CRC-on-a-Chip: A Predictive Platform for Colorectal Cancer Drug Testing

A 5-Fluorouracil (5-FU) Case Study

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The Challenge in CRC Drug Development

Colorectal cancer (CRC) is the second leading cause of cancer-related mortality worldwide. Despite intense research, **over 90% of oncology drug candidates fail in clinical trials**, largely because traditional preclinical models lack predictive power:

- **2D cell cultures** oversimplify the tumor microenvironment.
- **Animal models** are costly, time-consuming, and poorly mimic human tumor–vascular interactions.

Pharma companies need **clinically relevant in vitro systems** that bridge the gap between discovery and the clinic.

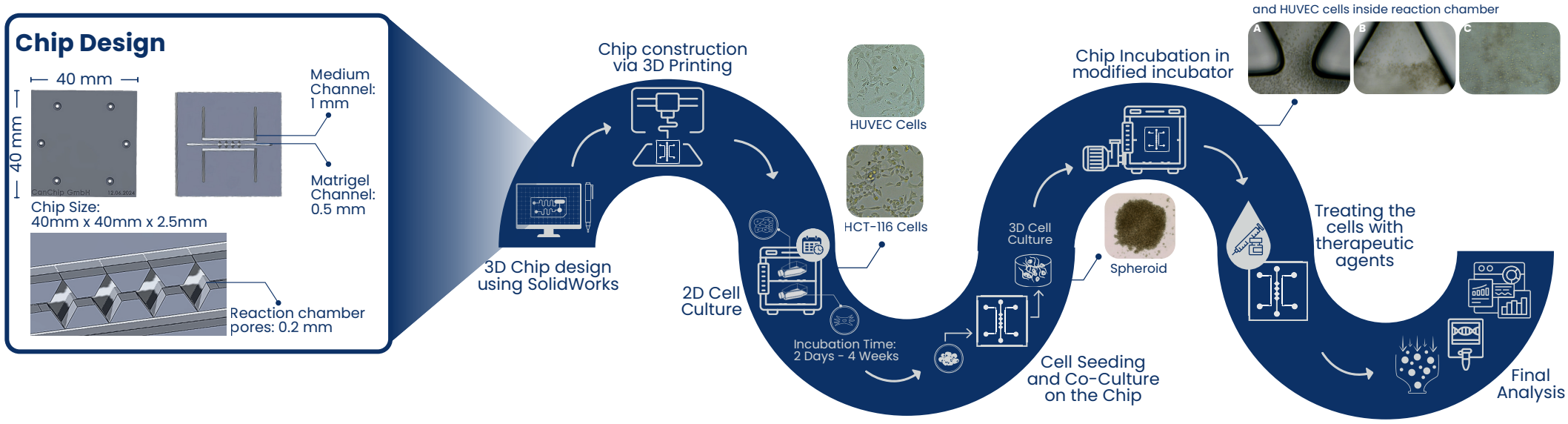
Our Solution: CRC-on-a-Chip

CanChip has developed a **3D microfluidic co-culture platform** that integrates HCT116 colorectal tumor spheroids with HUVEC endothelial cells under **continuous perfusion flow**.

- Preserves tumor–endothelial crosstalk.
- Mimics **in vivo-like pharmacokinetics**.
- Generates **mechanistic readouts** (gene expression, viability, morphology).
- Ensures reproducibility through **ISO 9001–aligned QA systems**.

This approach delivers **translationally relevant insights** for drug screening, mechanism studies, and resistance profiling.

Workflow

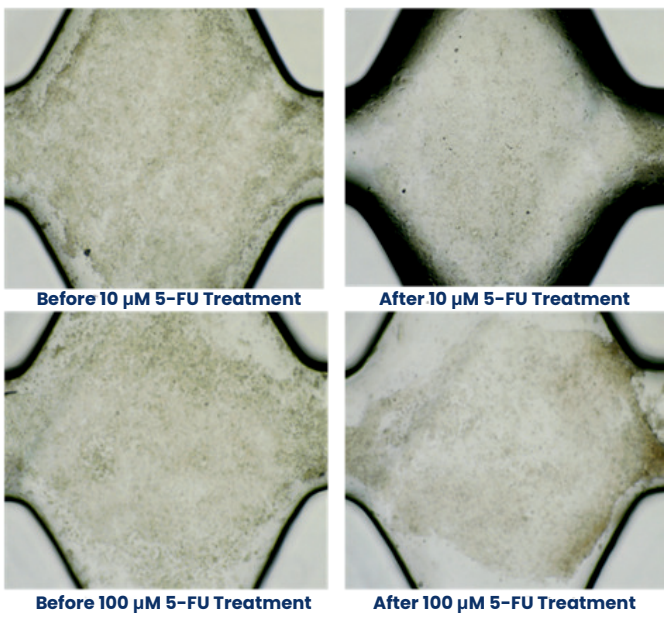


Case Study: 5-Fluorouracil (5-FU)

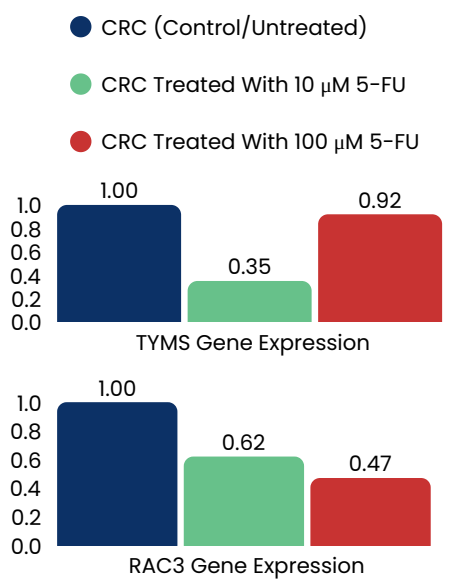
We evaluated 5-FU, the clinical standard for CRC therapy, at 10 µM (clinically relevant) and 100 µM (supra-physiological) for 48 hours.

Result

- **Morphology:** Dose-dependent shrinkage, 3D cell disintegration, and debris accumulation.
- **Viability (MTT):** HCT116 tumor cells highly sensitive at low micromolar concentrations, endothelial cells more resistant.
- **Gene expression (qRT-PCR):**
  - **RAC3:** Dose-dependent downregulation (0.69× at 10 µM; 0.47× at 100 µM vs. control).
  - **TYMS:** Maximal suppression at 10 µM (0.35× vs. control), less reduction at 100 µM (0.92×).



Microscopic images from the CRC chips before and after treatment.



Relative RAC3 and TYMS gene expression at 0, 10, and 100 µM of 5-FU.

Implications for Pharma R&D

- **Clinically aligned efficacy:** Matches patient plasma levels of 5-FU (~10 µM).
- **Mechanistic clarity:** Distinguishes between target engagement (TYMS) and broader cancer signaling (RAC3).
- **Predictive advantage:** Captures drug–vascular interactions missed in static assays.
- **Applications:** Candidate screening, biomarker validation, resistance studies, combination therapies.

Partner with CanChip

Our CRC-on-a-Chip platform demonstrates **scientific rigor and translational impact**. Partnering with **CanChip** enables pharma to:

- **Reduce** attrition in oncology pipelines.
- **Accelerate** preclinical decision-making.
- **De-risk** early clinical trials with mechanistically validated models.

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