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CROSS CARE

Cross-border cooperation to foster the resilience of clinical management in cancer patients by establishing best practices in personalized molecular-based diagnostics, treatment, and long-term care

RORS00040

From tumor “-on-a-” patient to tumor-on-a-chip

Building a Translational Pipeline for Personalized Surgical Oncology

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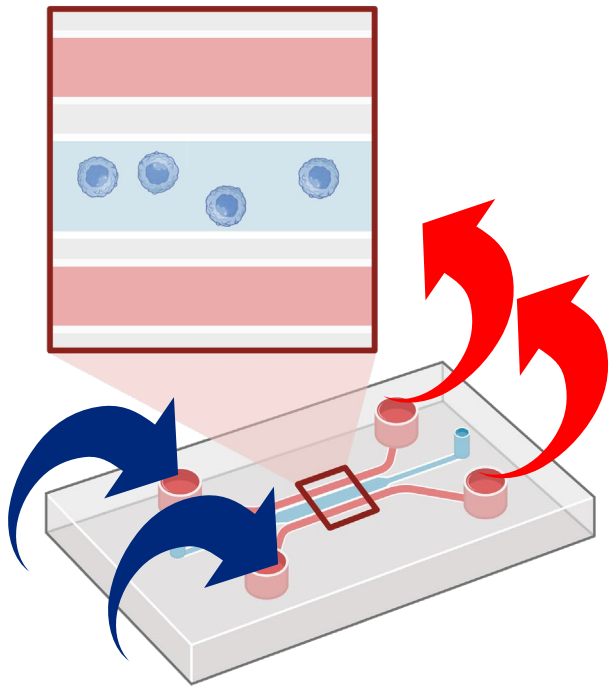
What are "on-chip" platforms?



- **Microfluidic in-vitro systems** that culture living human cells in controlled, perfused environments
- **Recreate key features of the tumor microenvironment** (architecture, flow, gradients, cell–cell interactions)
- **Integrate multiple cell types** (tumor epithelium, stroma, endothelium, immune cells)
- **Enable dynamic drug exposure and real-time monitoring** (viability, barrier function, metabolism, invasion)
- **Bridge the gap between static cultures and in-vivo models**

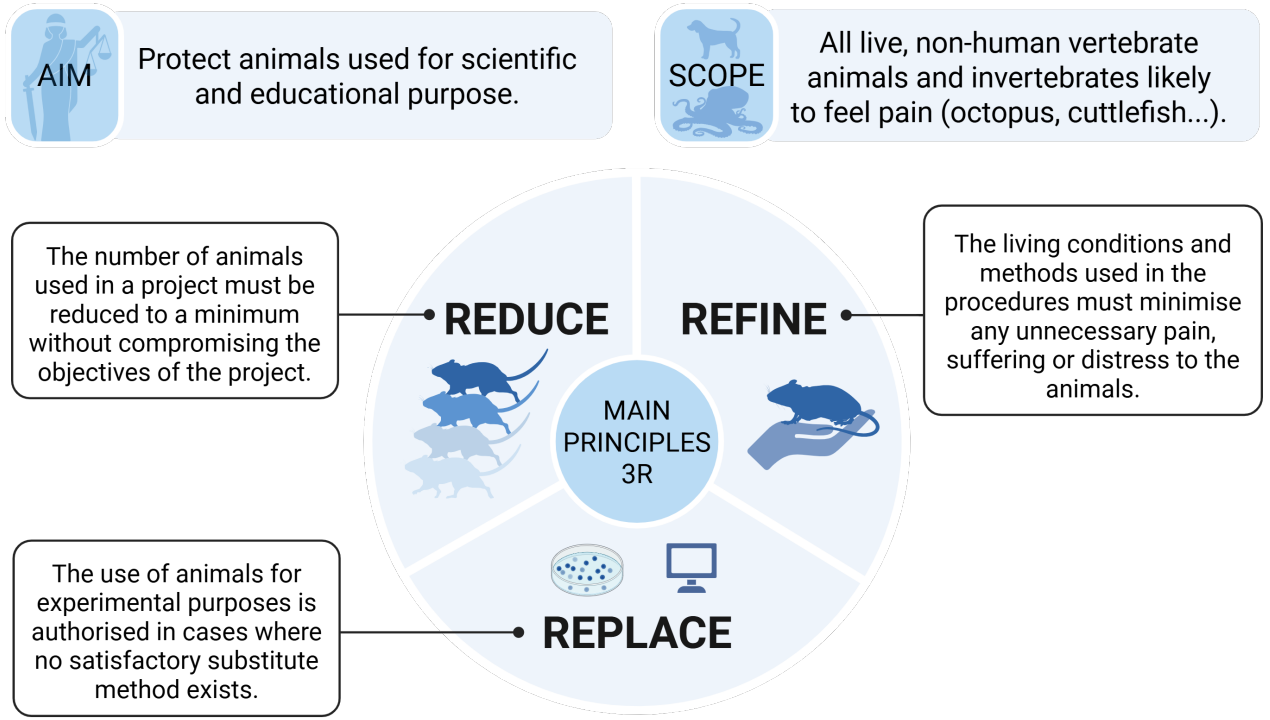
Rationale & Clinical Need

Why do we need tumor-on-a-chip?

- PDAC, CRC and HCC have poor prognosis despite guideline-based therapy.
- Current treatment decisions rely on population-level evidence, not individual tumor behavior.
- Patient-derived models (organoids, tumor-on-a-chip) ***could*** predict chemotherapy response **before** administering treatment.
- Implementation of *3R's*
- **Opportunity:** integrate personalized testing into surgical oncology workflow.

EU Directive 2010/63

3R



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Overall Concept of the Project

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INTRAOPERATIVE SAMPLING

CELLS ISOLATION AND SEEDING

ON CHIP CULTURING AND MONITORING

PERSONALISED DRUG TESTING

ENDPOINT COMPARISON

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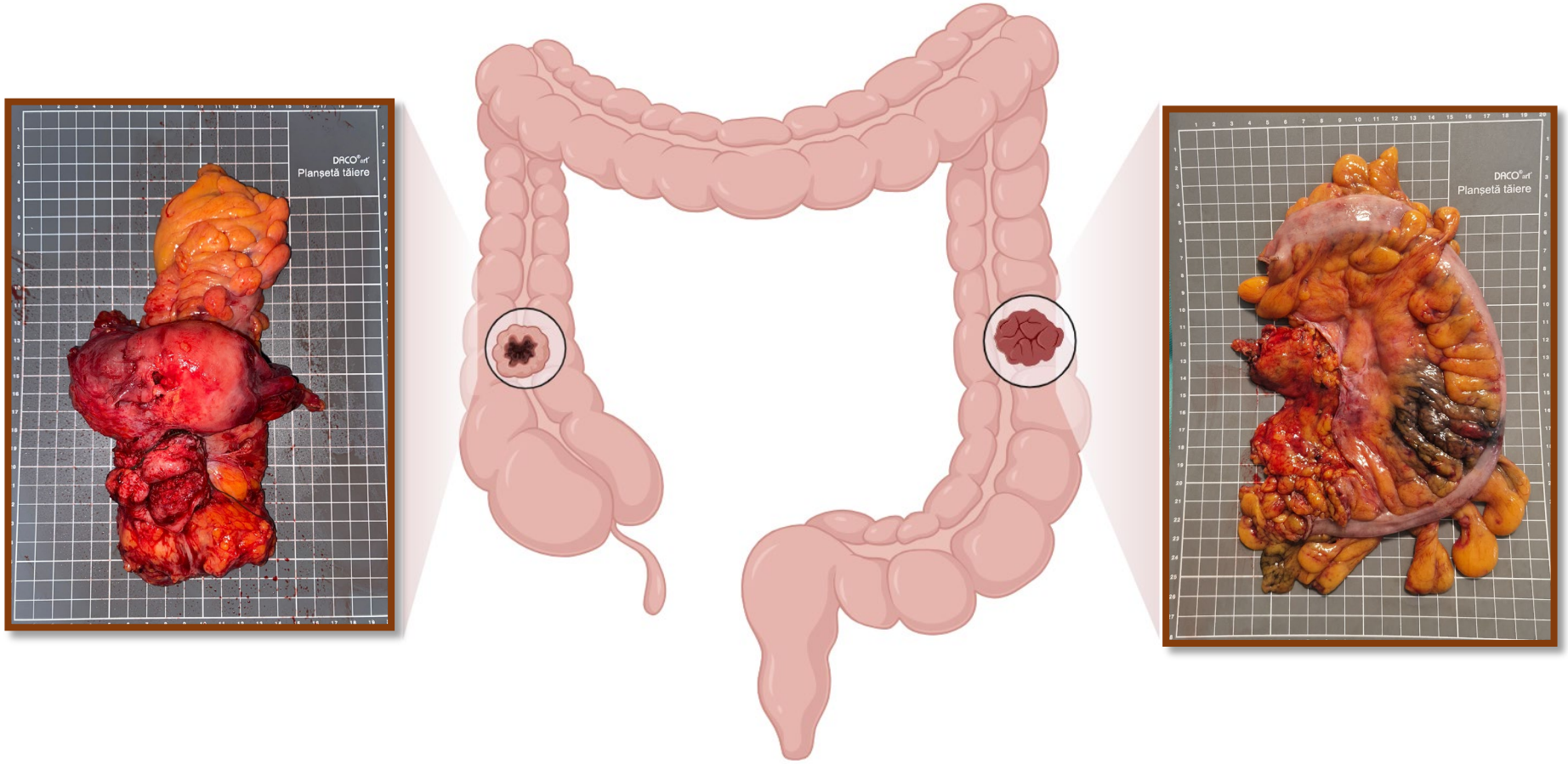
Intraoperative sampling

Colon Cancer

- T3–T4 tumors operated by open approach
- Tumor identified by preoperative endoscopic tattooing and palpation
- Sampling after *arterial exclusion*
- ≥5 *Tru-Cut biopsies* from different tumor regions



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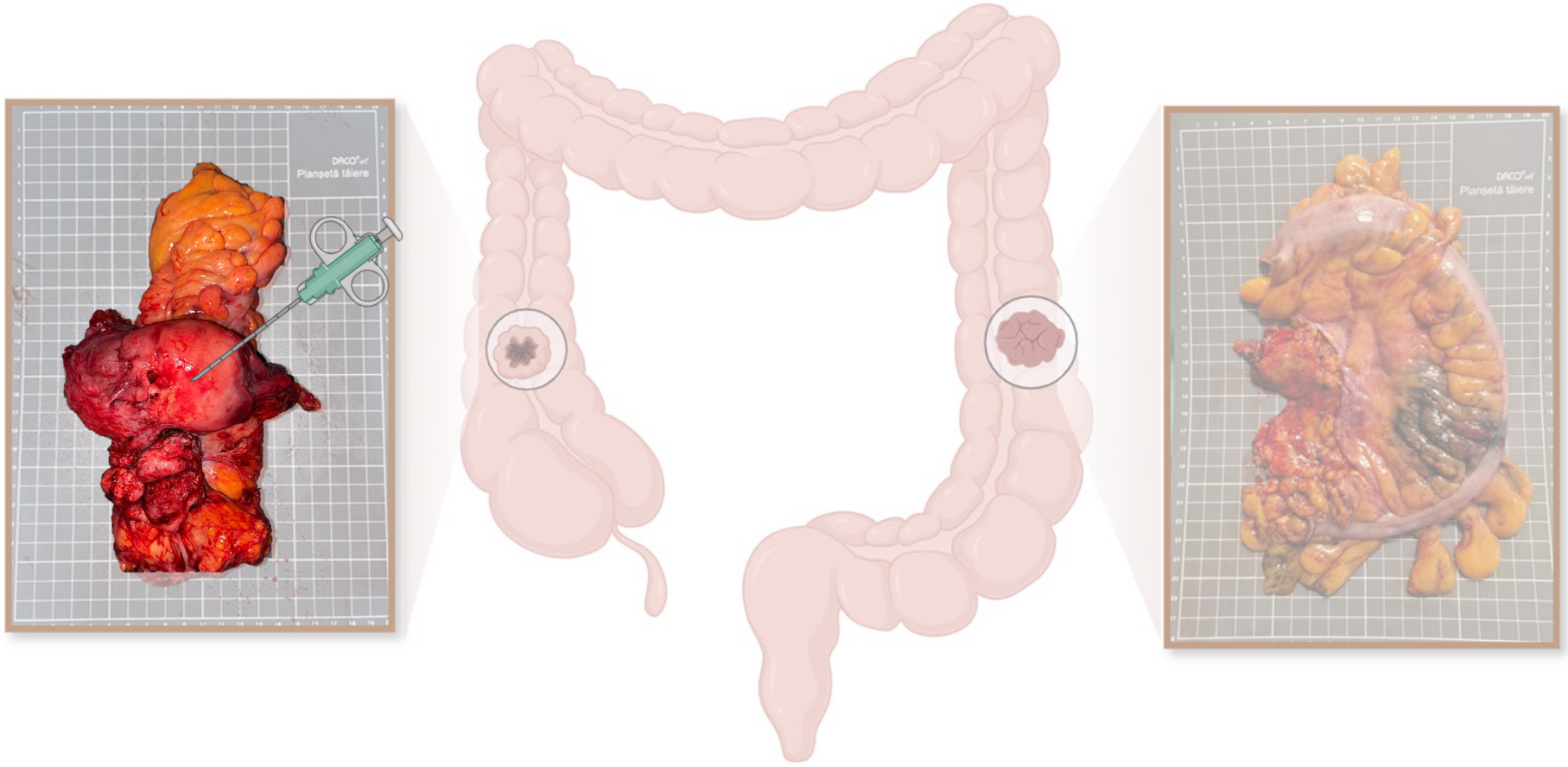
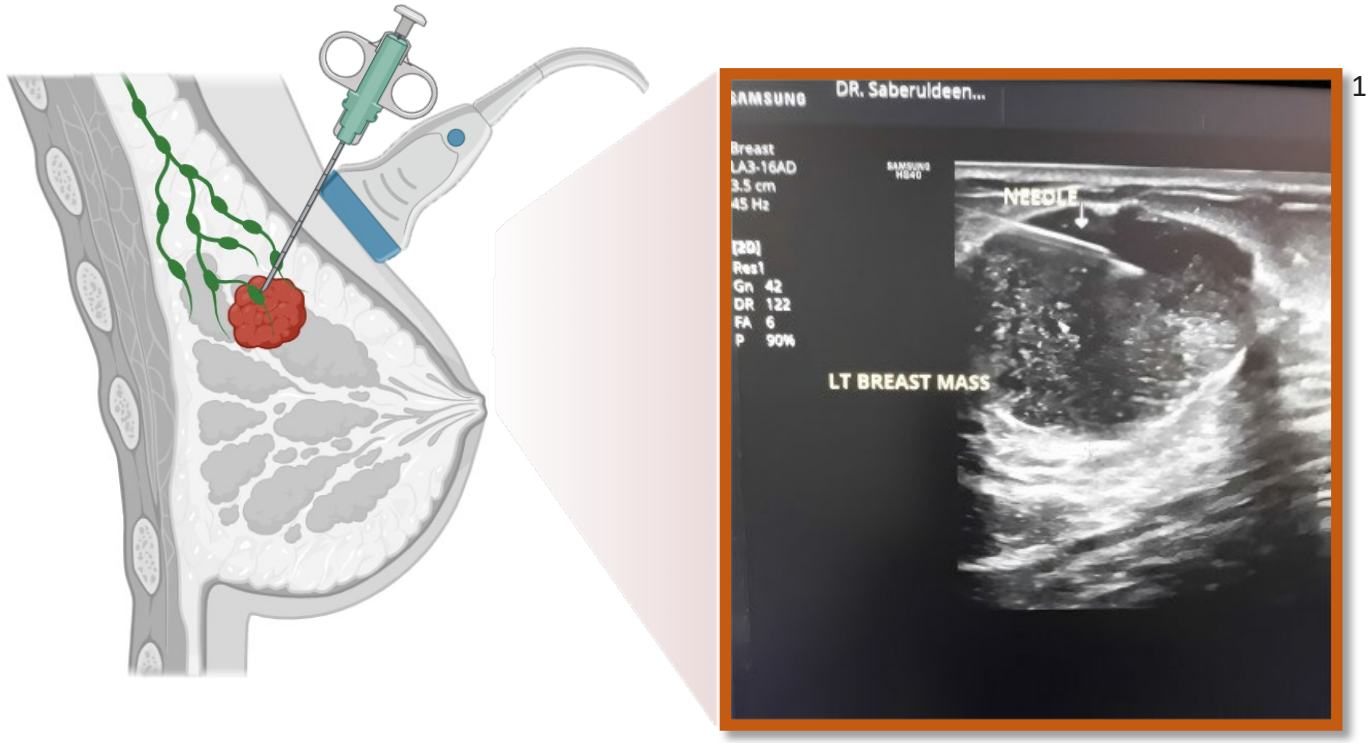


Pre-operative sampling

Breast Cancer

- Preoperative ultrasound-guided Tru-Cut biopsy
- BIRADS 4/5/6
- Minimal tissue trauma, high cellular yield

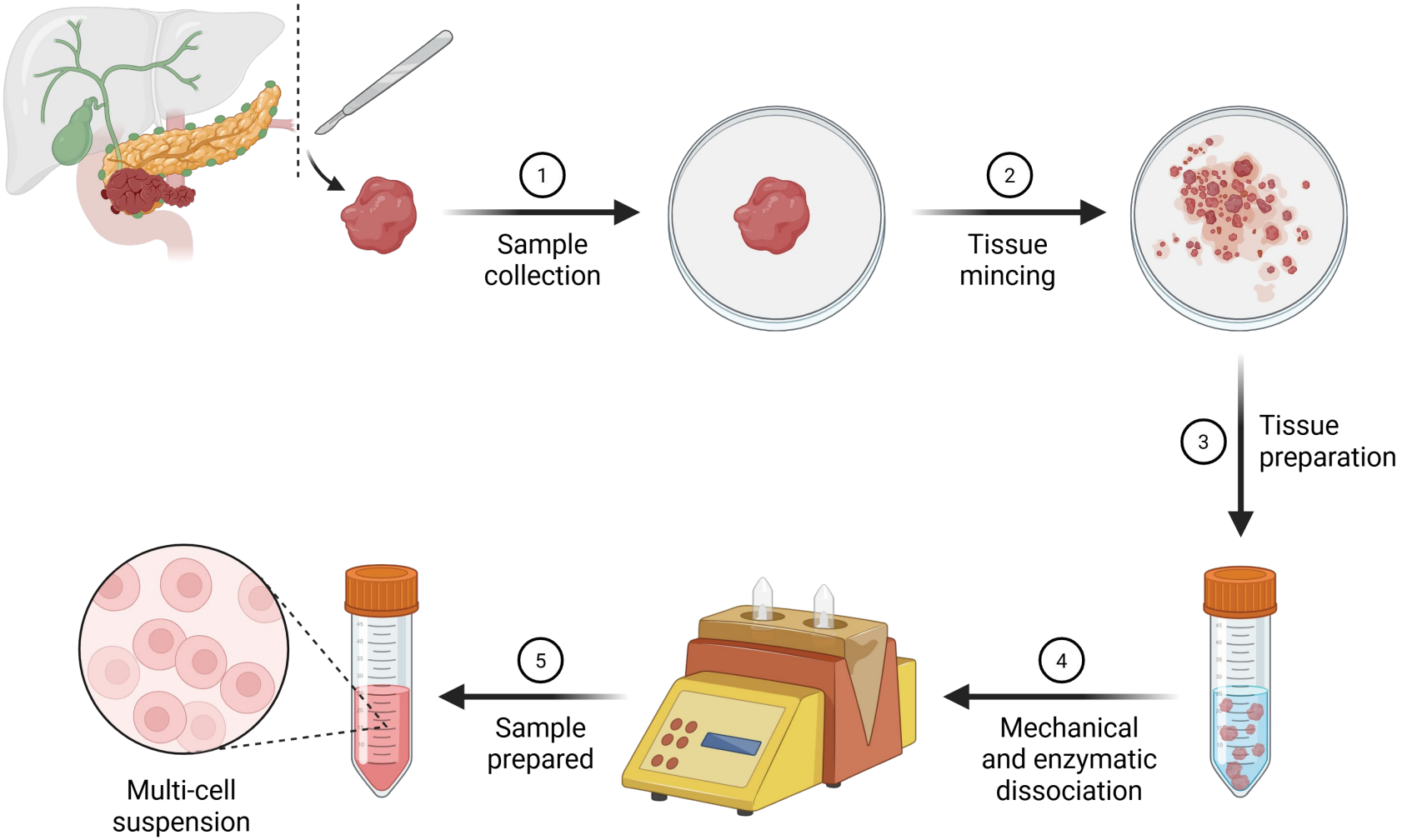


[1]

[1]Al Zobair AA, Al-Nauimy WM, Mohammed SM. Accuracy of Image-guided Tru-cut biopsy in the diagnosis of breast tumors. Cancer Treat Res Commun. 2025;44:100955. doi: 10.1016/j.ctarc.2025.100955. Epub 2025 Jun 17. PMID: 40543418.

Biopsy handling

Tumor cells retrieval and isolation



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Cell seeding

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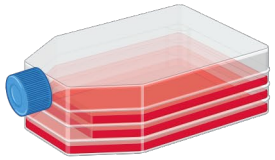
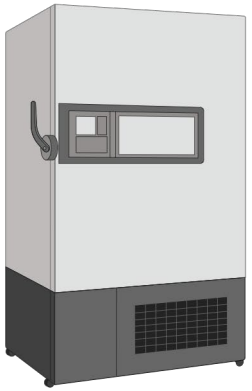
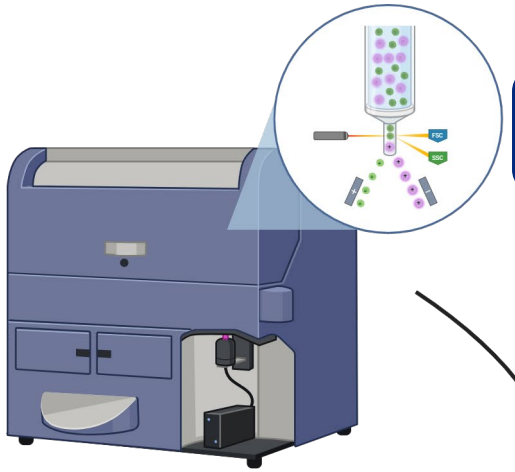
Culturing cells for 7-10 days



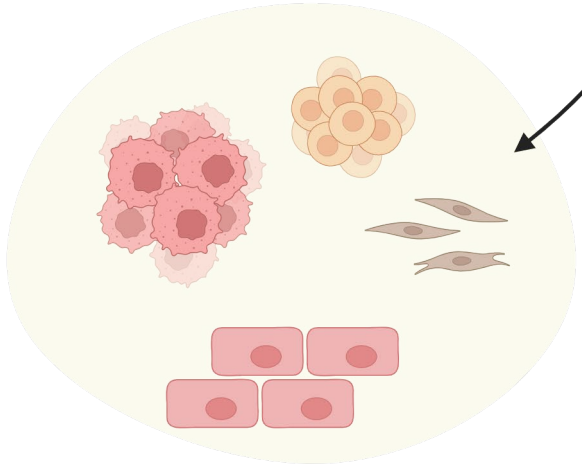
Freezing in -80 while colecting samples



Defreezing



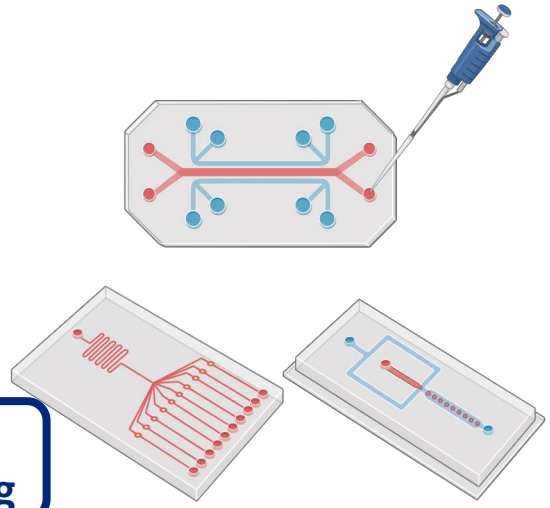
Flowcitometry



Culturing isolated cells

Choosing/ Engeneering the corect chip format

On Chip seeding



Culturing and microperfusing

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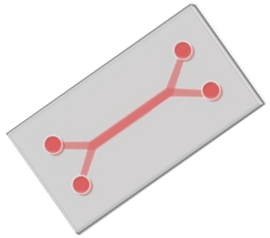
On chip Platforms

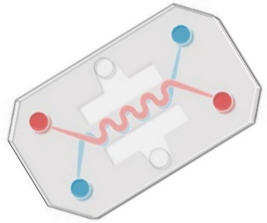
Single-Channel Chips

- Tumor cells in ECM under perfusion
- Simple viability & drug-response assays



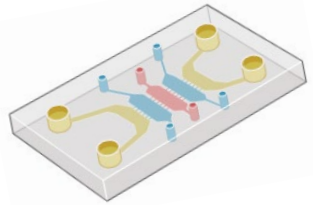
Dual-Channel (Barrier) Chips

- Two channels + porous membrane
- Tumor ↔ endothelium/stroma interaction
- TEER for real-time barrier monitoring



Multi-Compartment Chips

- 3+ channels: tumor, stroma, endothelium
- Recreates gradients (O_2, pH, nutrients)
- Supports **immune & CAF interactions**



Microfluidic Principles

- Controlled perfusion → **physiologic shear stress**
- **Dynamic flow** → realistic drug delivery profiles
- **Gradients** generated inside chip (oxygen, acidity, metabolites)
- Integration of **sensors** (TEER, pH, O_2)
- **Small volumes** → rapid, patient-specific testing

Personalised drug testing

Personalized Drug Testing on Chip

- **Patient-specific functional testing** before therapy
- Integration of **genetics, proteomics, and epigenetics**
- Dynamic assessment under **physiologic/ pathologic perfusion and microenvironmental conditions**
- Ability to test **multiple therapies and combinations ex-vivo**
- **Personalised toxicity response in Multi-tissue series Chips, (heart on chip, liver on chip, kidney on chip)**

Classical Oncologic Treatment

- Treatment guided by **population-based protocols**
- **Genetic testing** limited to predefined panels (e.g. KRAS, HER2, BRCA)
- Therapy selection based on **tumor type and stage**
- Chemotherapy, radiotherapy, and immunotherapy administered **without direct functional testing**
- Response assessed **after treatment**, through imaging and biomarkers

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Predicts efficacy and resistance prior to patient exposure

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Perspectives

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1. Minimally Invasive, Repeatable Sampling

Circulating tumor cells (CTCs), ctDNA, and exosomes can be collected longitudinally, enabling real-time monitoring without repeated tissue biopsies.

2. Early Detection of Treatment Resistance

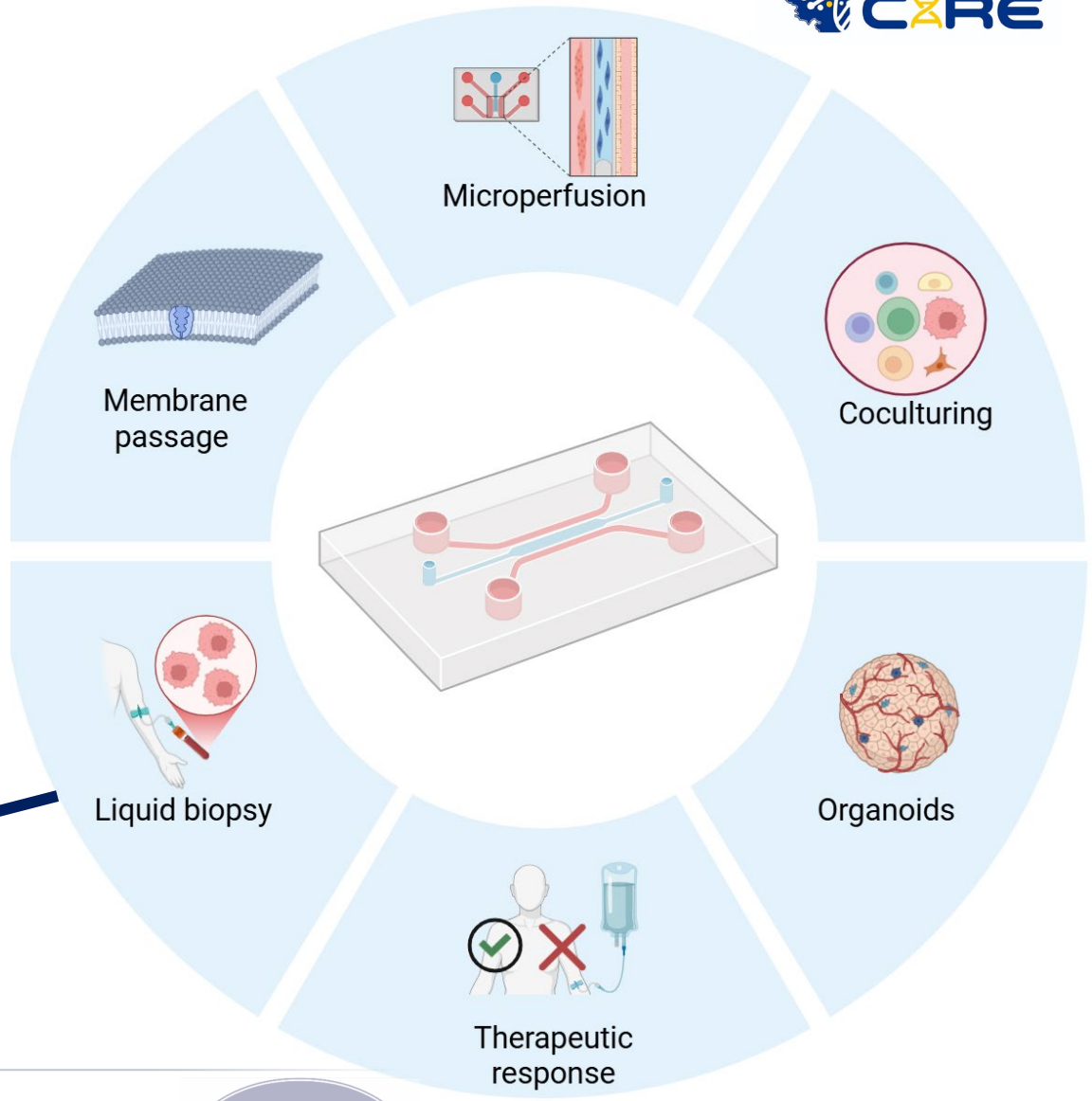
*Liquid biopsy detects emerging mutations, clonal evolution, and resistance signatures **before** they become clinically visible.*

3. Integration With Tumor-on-a-Chip Models

*CTCs or ctDNA-derived organoids can be seeded on-chip to create **dynamic, real-time models** reflecting tumor evolution during therapy.*

4. Pathway to True Personalized Therapy

*Combining liquid biopsy biomarkers with chip-based drug testing may allow **rapid adaptation** of treatment plans and identification of optimal therapy windows.*



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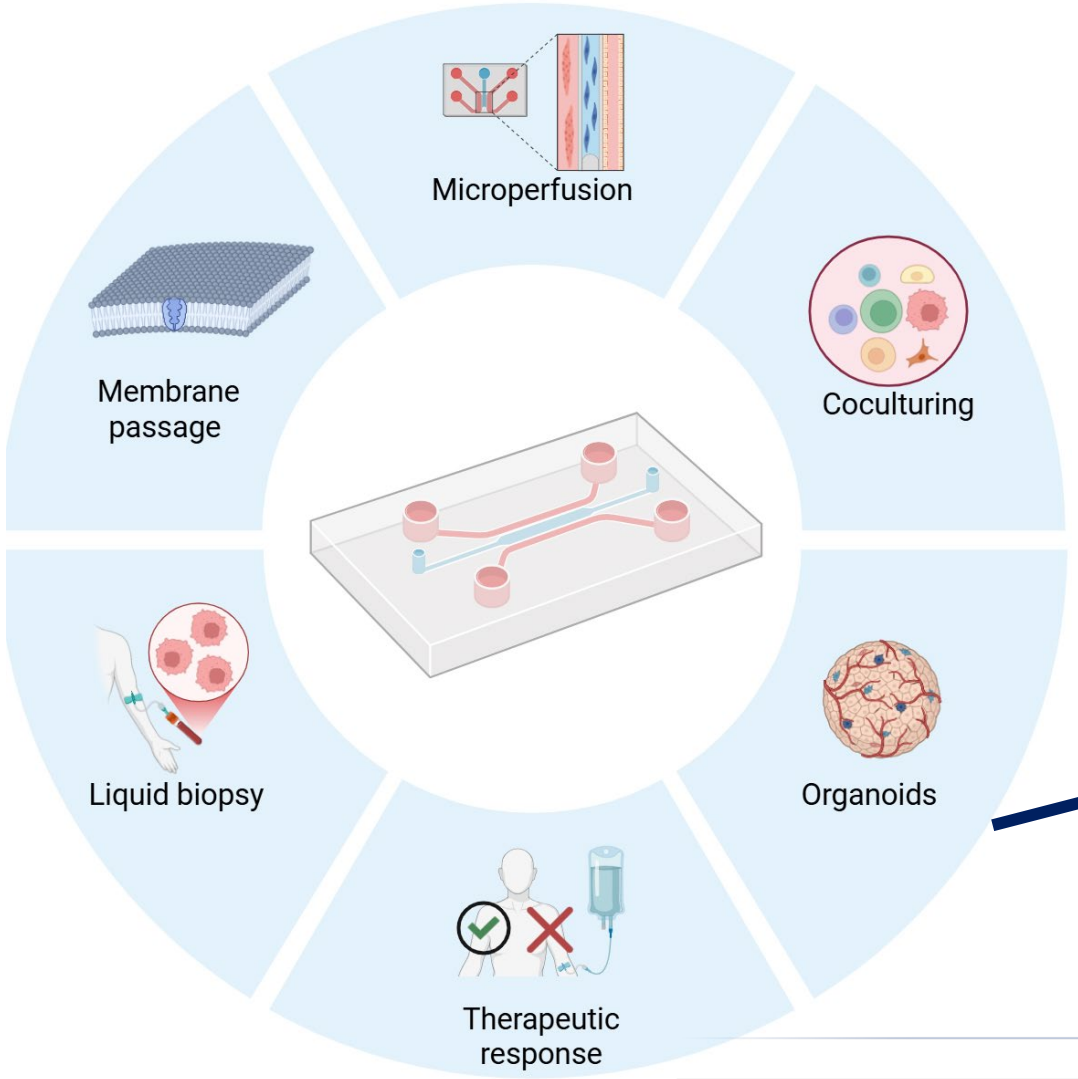
Perspectives



1. Enhanced Physiological Fidelity

*Combining organoids/aglutinoids with microfluidic perfusion recreates **vascular flow, biochemical gradients, and stromal interactions**, producing a model that more closely mimics in-vivo tumor biology than static cultures.*

2. Accelerated and Scalable Personalized Testing

*Organoid-derived chips enable **rapid drug screening** using minimal patient material, with higher throughput and faster readouts than traditional organoid platforms — ideal for personalized oncology workflows.*

3. Integration of Complex Tumor Microenvironment Components

*Chips allow controlled co-culture of immune cells, CAFs, endothelial layers, and ECM variants, enabling **immune-oncology studies, metastasis modeling, and microenvironment-driven therapy response prediction.***

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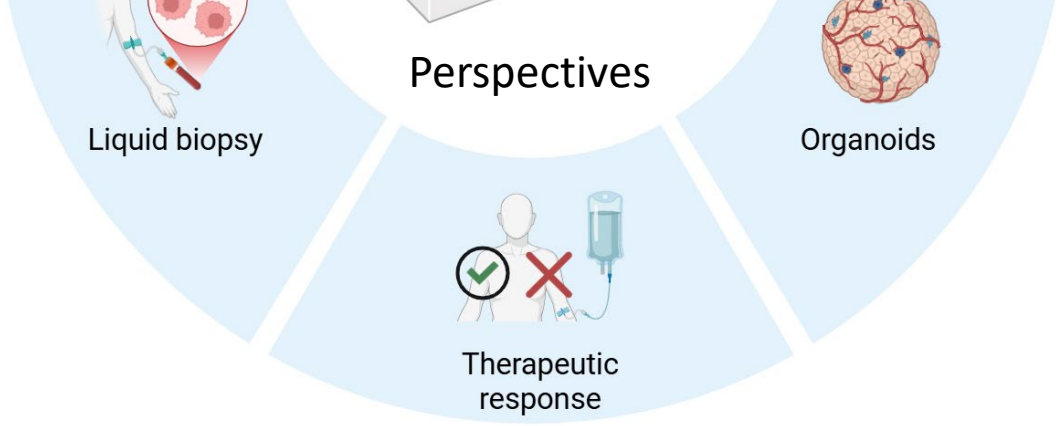

Oncologic Patients postoperative follow-up through their oncologic treatment- response to chemo-/ radio-/ imunotherapy

Patient's isolated tumor cells/ organoids follow-up through their treatment regime- response to chemo-/ radio-/ immunotherapy.

ENDPOINT DATA ANALYSIS

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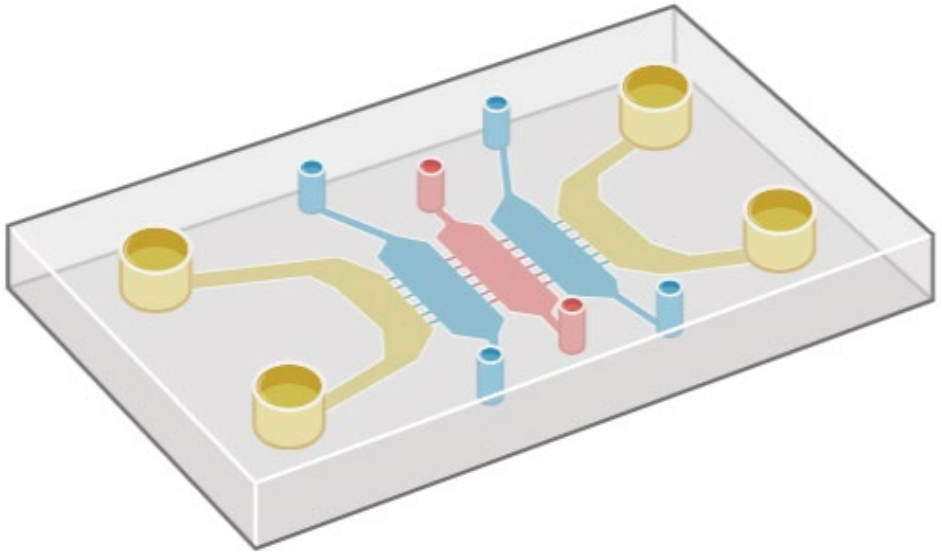
Conclusion



- **Tumor-on-a-chip platforms enable functional, patient-specific testing** beyond classical stratification
- **Microfluidic systems recreate key tumor microenvironment features** influencing therapy response
- **On-chip drug testing allows evaluation of molecular, proteomic, genetic and epigenetic responses** before patient treatment
- **This approach bridges the gap between experimental models and clinical decision-making**
- **Lays the foundation for future precision oncology strategies in aggressive solid tumors**

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Take-Home Message:

Test first — treat after.

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