Advancing Colorectal Cancer Research

3D-Printed "Cancer-on-a-Chip" Model for Studying Angiogenesis

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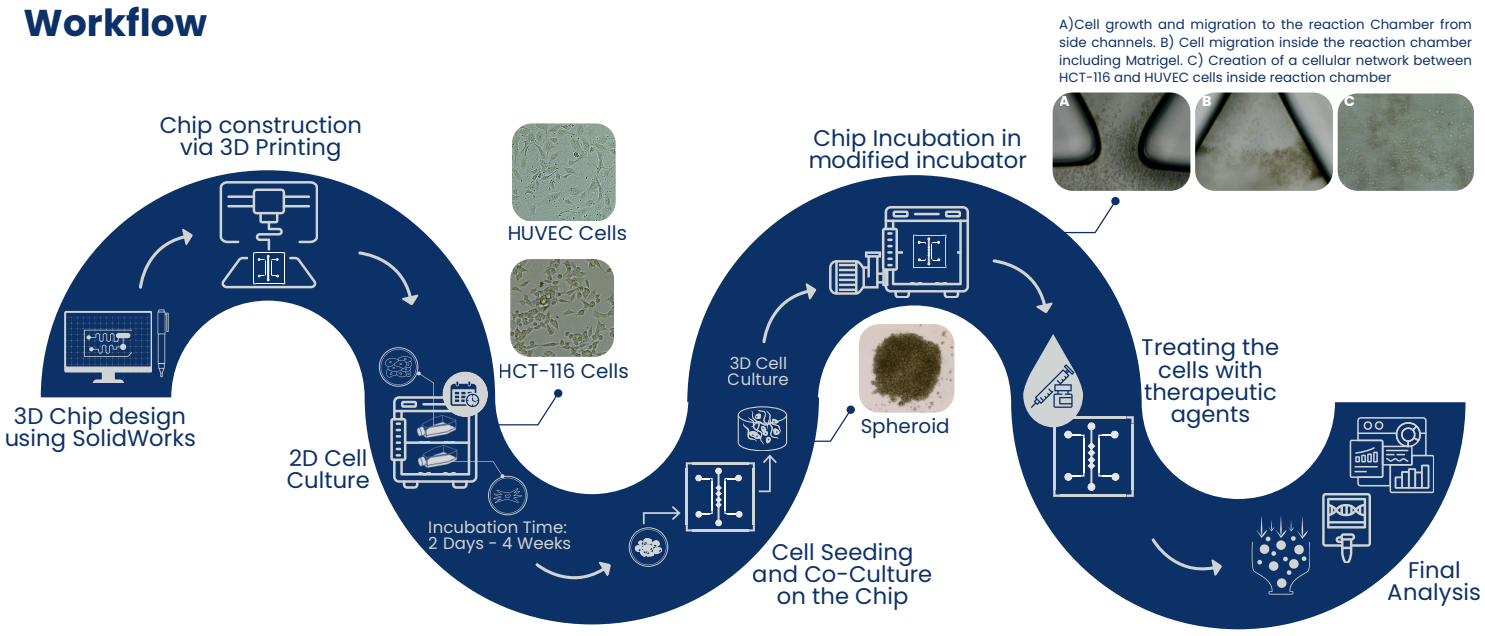
Introduction

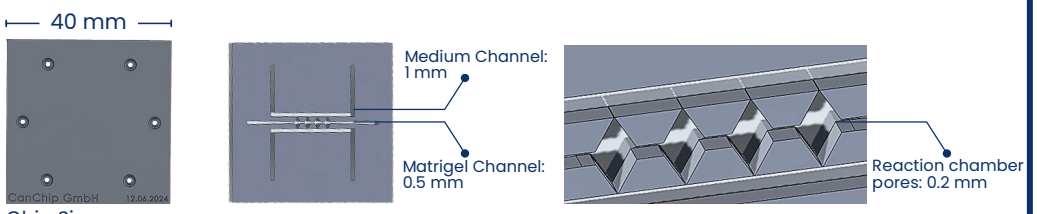
Tumor angiogenesis is central to CRC progression and metastasis, yet conventional 2D models cannot replicate the spatial and physiological complexity of the tumor microenvironment. This limits insights into cell–cell interactions and vascularization.

To overcome these gaps, we developed a 3D-printed "CRC-on-a-chip" system co-culturing HCT116 cells with HUVECs to mimic angiogenic interactions. This platform offers a more realistic model for studying CRC angiogenesis and provides a reliable foundation for drug testing and molecular research.

Workflow

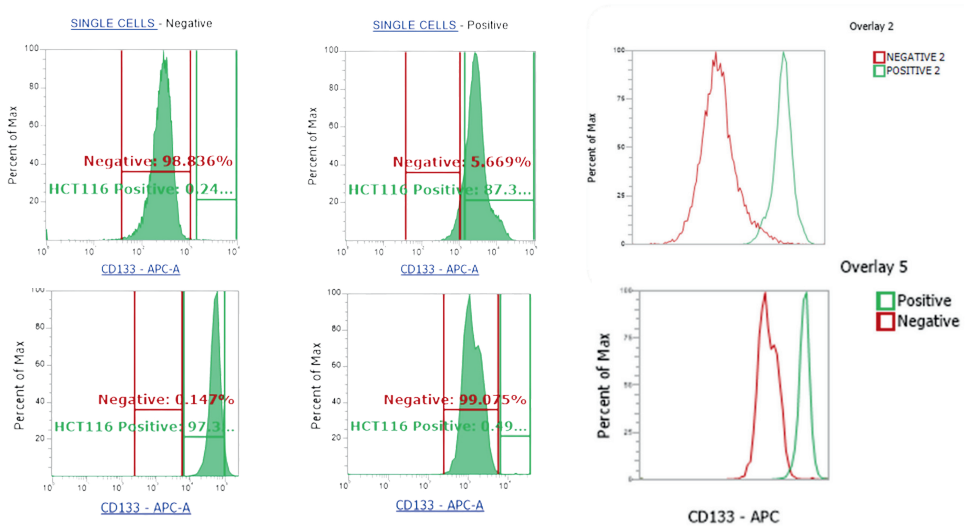


Chip Design



Chip Size:
40mm x 40mm x 2.5mm

Flow cytometry Analysis

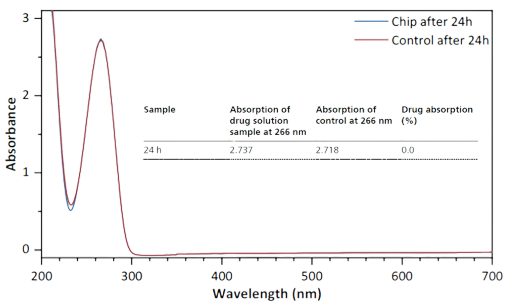


Flow cytometry of HCT-116 cells stained with APC-CD133 on the Attune cytometer shows single-cell gating for CD133-positive (green) and CD133-negative (red) populations. The plots display percentage distributions and overlay histograms comparing fluorescence intensities between positive and negative groups.

Drug Absorption Test

Testing drug absorption on 3D-printed microfluidic devices is key to evaluating material–drug interactions. Assessing how 5-Fluorouracil (5FU) behaves helps determine device compatibility and efficiency for delivery, testing, and screening.

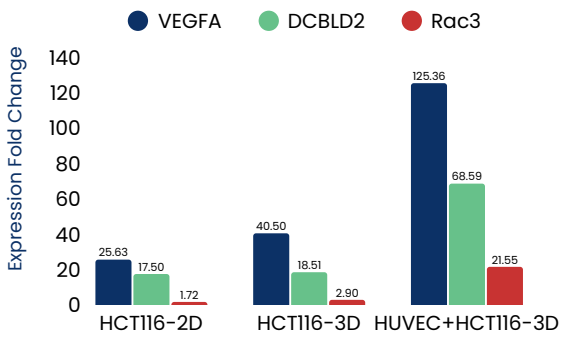
The lack of significant absorption indicates minimal interaction with 5FU, suggesting the devices are material-neutral and suitable for drug screening applications.



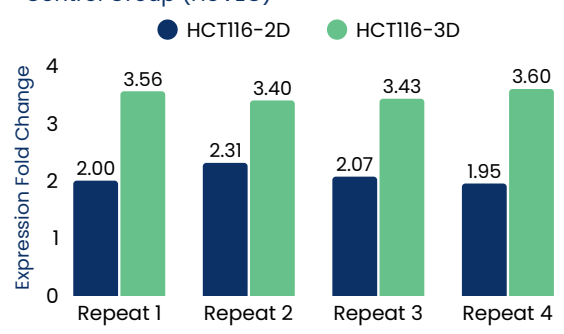
UV-Vis spectrum for drug solution pipetted out of chips after 24 hours. Control was a stock drug solution in 200 µL-microtubes.

Gene Expression Analysis

Comparison of Gene Expression Level Across Different Sample Types (Expression fold changes have been resulted as data normalization to HUVEC, as control group)



Rac3 Expression Fold Change Normalized to Control Group (HUVEC)



Genes used for qPCR

Rac3 – Promotes gene expression linked to cancer stemness and CRC progression.
DCBLD2 – Drives tumor growth, metastasis, and 5-FU resistance through EMT and angiogenesis.
VEGFA – Key regulator of angiogenesis; stimulates endothelial proliferation, migration, and vessel permeability.

In the HUVEC–HCT116 3D co-culture, VEGFA, DCBLD2, and Rac3 expression was significantly higher than in HCT116 3D monoculture or 2D systems, highlighting the role of cell–cell interactions in driving complex biological processes.
Chip performance was validated for reproducibility through Rac3 expression assays in four repeats over four months.

Experimental Results

Gene expression analysis and flow cytometry have revealed the role of the Rac3 gene in CRC angiogenesis. Quantitative PCR data showed a 2.54-fold increase in Rac3 expression in HCT116 cells compared to HUVEC controls. Further experiments with spheroids demonstrated a 1.36-fold increase in Rac3 expression compared to monolayer cultures, highlighting the importance of 3D tumor structures in modulating gene activity.

Conclusion

The 'CRC-on-a-chip' model presents a transformative leap in colorectal cancer research, offering an ethical, cost-effective, and scalable alternative to animal testing. By accurately mimicking the tumor microenvironment, this platform provides new insights into CRC biology, angiogenesis, and drug response, paving the way for innovative treatments and therapies.

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