

## PANCREAS-ON-A-CHIP: A NEW ERA FOR PANCREATIC CANCER RESEARCH

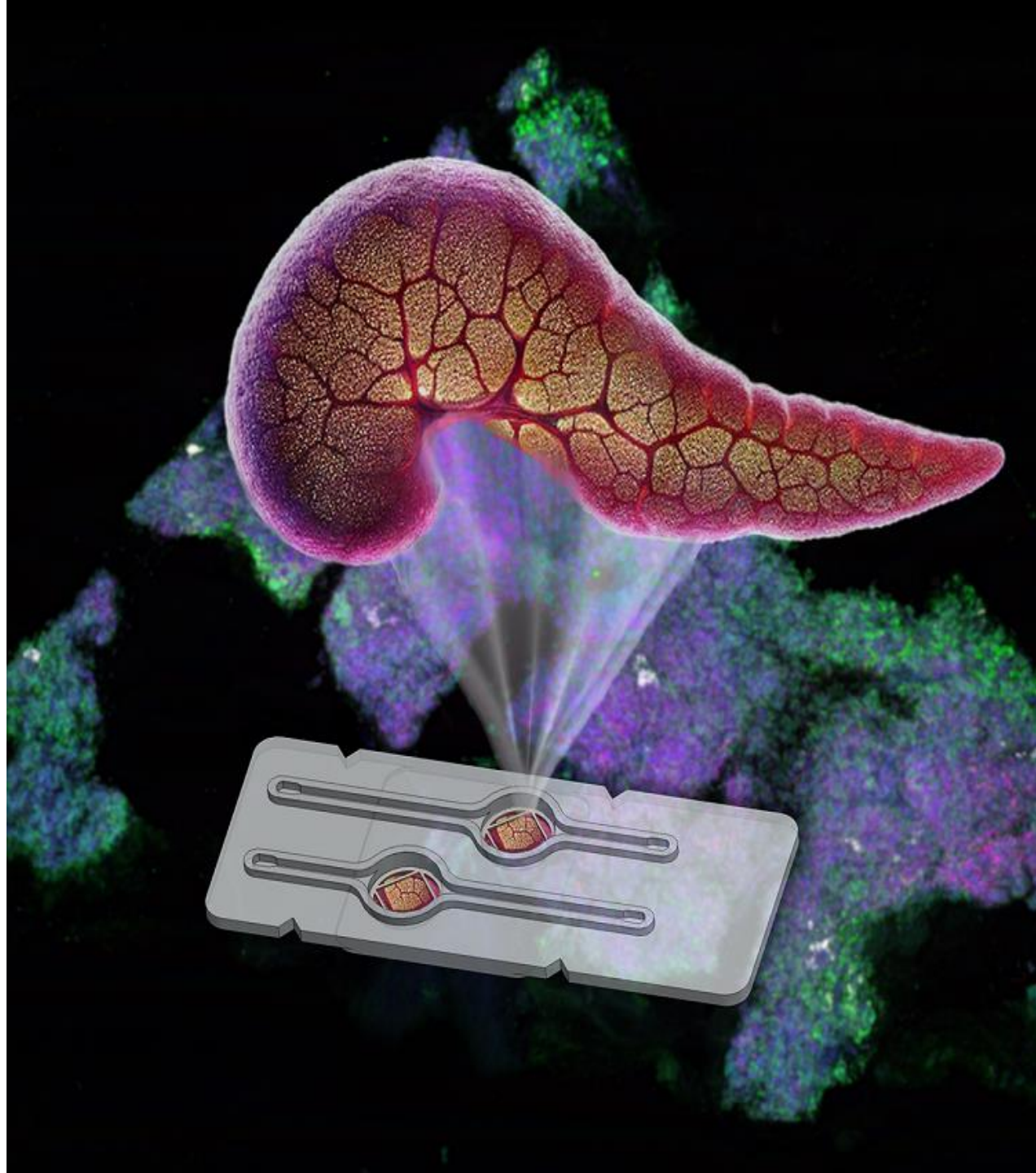
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MICRO-568

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Based on the following articles:

- 1) **Patient-derived pancreatic cancer-on-a-chip recapitulates the tumor microenvironment. 2022**
- 2) **Personalized PDAC chip with functional endothelial barrier for tumour biomarker detection: A platform for precision medicine applications. 2024**

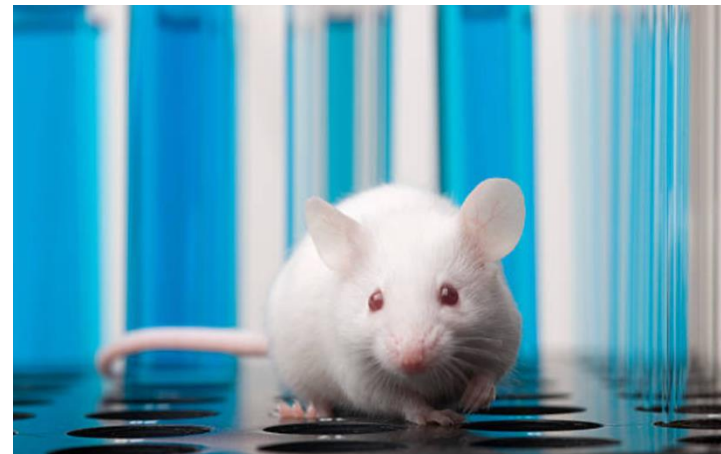
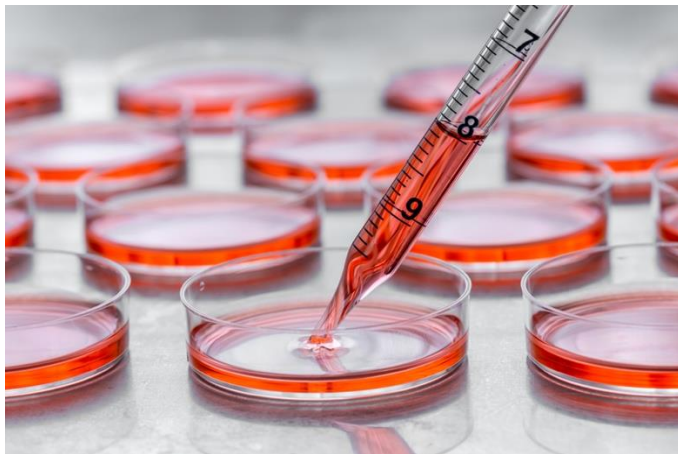
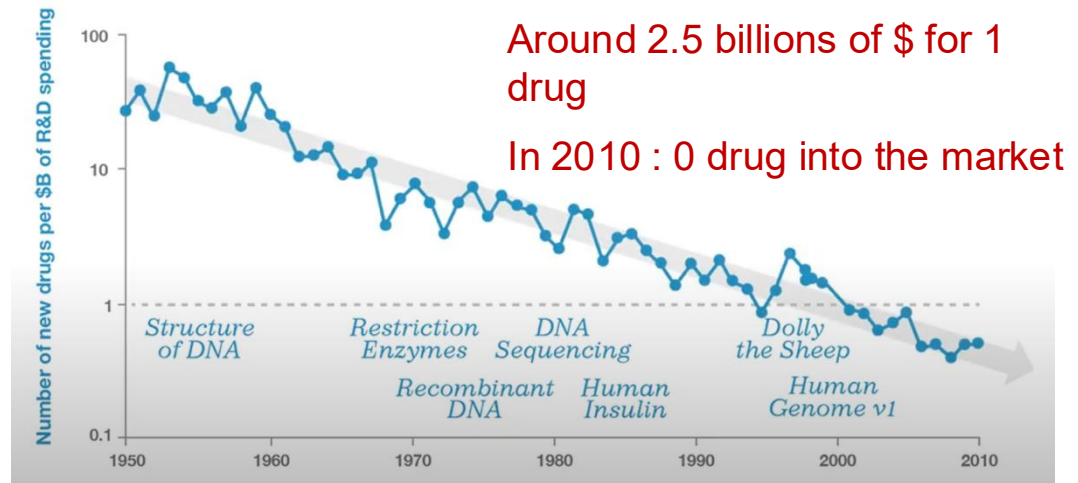


# 1. INTRODUCTION TO OOC TECHNOLOGY

OoC is a massive discovery for research :

- Drugs are too **expensive** to develop and test
- Labs dishes and animals are not good at mimicking a human body
- Our body cells are under constant **mechanical stress and forces**
- Need for more physiologically relevant human models

## R&D Productivity Is On The Decline



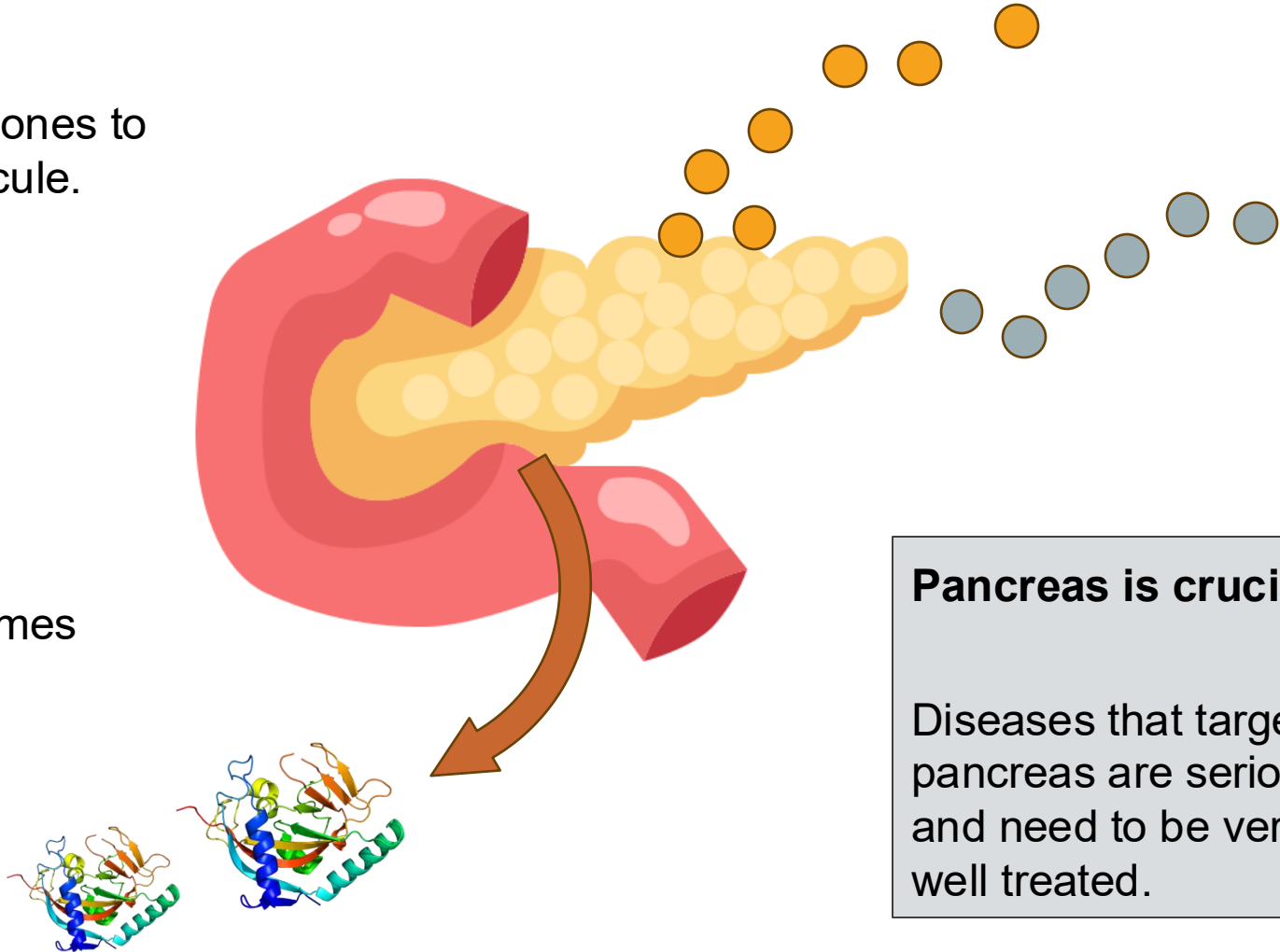
## 2. WHY THE PANCREAS ?

### ENDOCRINE

secretes hormones to regulate molecule.

### EXOCRINE

secretes enzymes to help the digestion.



**Pancreas is crucial :**

Diseases that target pancreas are serious and need to be very well treated.

# The technical sheet of the: Pancreatis Ductal Adenocarcinoma

One of the **deadliest** cancers

## PDAC OVERVIEW

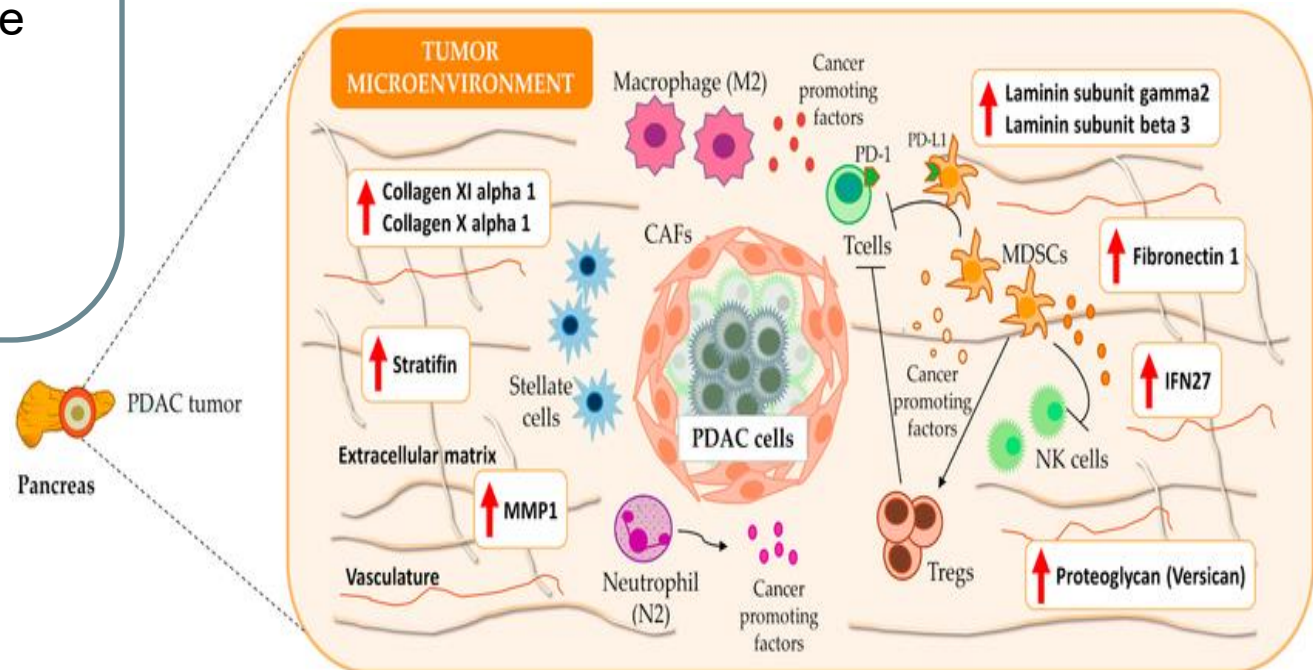
- 93% of all pancreatic cancers
- Aggressive and deadly (<10% survival chance)
- Current therapies are insufficient
- Large molecular heterogeneity

## CURRENT THERAPIES

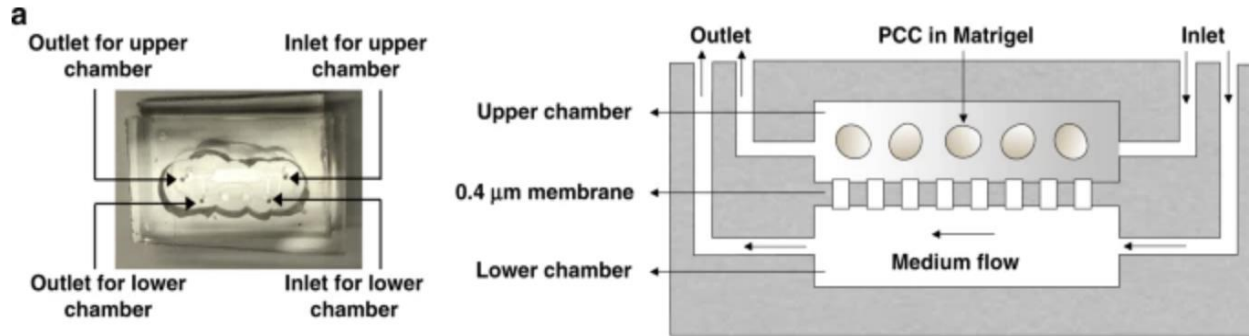
- Surgery
- Chemotherapy
- FOLFORINOX

## PRECISION MEDICINE

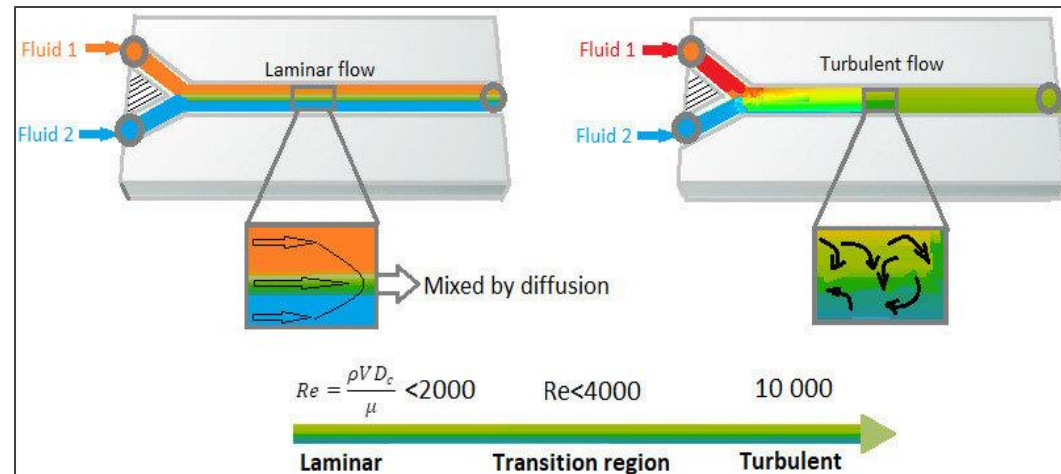
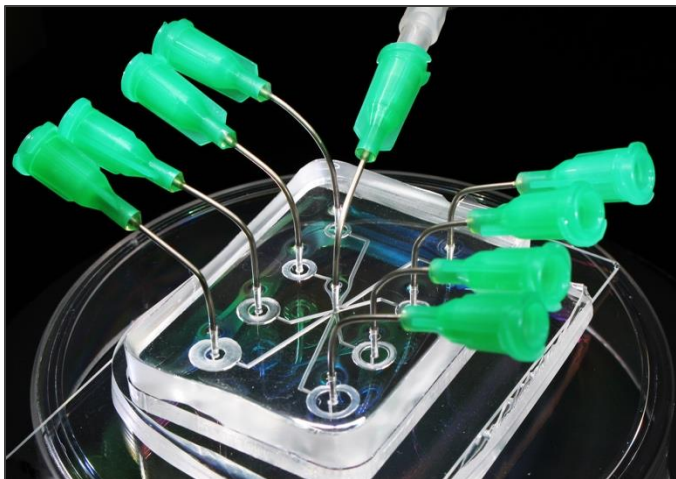
- Use the patient's cells
- Target the stroma



# 4. POC TECHNOLOGY REVIEW

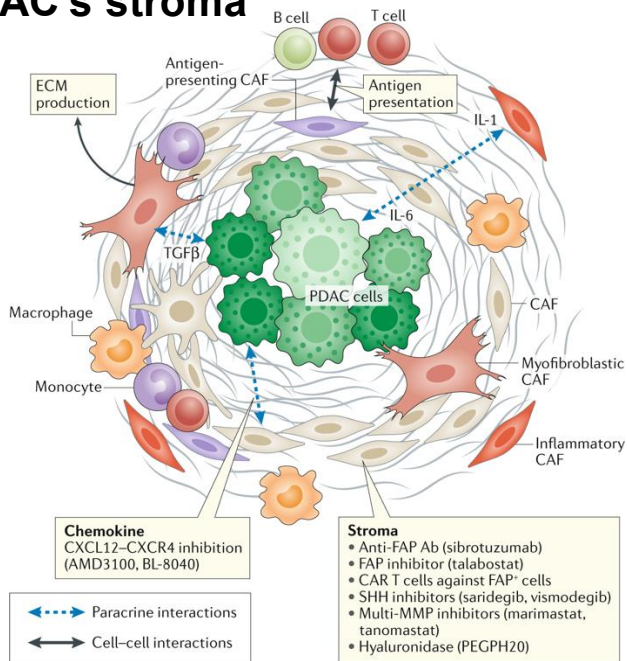


- Recreate the pancreas's complex cellular microenvironment with high fidelity.
- Monitor cellular behavior and interactions in real time.
- Uses fewer biological materials; allows **faster, cost-efficient testing**
- Accelerate experimental workflows and data acquisition.
- Applications: **disease modeling, drug screening, personalized medicine**

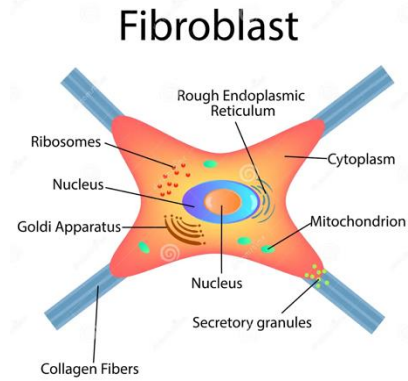


# PANCREATIC TUMOR-ON-A-CHIP (2022)

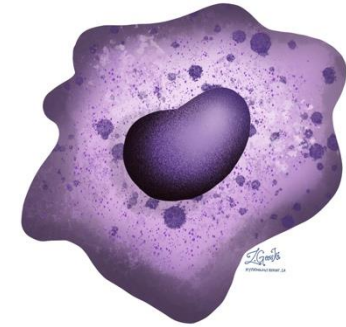
## PDAC's stroma



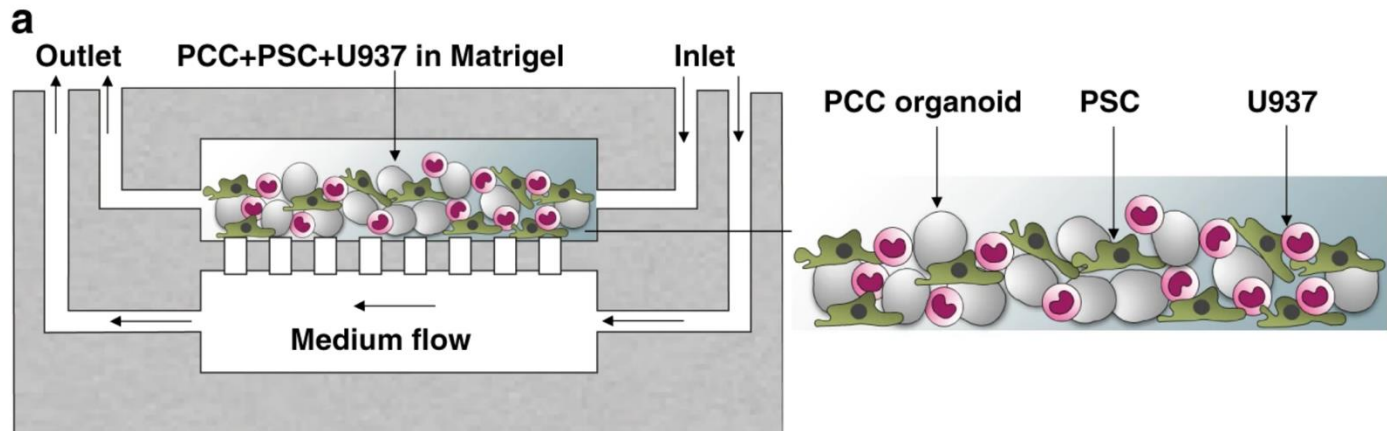
## PDAC's stroma recreation



## MACROPHAGE



## Chip of the 2022 paper structure

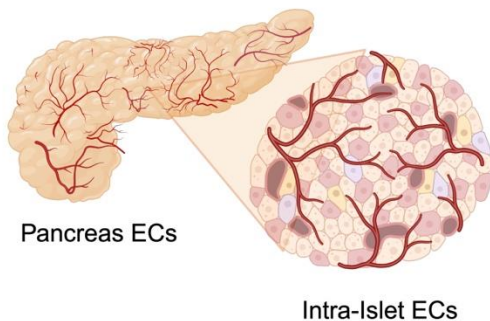


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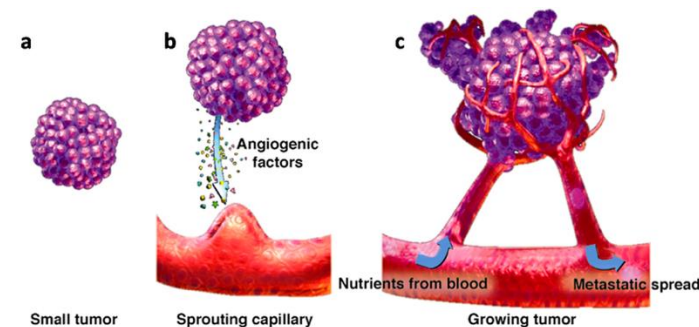
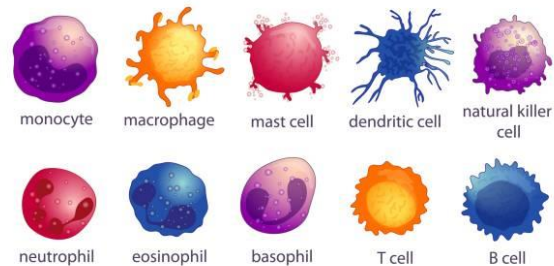
*What are the limitations of this device in the 2022 paper ?*

- 1) Only tested on 1 patient's cells
- 2) Stroma cells from commercial lines and not from the patient directly.

*What can we add to bring the technology even further ?*



## IMMUNE SYSTEM CELLS



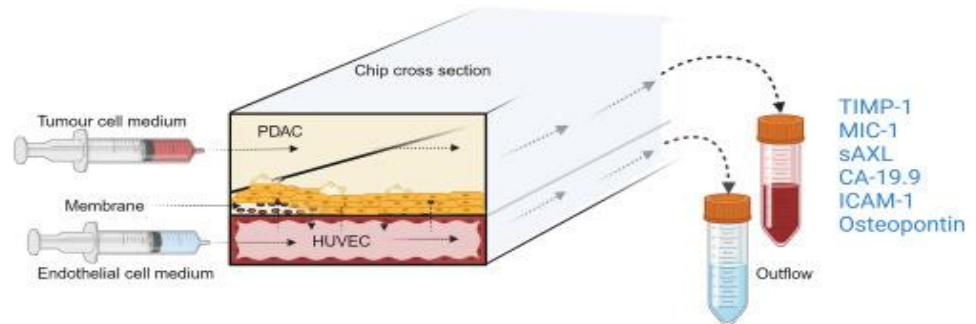
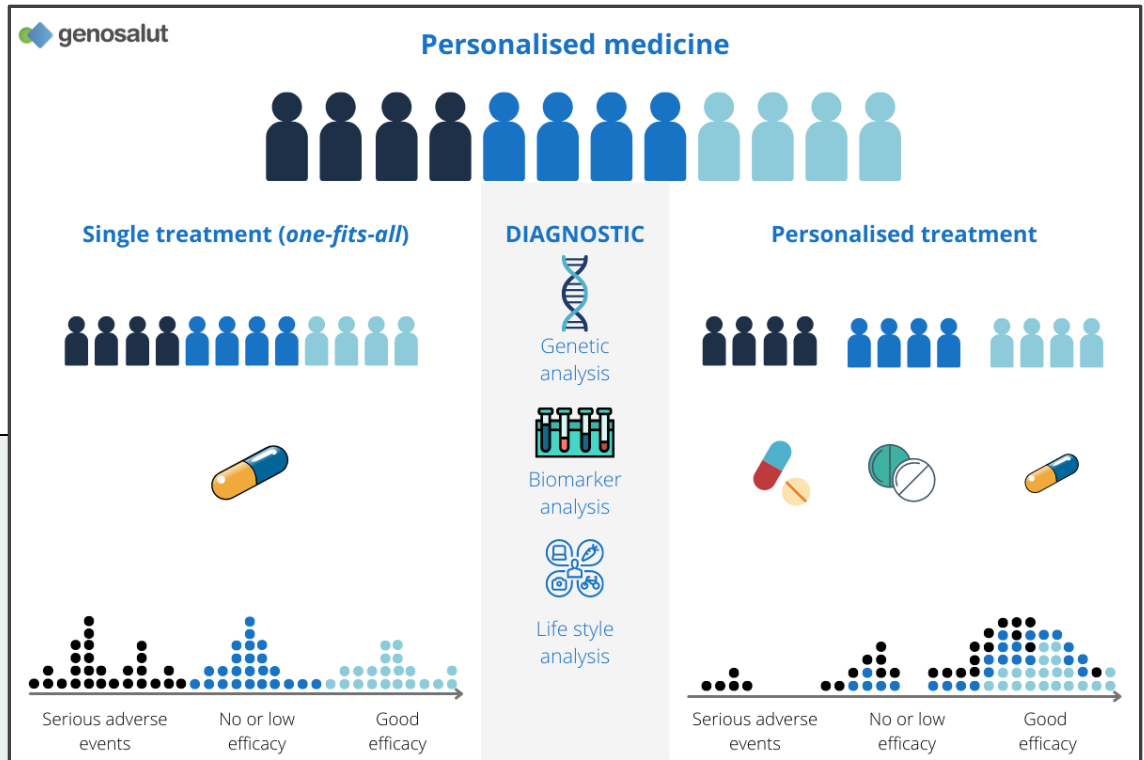
Use Endothelial cells to mimic even more the *in-situ* environment.

Use the entire patient's immune system and not only commercial cells.

Mimic tumor angiogenesis and mechanical stress.

# BREAKTHROUGH IN PERSONALIZED MEDICINE (2024)

- Recent advancement: Development of personalized pancreas-on-a-chip models.
- Use of patient-derived tumors, human pancreatic organoids (hPOs), and human umbilical vein endothelial cells (HUVECs).
- Recapitulates physiological vascular barrier and tumor interactions.
- Platform for precision medicine applications.



## KEY FEATURES OF THE PERSONALIZED PDAC CHIP (2024)

- PDMS-free chip design.
- Syringe pump for controlled, constant flow simulating blood vessel perfusion.
- Tumor and endothelial channels with continuous monitoring.
- Over 50 days of hPO culture with cell viability monitoring.
- Reliable detection of tumor biomarkers in outflows: CA-19.9, TIMP-1, Osteopontin, MIC-1, ICAM-1, sAXL.
- Gradual increase in tumor cell density and turnover.

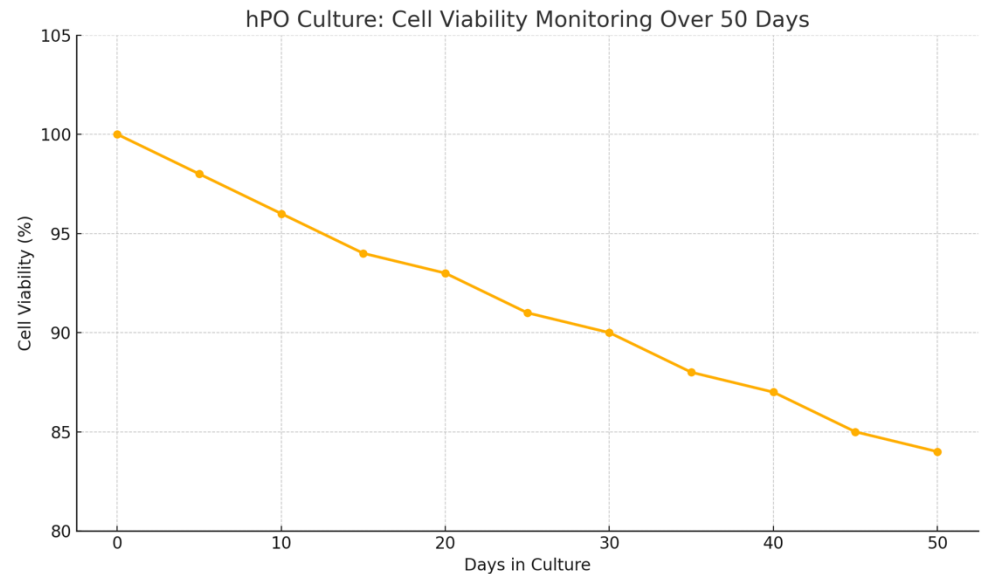
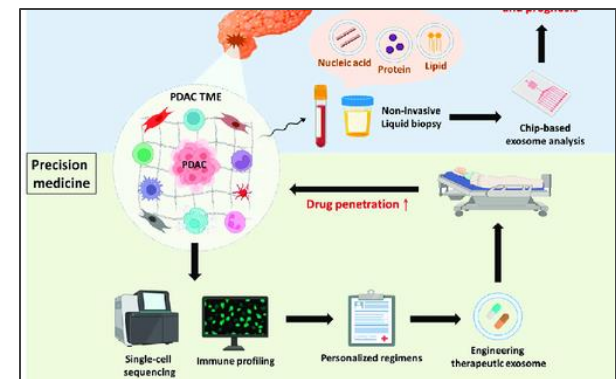
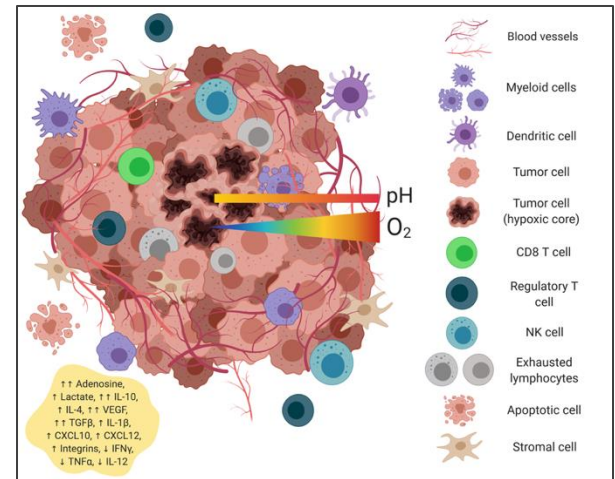


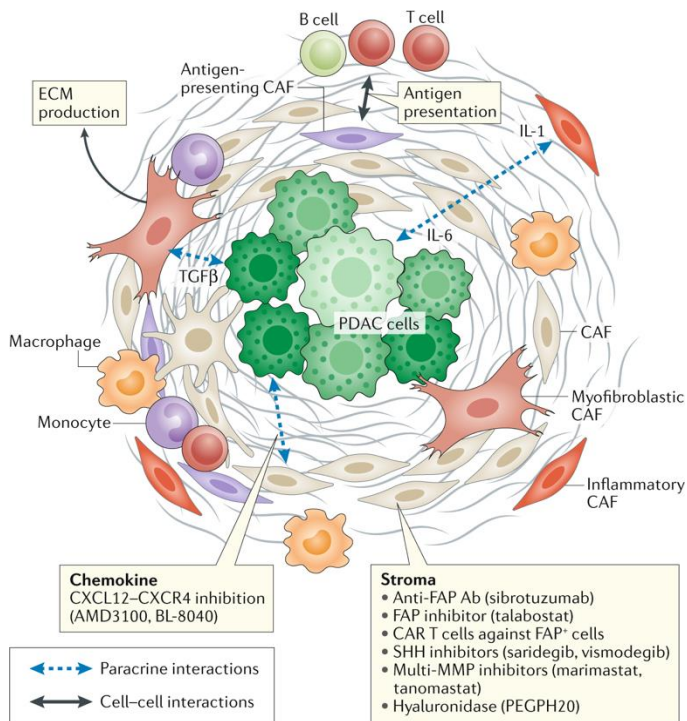
Figure: graph showing cell viability over 50 days of human pancreatic organoid (hPO) culture. It visually represents how viability remains relatively stable with a gradual decline, helping explain the long-term monitoring and robustness of pancreas-on-a-chip systems for personalized medicine.

# FUTURE APPLICATIONS OF THE PDAC CHIP

- Study aspects of tumor biology:
- Metastasis initiation.
- Drug-induced vascular damage.
- Impact of vascular deprivation and hypoxia on drug delivery.
- Potential to incorporate additional tumor microenvironment components.
- Expansion and Multi-Organ Models
- Two-compartment design for studying biologically relevant barriers (e.g., blood-brain barrier, placenta, lung, gut, kidney, skin, oral mucosa).
- Platform for multi-organ chip models.



# LIMITATIONS IN CANCER THERAPY RESEARCH



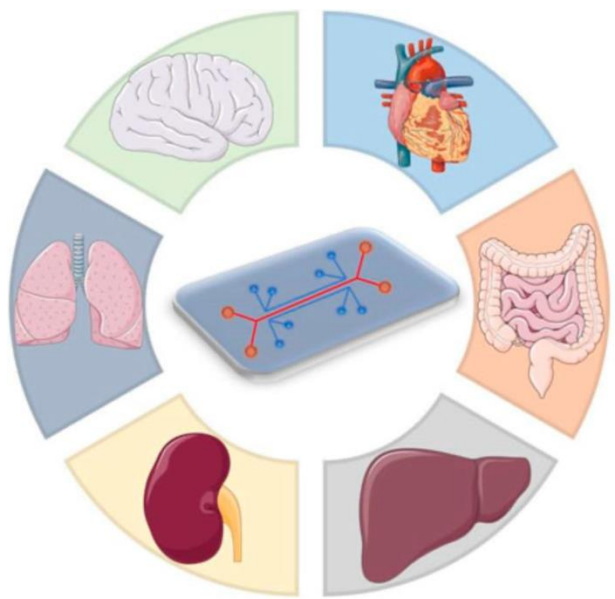
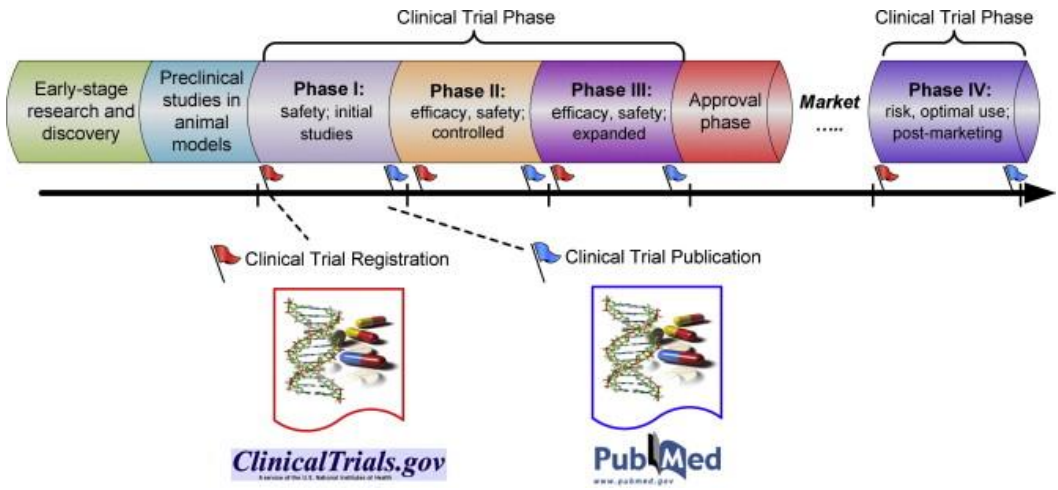
High heterogeneity → difficult to establish a standardized lab protocol

Clinical drugs trial are highly expensive to perform :

- 1 ) Design and manufacture the chip
- 2 ) Maintaining the systems (pump, cells, ...)

**Personalized medicine = Personalized chip = 1 chip for 1 patient**

# CONCLUSION



Drug development pipeline – ResearchGate (2012)

Big step in the future : body on a chip

Time from the pre-trials stage to the released into the market :

Previous models : 10-15 years  
PoC model : ? years

Drugs metabolized in 1 and only 1 OoC could be differently metabolized in many OoCs

# REFERENCES

## Scientific papers:

**Human organs-on-chips for disease modelling, drug development and personalized medicine**

<https://www.nature.com/articles/s41576-022-00466-9>

**Personalized PDAC chip with functional endothelial barrier for tumour biomarker detection: A platform for precision medicine applications**

<https://www.sciencedirect.com/science/article/pii/S2590006424003235>

**Patient-derived pancreatic cancer-on-a-chip recapitulates the tumor microenvironment**

<https://www.nature.com/articles/s41378-022-00370-6>

## YouTube Videos :

**Pushing boundaries with human organs-on-a-chip | Janick Stucki | TEDxBern**

**Why organs-on-chips raise the odds in drug development | Jos Joore | TEDxBoerhaavedistrictStudio**

**Geraldine Hamilton: Nos organes sur une puce.**

**What is organ-on-a-chip technology?**

**A guide to the organ-on-a-chip**

<https://www.nature.com/articles/s43586-022-00118-6>

<https://wyss.harvard.edu/technology/human-organs-on-chips/>

