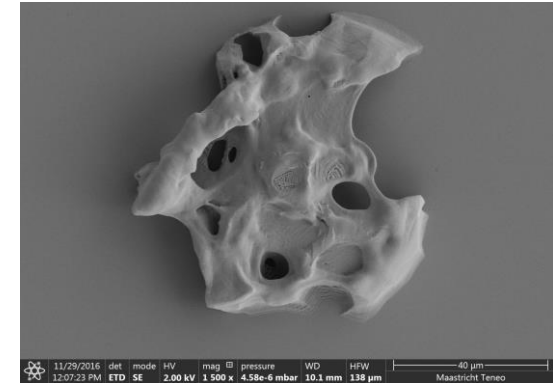
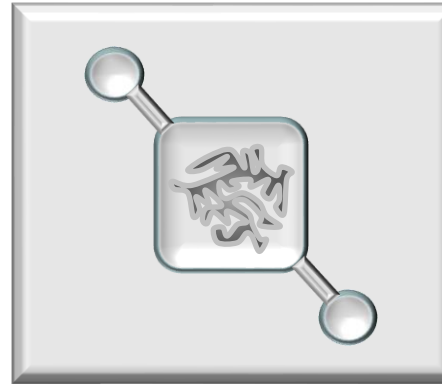
Osteoprint



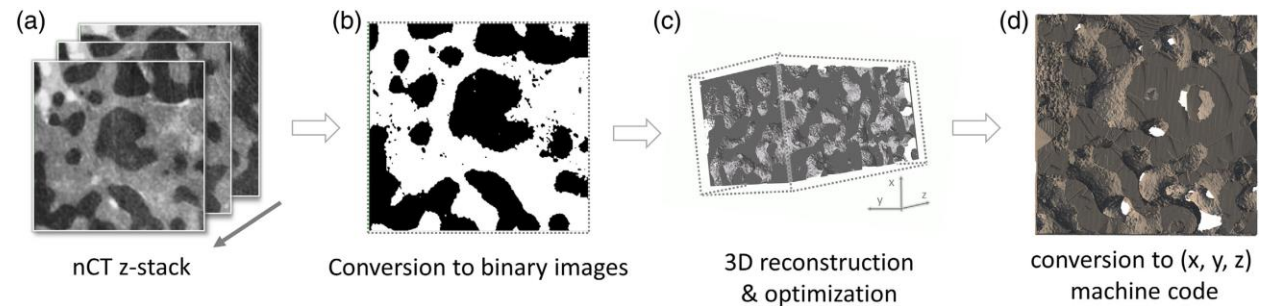
Physiologically relevant geometries

+ Correct chemistry at interface with Calcium Phosphate

Bone-on-chip

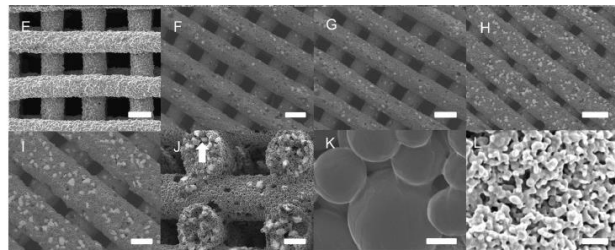


Acquisition and processing workflow from nano-computed tomography images into a volumetric model of trabecular bone

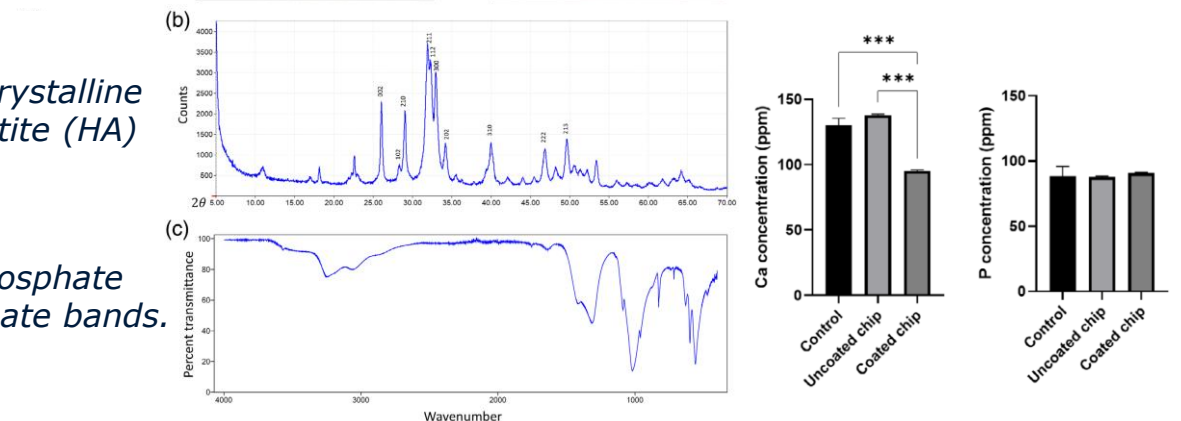
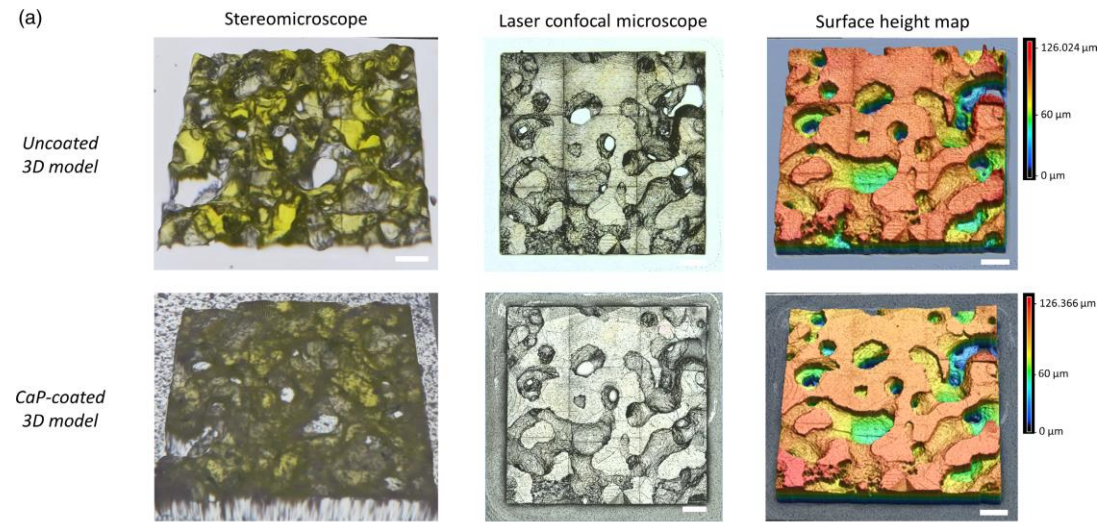
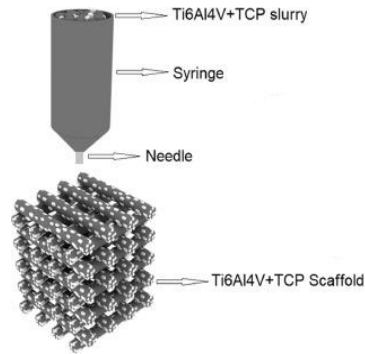


Scaffolding by 3D printing of instructive biomaterials

Precipitation of a Hydroxyapatite thin coating obtained by enzymatic degradation of urea by urease
 → slow increase of pH of a solution with calcium and inorganic

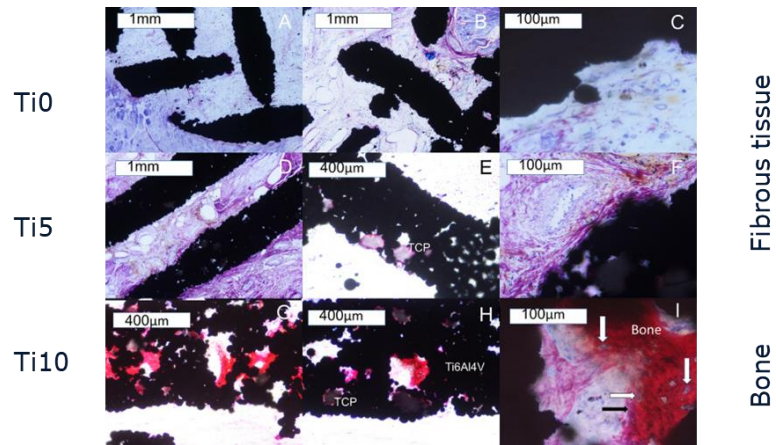


SEM images of moulded and 3D manufactured Ti6Al4V-TCP scaffolds.



XRD: semicrystalline hydroxyapatite (HA)

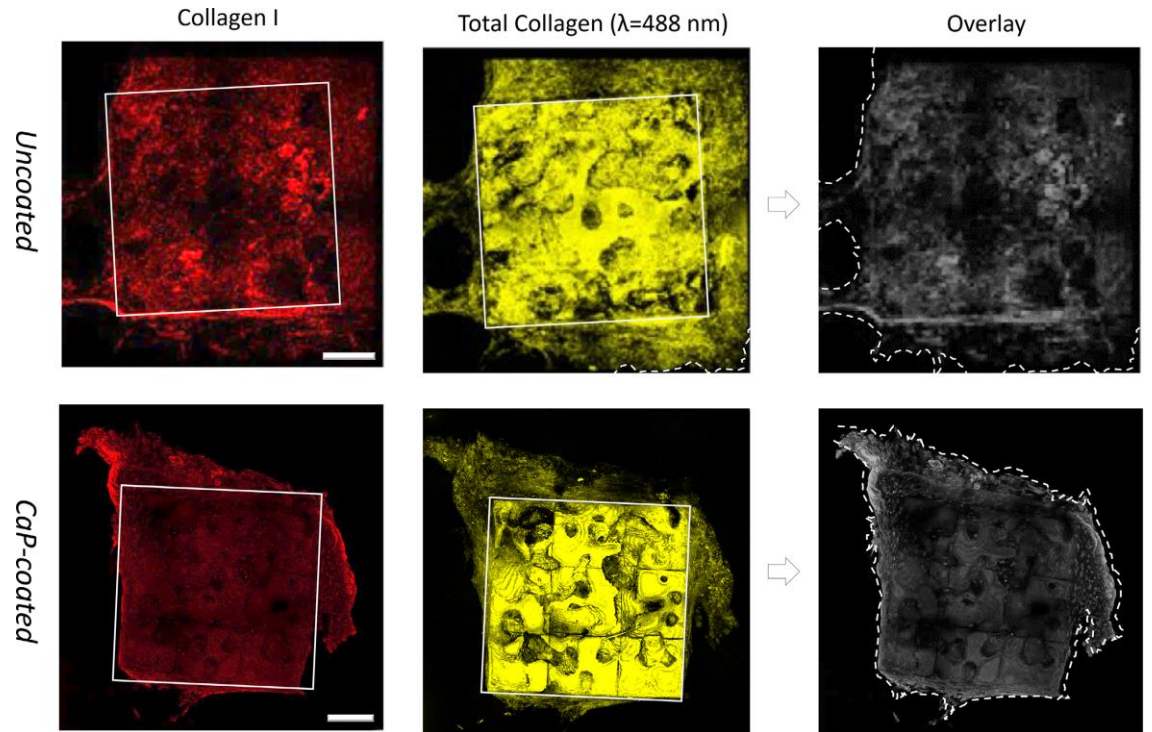
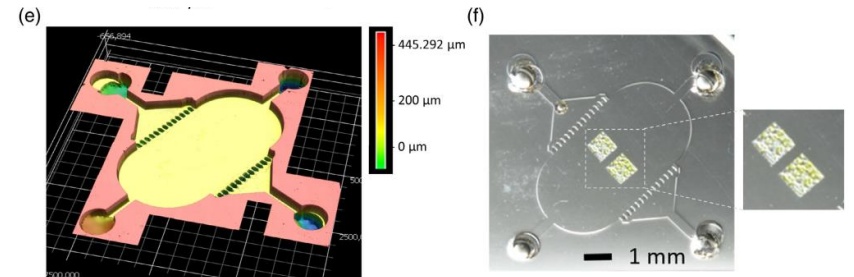
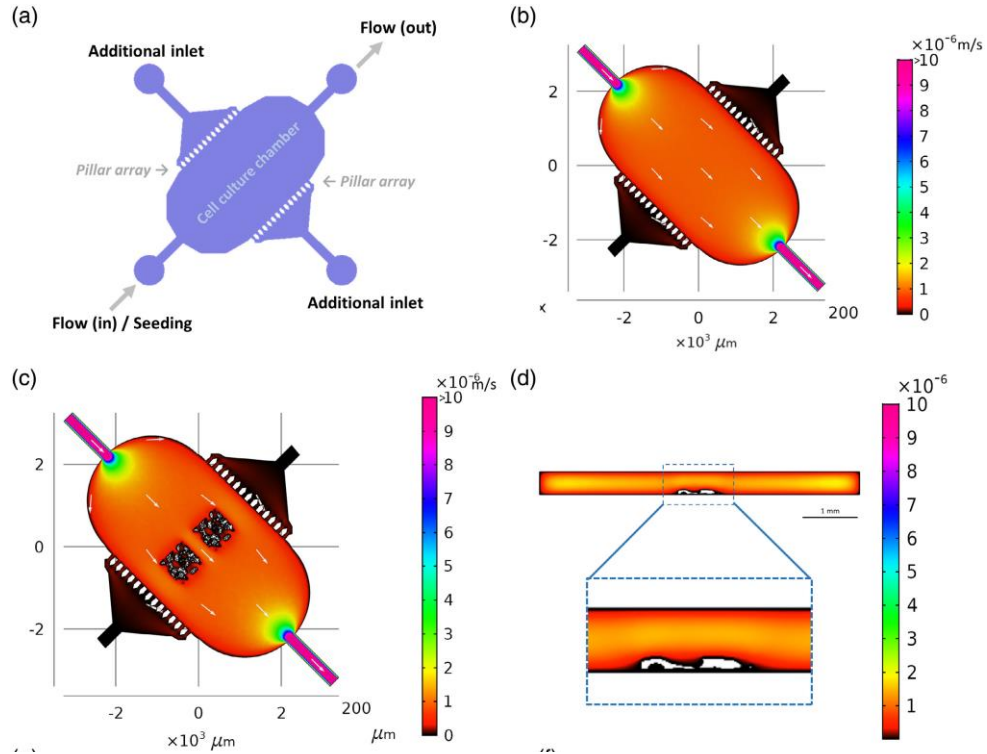
FTIR: phosphate & carbonate bands.



Fibrous tissue

Bone

Optimising seeding and culture on microfluidic chip

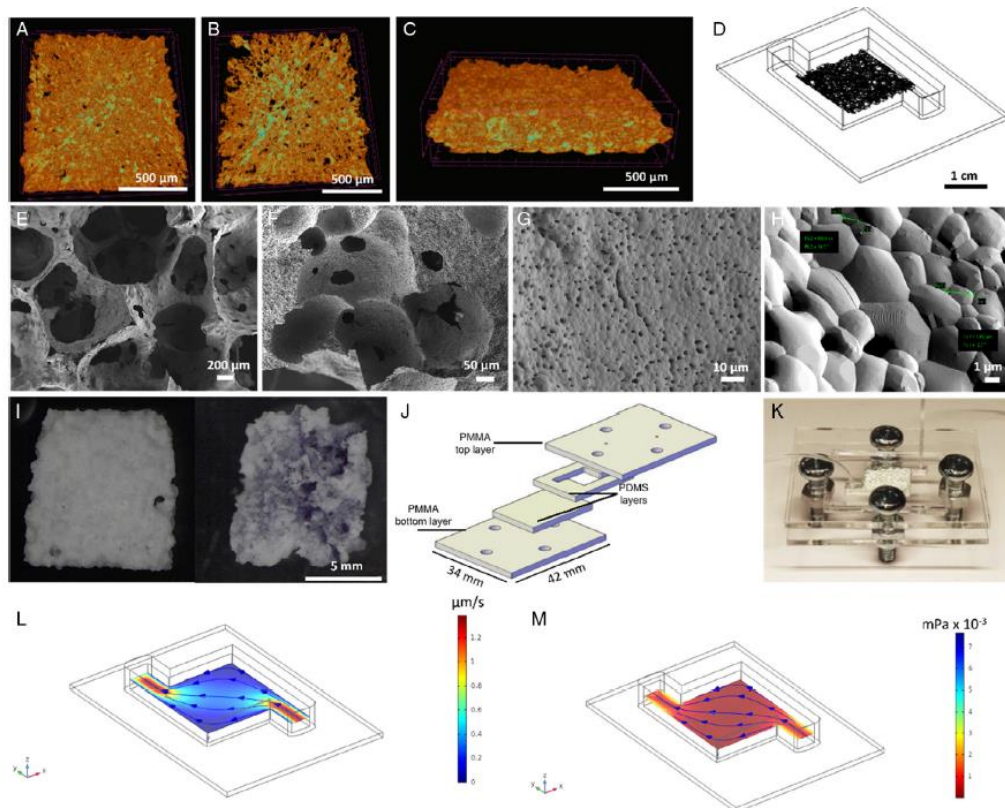


21 days Collagen production

Media perfusion at low perfusion rate in equal condition for all replicas of 3D bone model

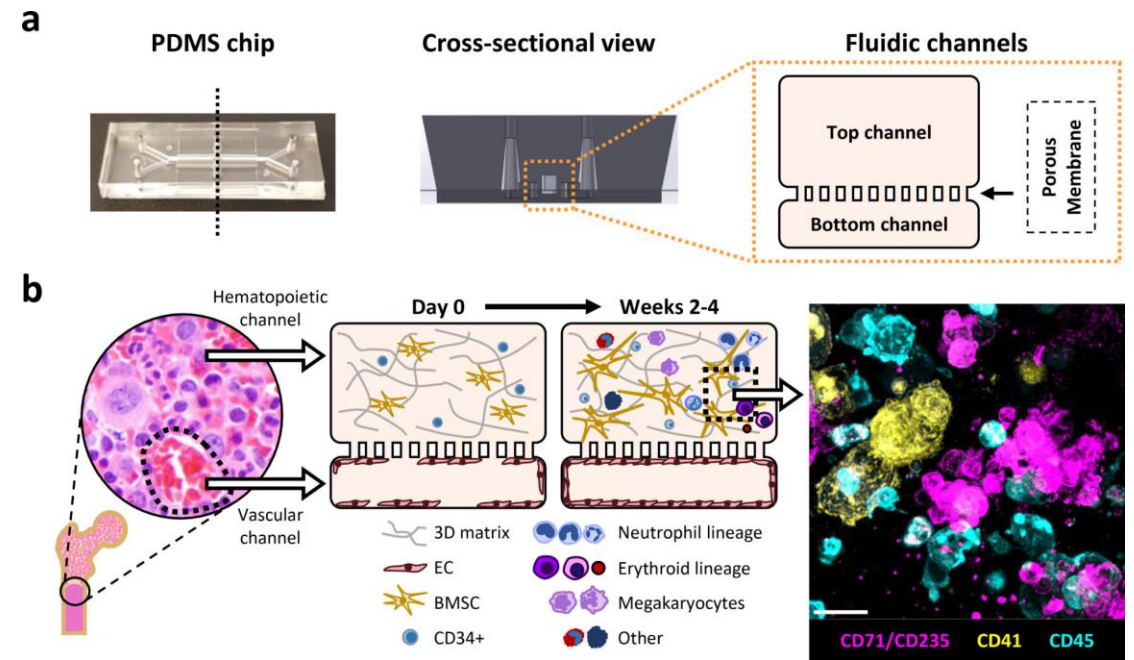
Other inspiring bone-on-chip systems

β -TCP based scaffold seeded with primary osteoblast and osteoclast precursors, then implanted.



Erbay et al. (Adv. Eng. Mater. 2023)

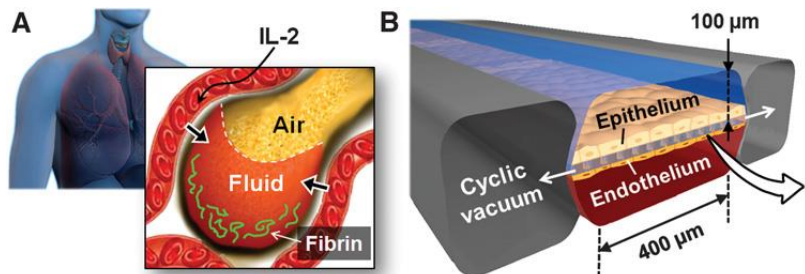
Primary human Bone Marrow Chip supports in vitro hematopoiesis over 4 weeks in culture



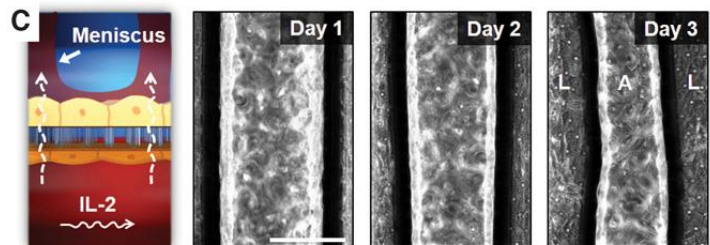
Chou et al. (Nat Biomed Eng. 2020)

Lung-on-chip

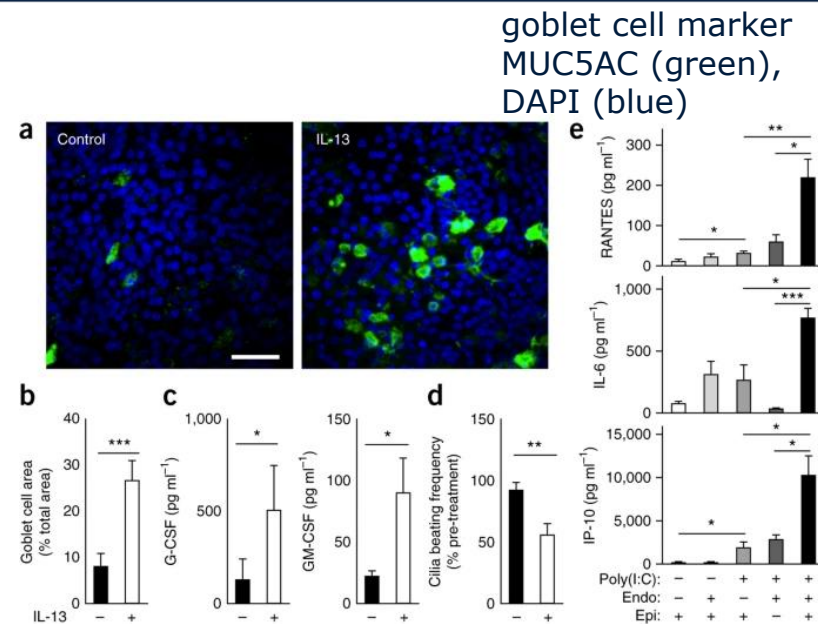
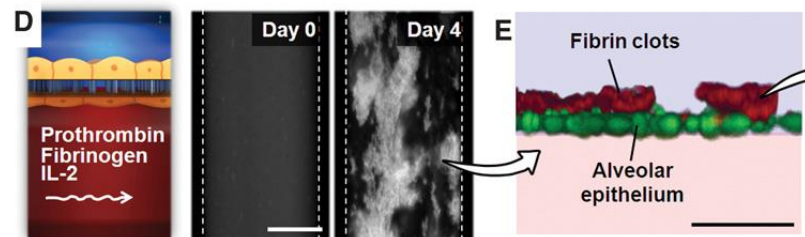
Mimicking the upper airway and testing barrier function



Modeling asthma and lung inflammation on-chip.

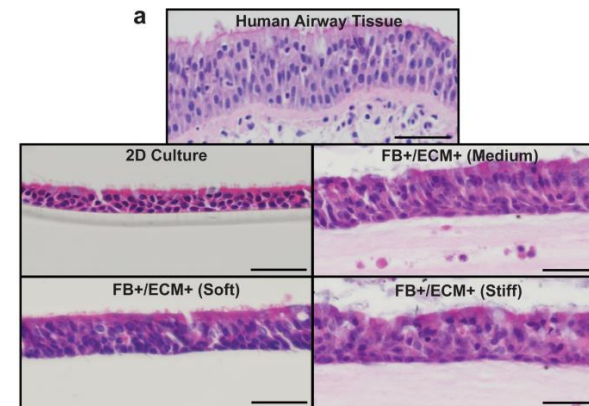
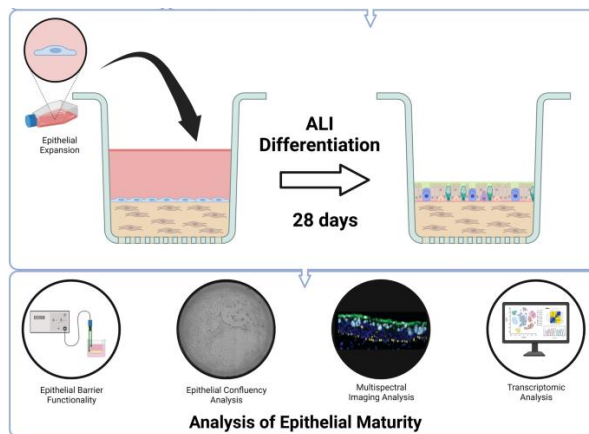


Leakage on membrane induces clots by IL-2



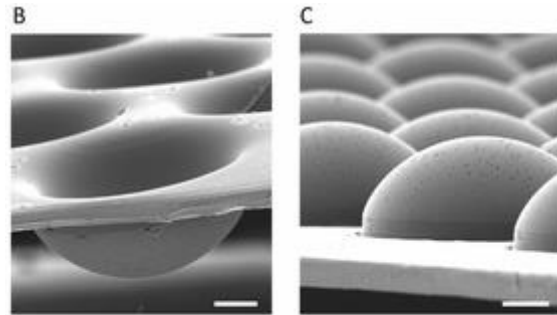
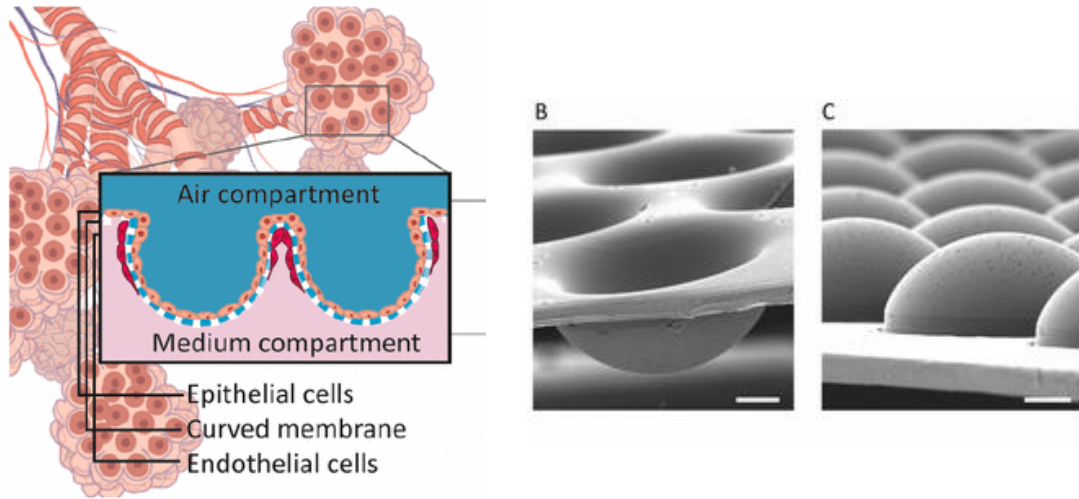
Benam et al. Nature Methods (2015)

Engineering the supporting ECM

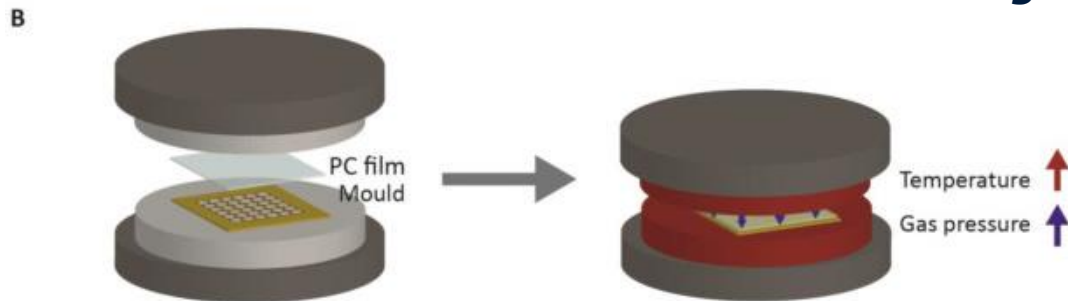


Leach et al. Scientific Reports (2023)

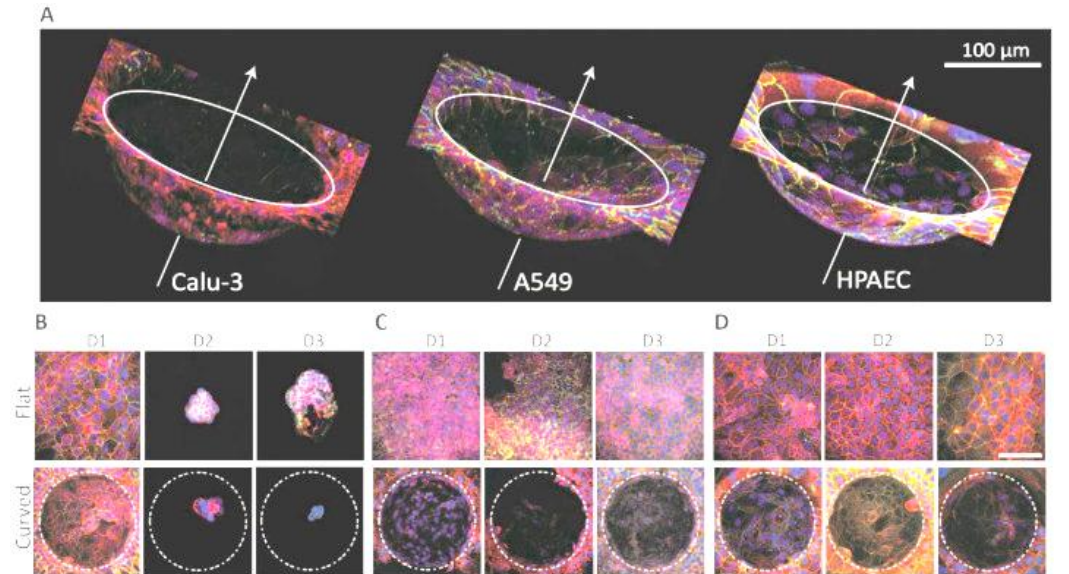
Engineering the alveolar microanatomical features



Membrane thermoforming

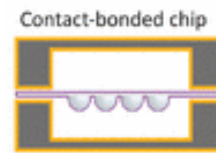
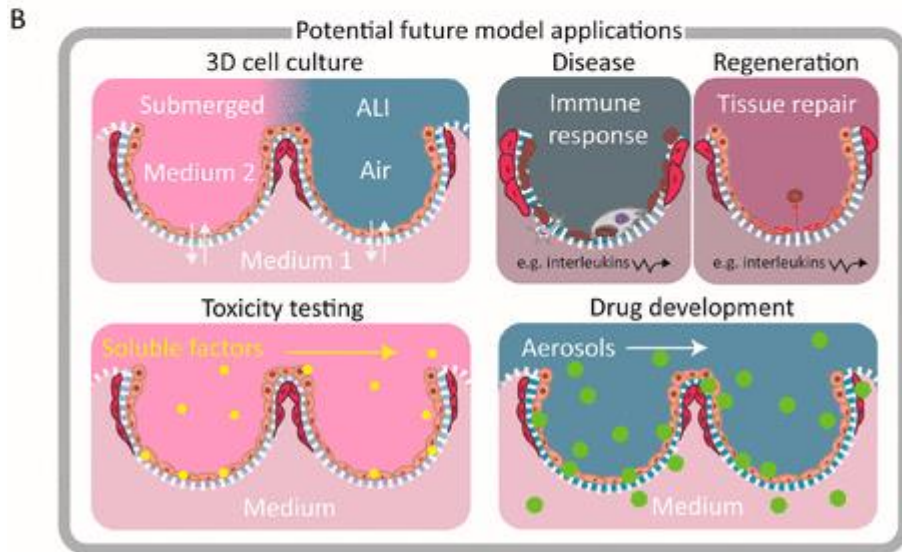
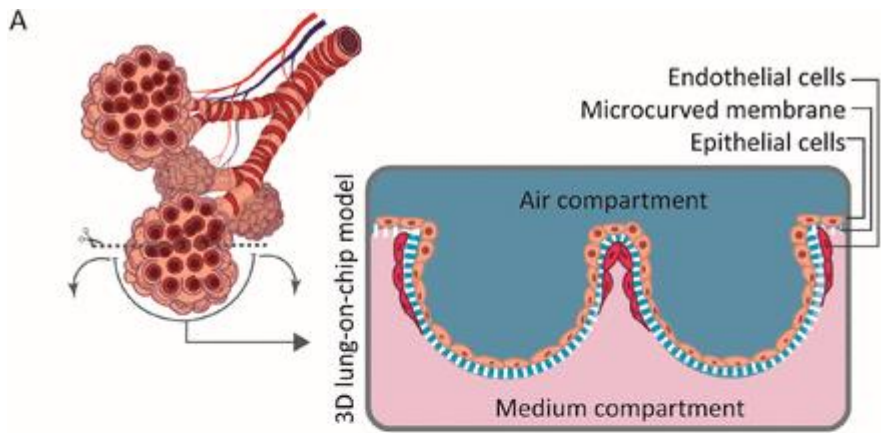


Culture of cell lines and primary cells in cell culture inserts

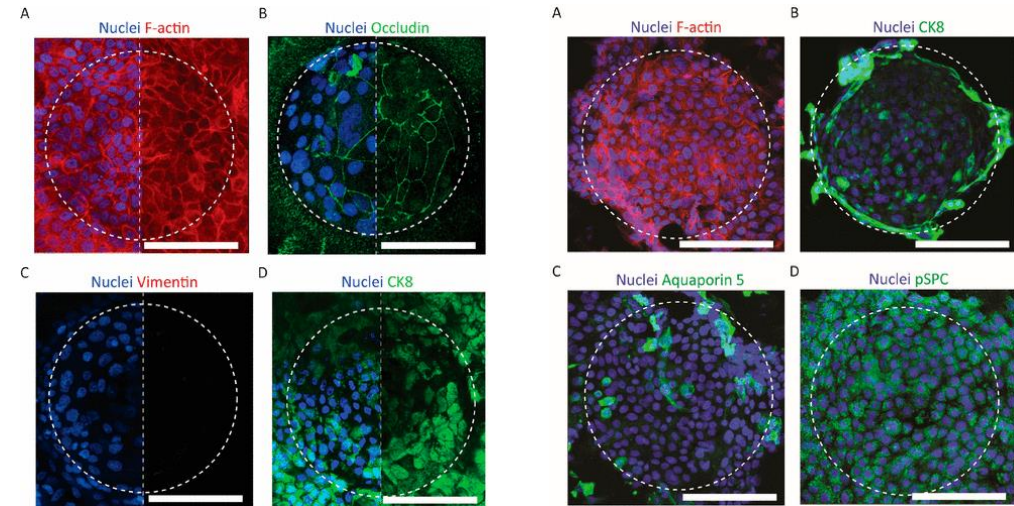


cells cultured for 11 days on curved and flat membranes

Engineering the alveolar microanatomical features



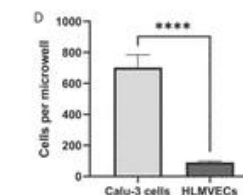
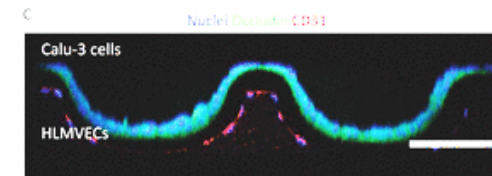
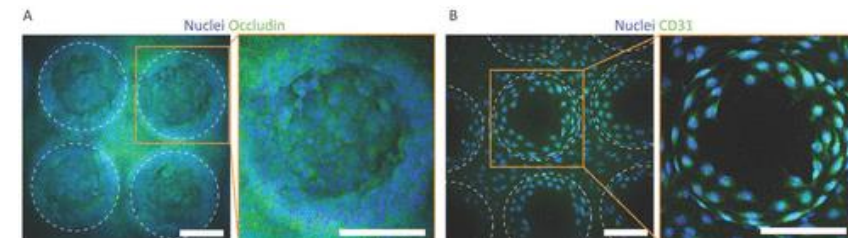
Microfluidic cell culture



HAECs, 7d sub.

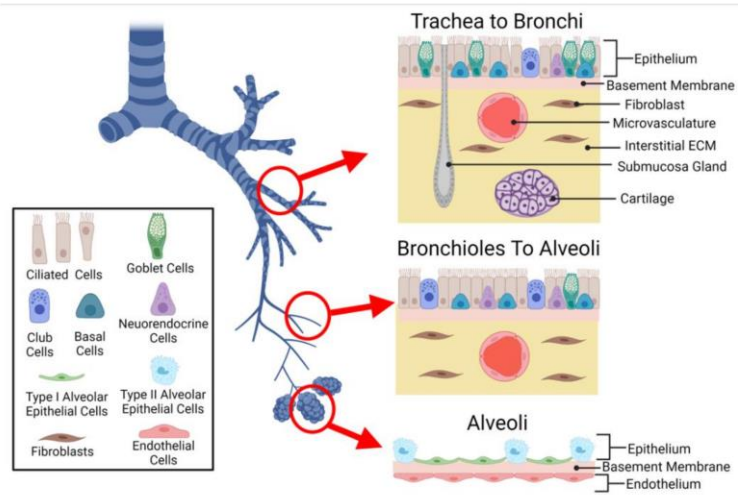
HAECs, 7d sub. = 14d ALI

Epithelial / Endothelial co-culture



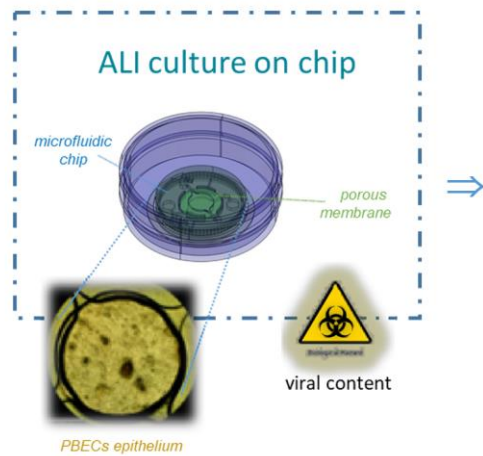
11d, sub.

Simple and high-containment LoC for viral infections – upper airway

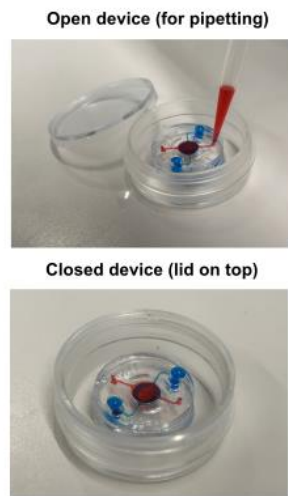


Bennet et al, Cells (2021)

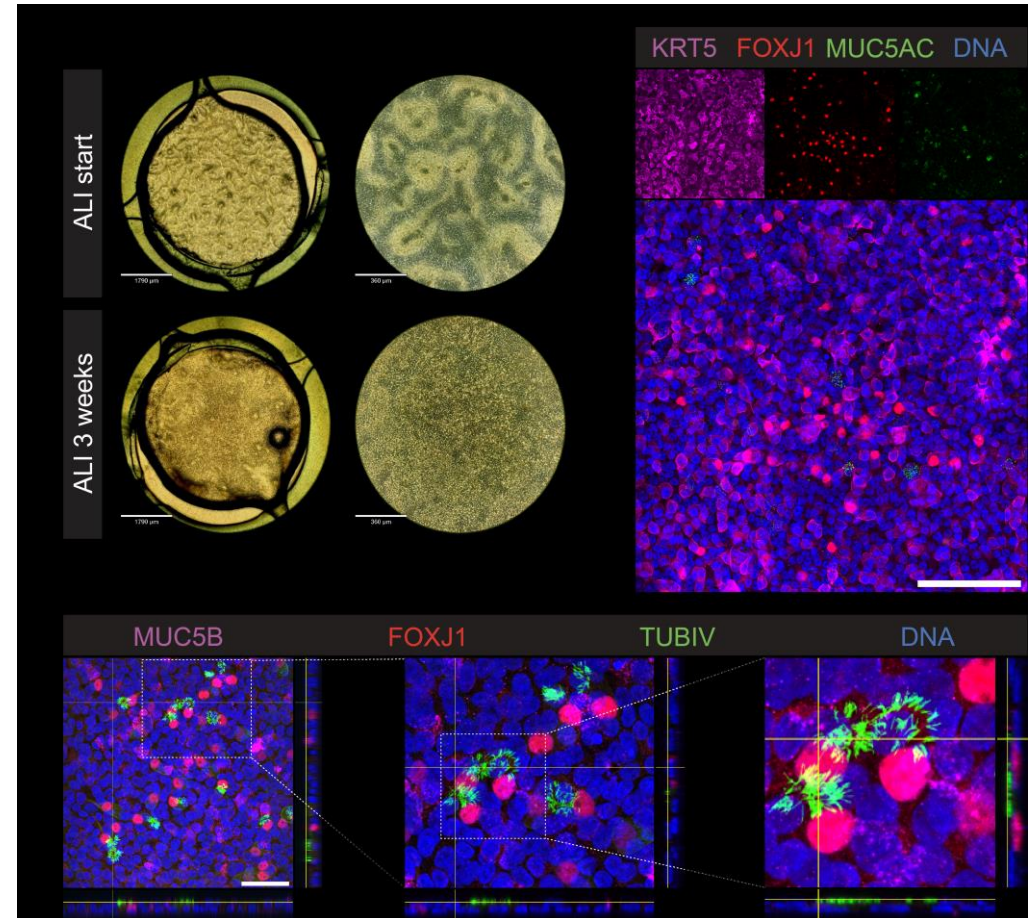
Simple and high-containment lung on chip



Fluid injection



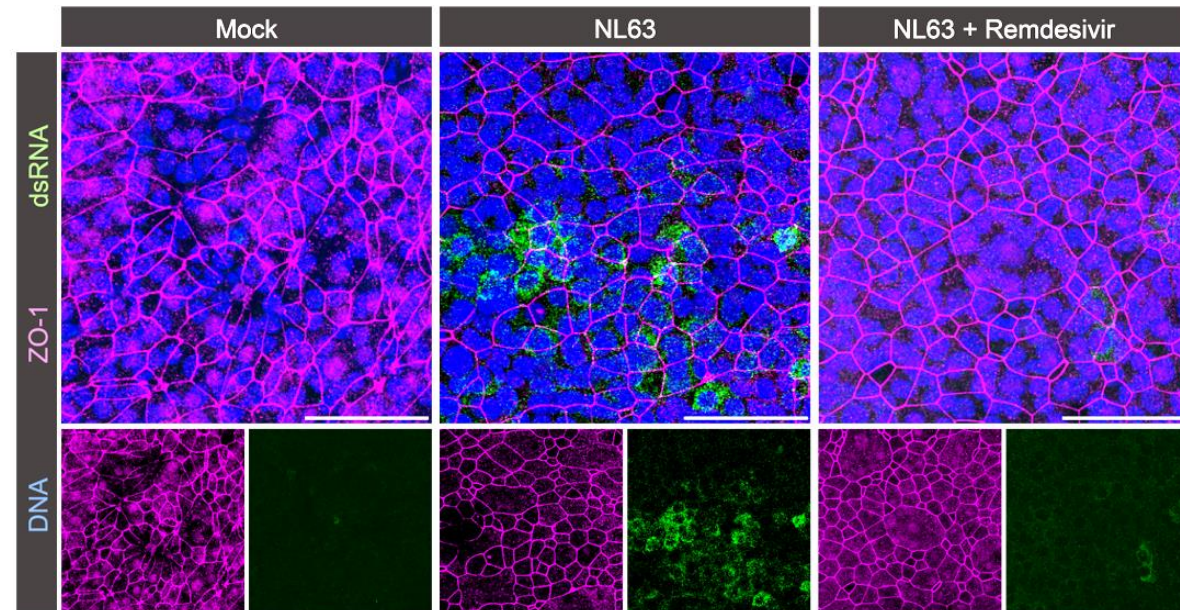
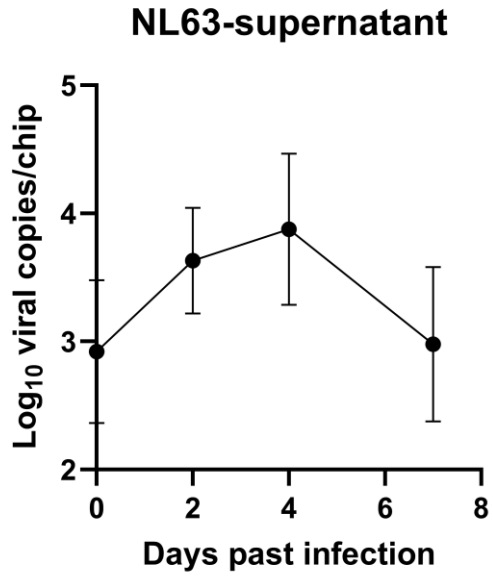
Maturation of apical side on-chip



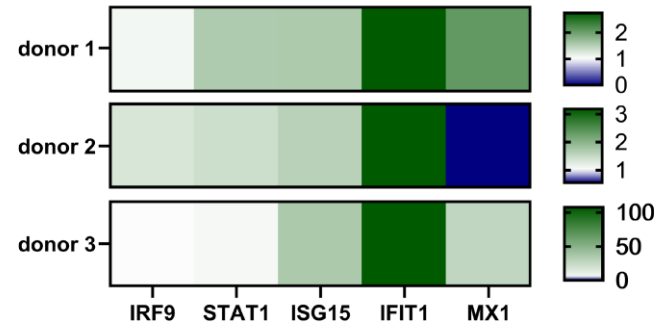
Barata, Koornneef et al, under revision (2025)
 SSRN preprint available <https://dx.doi.org/10.2139/ssrn.5357561>

Studying human coronavirus infection and cell response mechanism

Detecting the virus on the epithelial layer

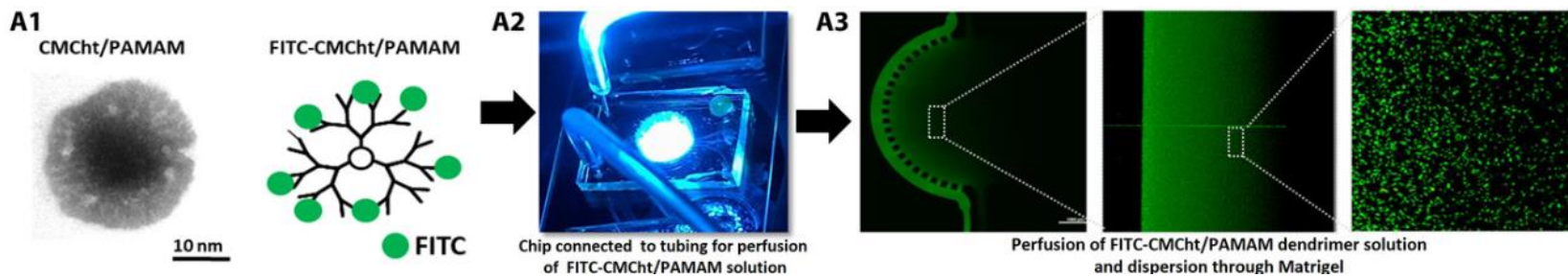
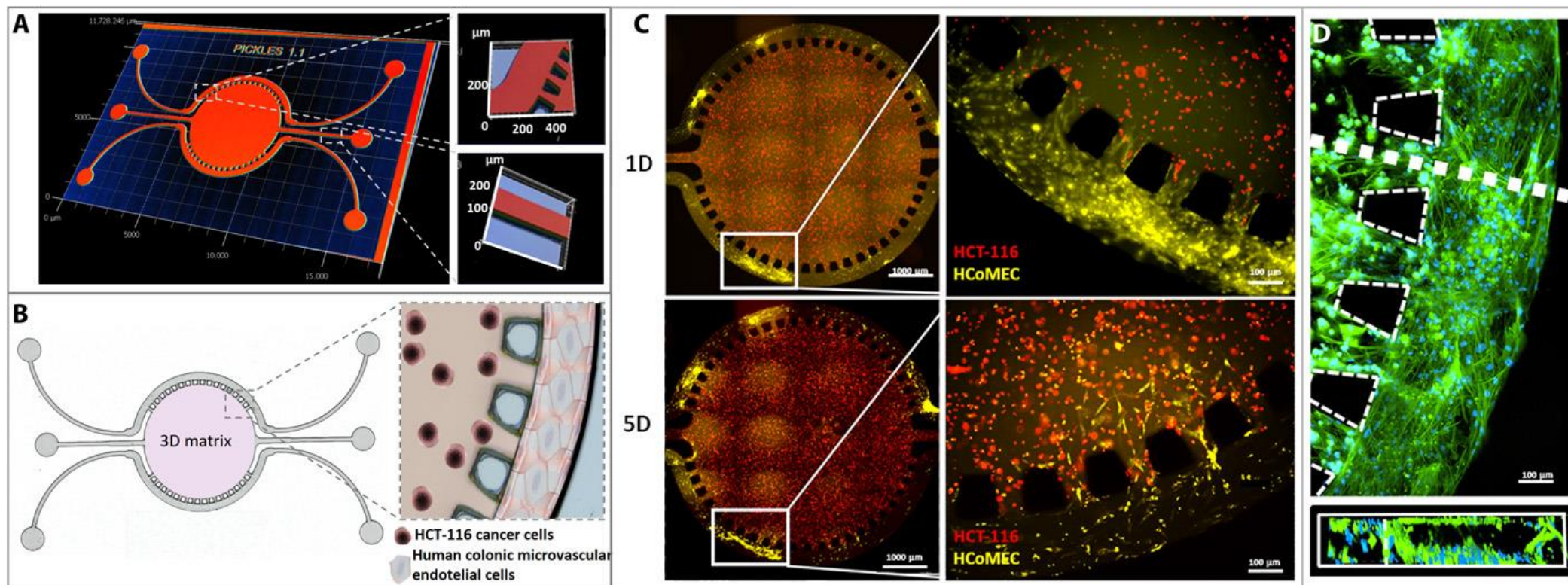


Donor variability on response to viral infection

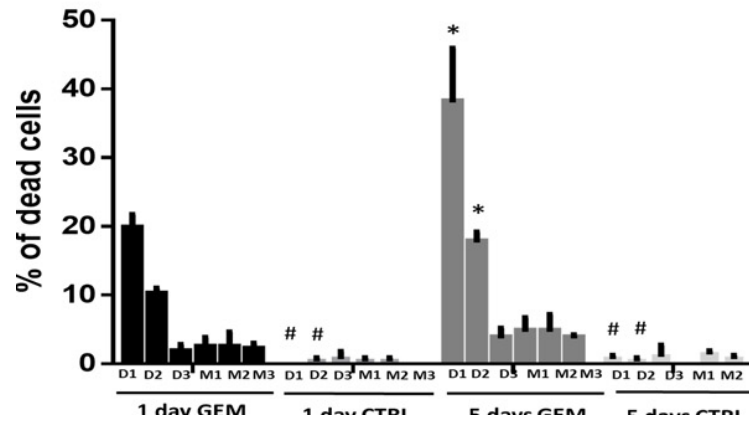
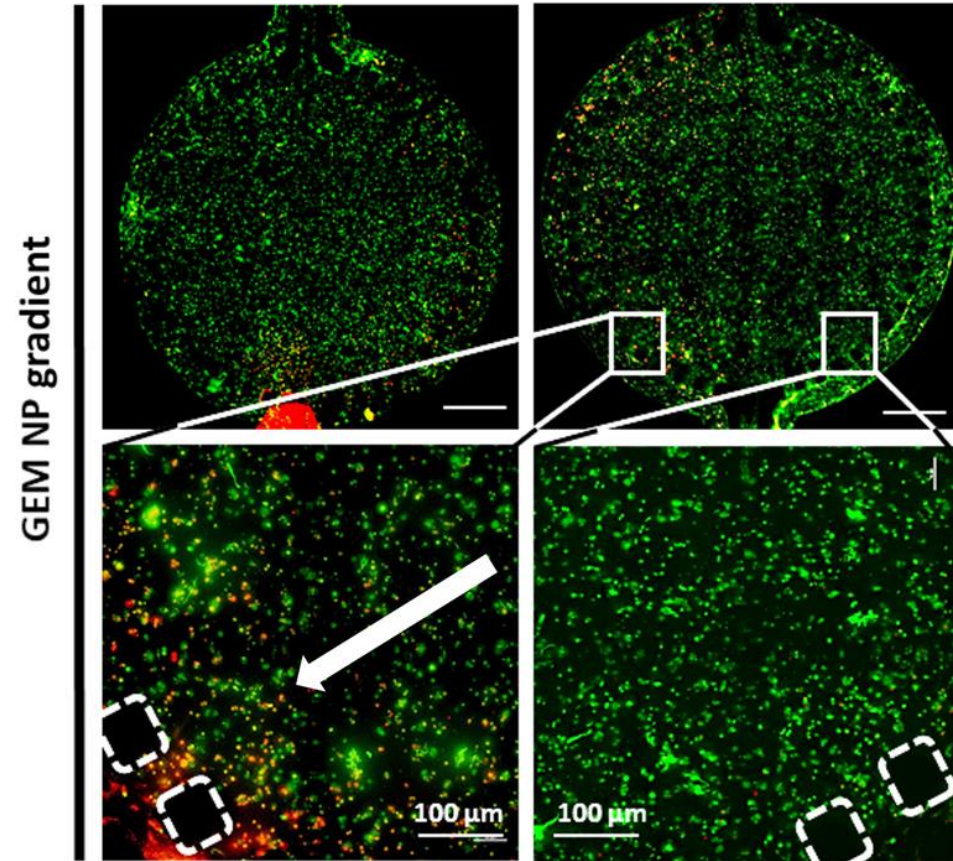
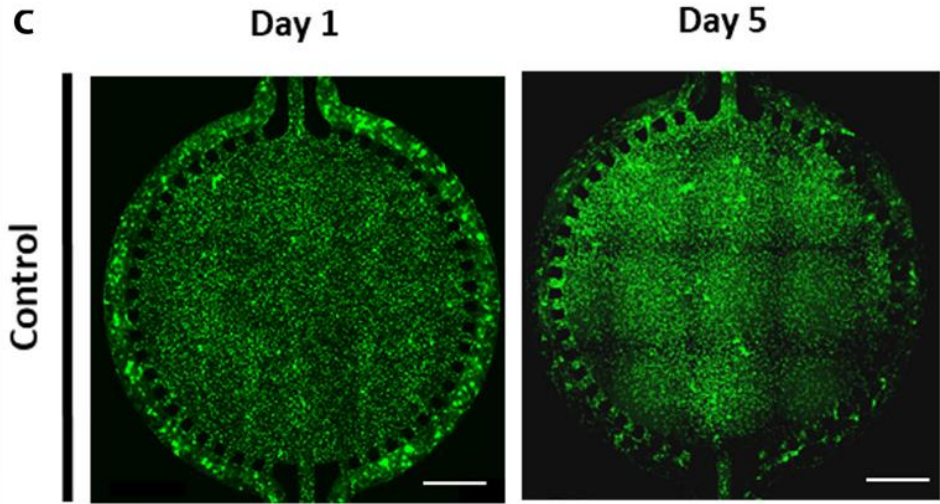


Cancer-on-chip

Colorectal tumor-on-a-chip system: a tool for precision onco-nanomedicine



Perfused NPs (with Gemcitabine) slowly permeates endothelial vessel and induces apoptosis



Looking forward :: Biosensing for 3D microtissue monitoring



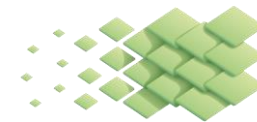
*344P tumor spheroids
growth and viability*

*Skeletal muscle
growth, viability, atrophy*

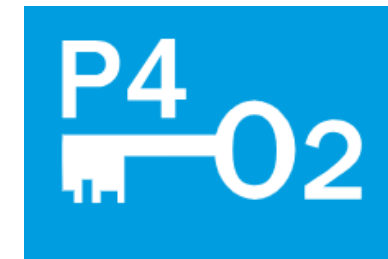
Questions ?

david.baiaobarata@maastrichtuniversity.nl

Thank you!



materials-driven regeneration



Prof. Dr. R. Langen
Dr. C. Mota
Prof. Dr. R. Truckenmüller
Prof. Dr. P. Habibovic