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Cancer metastasis-on-a-chip

Hossein Eslami Amirabadi*, Regina Lüttge, Jaap den Toonder
Department of Mechanical Engineering, Eindhoven University of Technology

Aim of the project

The aim is to create microfluidic devices that can be used to model and study (in vitro and real time) cancer metastasis from a primary tumor to a secondary site as happens in the human body.

Introduction

Cancer:

- number one cause of death in the Netherlands
- 12 million new cancer cases in 2008 globally
- WHO: this number will be doubled by 2030

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urgent clinical need for new treatment options

Animal based models

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Limitations

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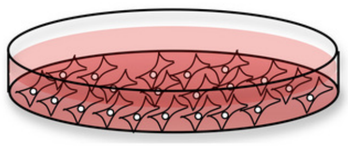
- not representative of what happens in humans
- no direct and live observations of the processes
- ethical issues



Cell based models

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Limitations

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- no control on bio-physical and bio-chemical factors
- not able to visualize the process of metastasis
- No relevant micro-environment

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New in-vitro models needed

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Organ-on-chips: Creating a microenvironment inside a microfluidic chip where “mini-organs” can grow within their own specified microenvironment, and function and interact as in intact organs.[1] Lung-on-a-chip (fig. 1) is one of the first examples in this field.

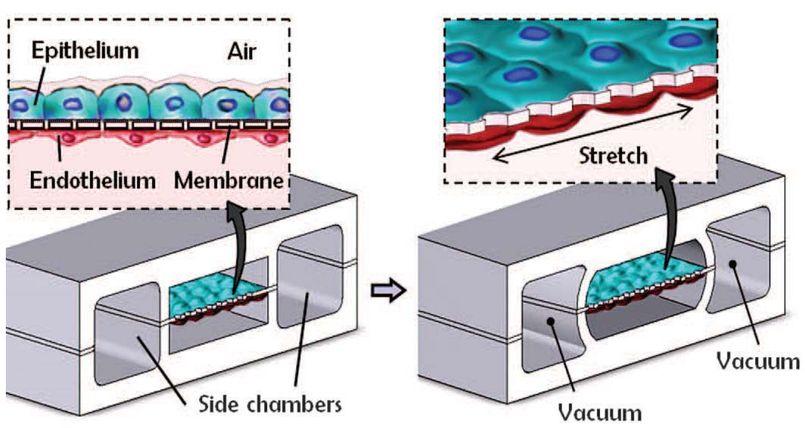

Fig. 1 – Lung-on-a-chip device developed by Huh et al.[2] at Harvard University. Using a stretchable and porous membrane in the device the alveolar-capillary interface in the human lung is modeled.

Cancer metastasis-on-a-chip device

Conceptual design:

The device contains a microchannel representing a blood vessel (bottom block) and organ micro-chambers (top block) where tumor cells and cells of the metastatic site are cultured. A porous membrane is also sandwiched between the blocks. In this configuration, the membrane is used as a substrate to culture cells on both sides, and forms the interface between the organs and the blood vessel.

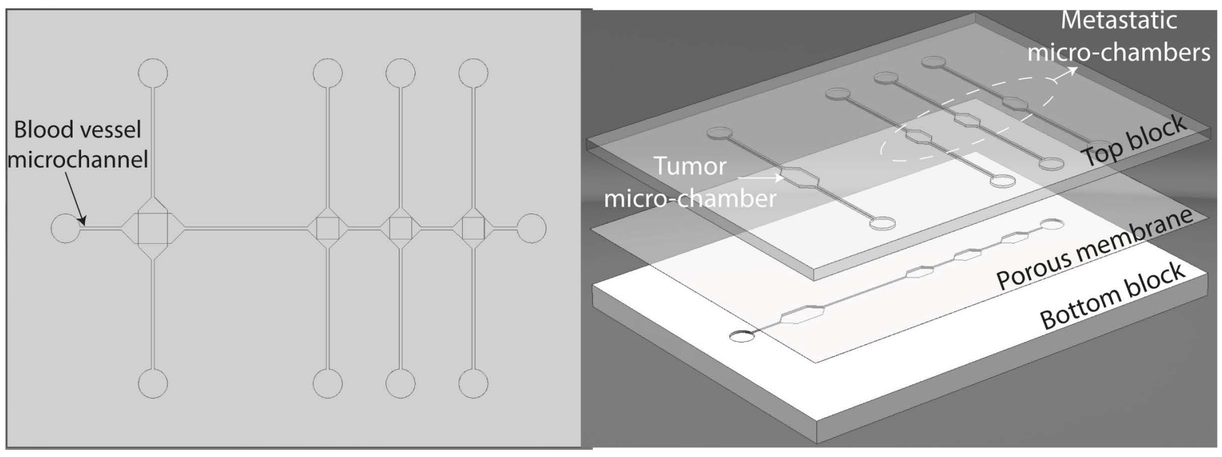

Fig. 2 – Top view (left) and exploded view (right) of the conceptual design for the cancer metastasis-on-a-chip.

As shown in fig. 3, the chip is designed to study the invasiveness of the tumor cells and also the metastasis of the circulating tumor cells into a second organ.

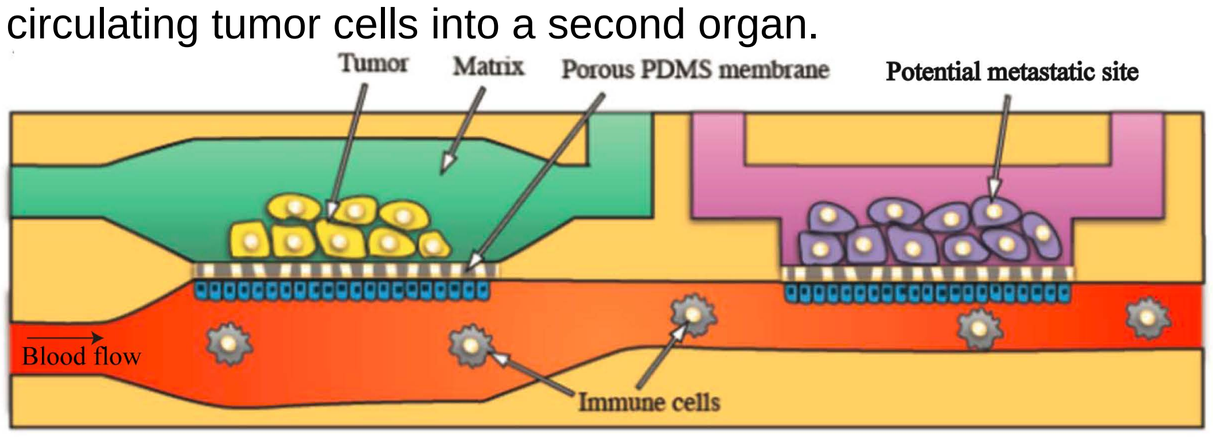

Fig. 3 – Schematic representation of the desired mircofluidics system after the cells are seeded.

What is new?

- Mimicking the contact between the blood vessel cellular layer and the tumor cell cultures
- Having different cell types in the organ chamber co-cultured in a structured and realistic manner
- Including static/dynamic stimulating elements for tumor cell migrations: chemical, mechanical and geometrical.

Collaborations:

Philips Research, Eindhoven, the Netherlands
Erasmus Medical Center, Rotterdam, the Netherlands

References:

1. van de Stolpe, Anja, and Jaap den Toonder. "Workshop meeting report Organs-on-Chips: human disease models." *Lab Chip* (2013).
2. Huh, Dongeun, et al. "Reconstituting organ-level lung functions on a chip.“ Science 328.5986 (2010): 1662-1668.

*Email: h.eslami.amirabadi@tue.nl