Organ-on-chip, the end to animal testing?

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IMPERIAL

Motivation & Aims

$ 15 billion is spent on animal testing in the US every year with <10 % of drugs that pass animal testing, passing the first round of clinical trials. This project aims to develop a lung-on-chip with an aerosol delivery interface to improve pre-clinical drug screening procedures.

What is an Organ-on-chip?

An organ-on-chip aims to recapitulate organ-level function in a microfluidic device.

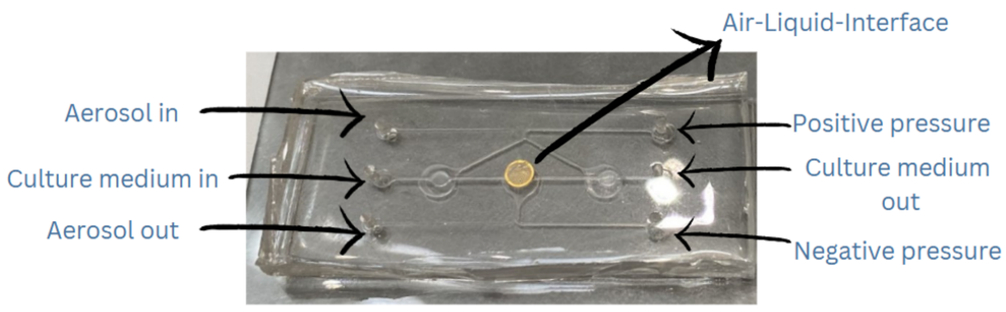

Figure 1: Illustration of the alveolus on a chip currently developed in the lab that will be used to interface with an aerosol delivery system.

Methods.

- Microfabrication of PDMS chip by 3D printing and soft lithography.
- Synthesis of hydrogel ECM mimic.
- Epithelial cell manipulation to express transmembrane protein GLP1-R, and seeding onto ECM mimic.
- Characterising the microfluidic chip by TEER and microscopy.
- Computational fluid dynamic, (CFD), model of aerosolised nanoliposomes through the chip.
- Interfacing the chip with aerosol delivery system.

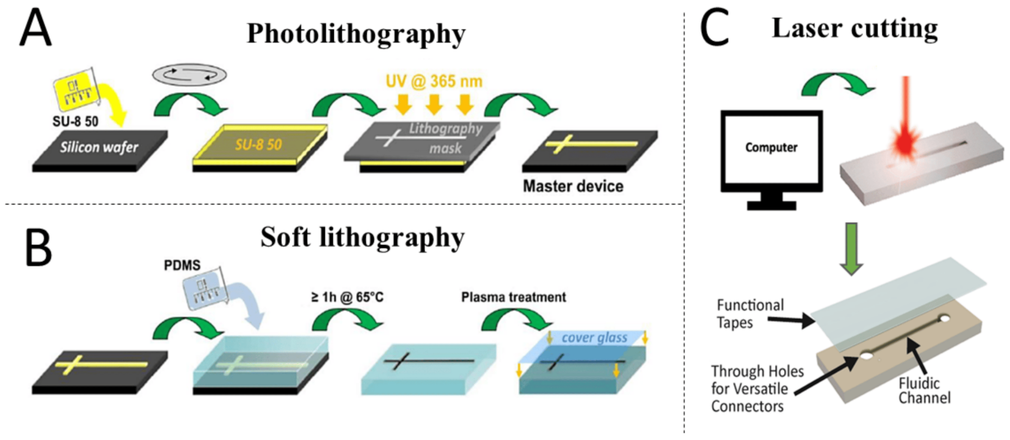

Figure 4: Fabrication methods of Organ-on-chips.

References

From First to Second to Future Gen.

Organ-on-chips have emerged out of advancements in tissue engineering, microfluidics and material science. The fisrt accepted organ-on-chip was developed by Huh *et al* at Harvard, Figure 2:.

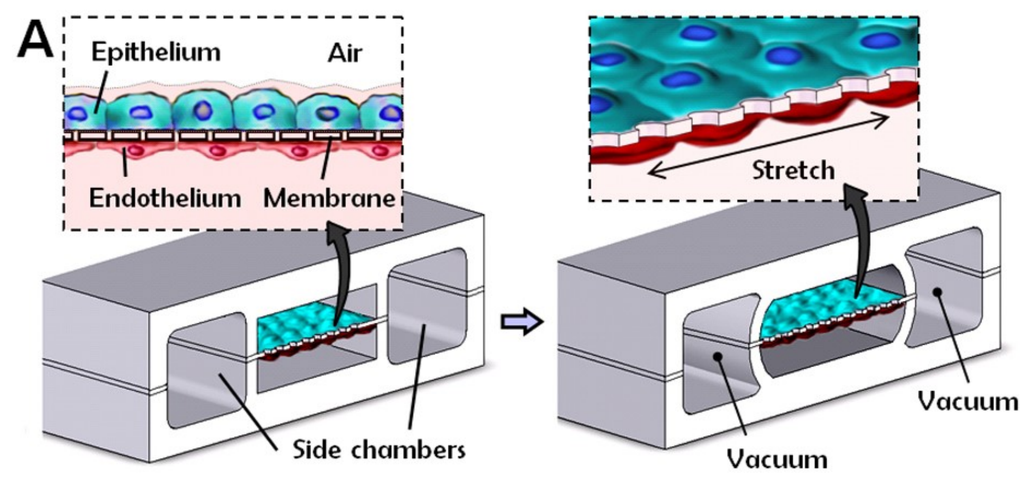

Figure 2: Huh *et al* First organ-on-chip, Emulate still use this design commercially. First generation design as the membrane only considers a single alveolar membrane as an extended structure.

This publication sparked the commercialisation of organ-on-chip technology with companies such as Emulate in the states and AlveoliX in Europe. Since, a variety of first generation chips have been produced. **First generation chips only consider the alveoli as an extended planar structure.**
More recently, second generation designs have been published. **Second-generation lung-on-chips consider an array of alveoli in 3 dimensions.** Allowing bidirectional airflow into and out of the alveoli to be modelled, as well as inter-alveoli interactions. Two notable designs by Zamprogano *et al.* and Huang *et al* are below:

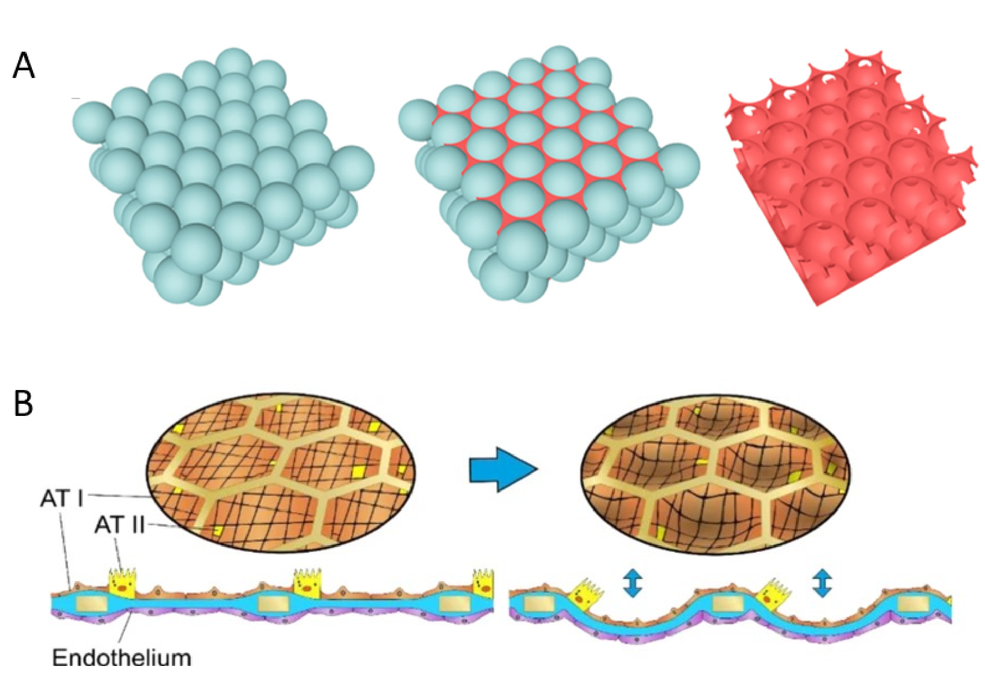

Figure 3: Second generation membrane designs for lung-on-chips. A) Reverse opal structure published by Huang *et al* [37] B) Zamprogano *et al* gold hexagonal mesh with collagen:elastin membrane.[29]