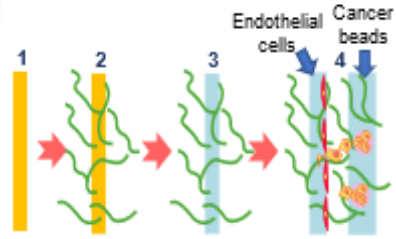
TU/e MICRO SYSTEMS TU/e ICMS

TU/e EINDHOVEN UNIVERSITY OF TECHNOLOGY

Cancer-vasculature on a Chip

MSc thesis theme



Introduction

Most of the cancer death cases occur due to cancer metastasis, not the initial tumor. Metastasis is a complex process in which, cancer cells invade the surrounding tissue and vasculature (invasion and intravasation), migrate through blood recirculation, and disseminate in the second organ (extravasation) (Fig. 1). Microfluidic devices are introduced as new in-vitro models to mimic the cancer microenvironment close enough to the native tissue for studying metastasis.

There are several types of cancer chips to mimic and study metastasis [1]; compartmentalized (Fig. 2), membrane, and lumen chips are among the most used. They all have microfluidic chambers for 3D cell culture and perfusion, with different types of barriers, such as micropillars or a porous membrane. The barrier inhibits the leakage of hydrogel to the other channel and simultaneously keep them interconnected; however, presence of an artificial material may affect the result of cellular studies. Hence, we move toward new generation of chips in this project: Hydrogel embedded lumens.

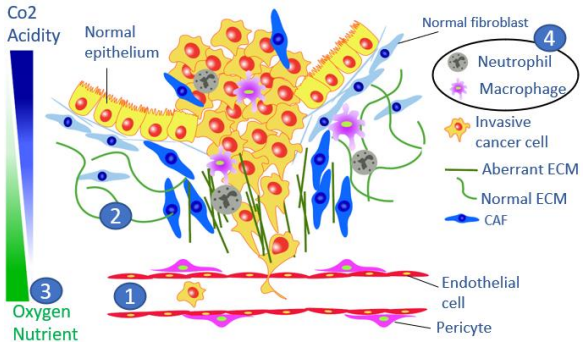


Figure 1 *Schematic view of cancer metastasis and its microenvironment: 1) Microvasculature, 2) ECM heterogeneity, 3) Oxygen gradient and 4) immune components. In this project we focus on (1) and (2).*

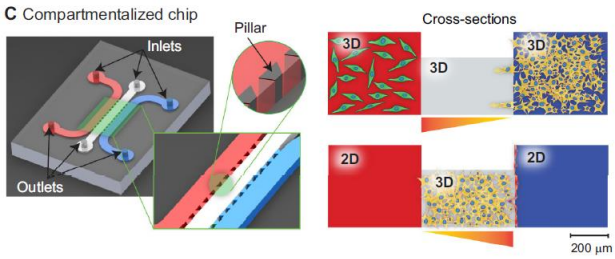


Figure 2 *Schematic view of a cancer metastasis chip. One of the mot common cancer chips composed of microfluidic chambers with micropillars barrier to provide the interaction between cell culture and perfusion channels [1].*

Project topics

In our lab, we design and fabricate new generation of microfluidic devices, in which perfusable lumens are cast in Extracellular Matrix (ECM) [2]. When seeded with endothelial cells, these form the (micro) vasculature. Combined with a neighboring channel for cancer cell culture, the process of cancer invasion, migration through ECM, and intravasation can be studied. In our model, as schemed in Fig.3, sugar fibers are printed and then coated. Sugar fibers are cast in hydrogel and cross-linked; subsequently, they are washed to create hollow perfusable lumens for either cancer beads seeding or endothelial cells.

In step 2 of this protocol (Fig.3 a), we coat the fibers with a material insoluble in water to prevent solving the sugar fibers in surrounding ECM before crosslinking. The MSc thesis project can focus on testing different coating options, but also device fabrication, 3D sugar printing, and cell culture.

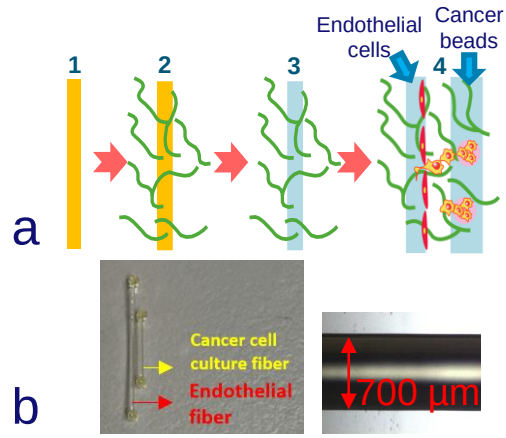


Figure3 *Sugar printing: (a) Schematic protocol from sugar fiber towards cell culture: 1. Sugar-print fiber, 2. Coat fiber, embed in ECM, 3. Crosslink ECM, dissolve sugar, and 4. Culture cells in obtained lumens; (b) sugar-printed parallel fibers, and enlarged view of a fiber.*

References

[1] Jelle J. F. Sleeboom, Hossein Eslami Amirabadi, Poornima Nair, Cecilia M. Sahlgren, Jaap M. J. den Toonder; Metastasis in context: modeling the tumor microenvironment with cancer-on-a-chip approaches. Dis Model Mech 1 March 2018; 11 (3): dmm033100. doi: https://doi.org/10.1242/dmm.033100

[2] Pollet, A.M.A.O.; Homburg, E.F.G.A.; Cardinaels, R.; den Toonder, J.M.J. 3D Sugar Printing of Networks Mimicking the Vasculature. Micromachines 2020, 11, 43. doi.org/10.3390/mi11010043

/ Interested? → **Prof. Jaap den Toonder (j.m.j.d.toonder@tue.nl)**