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Cotyledon-on-a-chip: Replicating the function of the placental barrier as an in-vitro model

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Abstract

The research with Organ-on-a-chip devices has allowed for the exploration of the possibilities of building a cotyledon-on-a-chip, replicating functions of the placenta in a microfluidic device. The prototype design consists of three PDMS layers, each separated by a membrane. This design enables a greater surface area for transport and provides a dynamic environment for the cells, creating a more accurate model of placental functions.

Introduction

Before a new drug is released in the market it must go through intensive testing. It first needs to be tested for safety through animal testing before it can be approved for human testing. This is considered immoral by many, but is also very expensive, and time consuming. Organ-on-a-chip technology provides a practical solution to these problems.

An organ-on-a-chip is basically a 3D cell culture model with microfluidic channels flowing through it. It simulates the activities and physiological responses of an entire organ. This type of device creates a uniquely accurate method to replicate the organ structure with human tissue and observe the biological responses as opposed to predictions based on extrapolated data from animal testing.

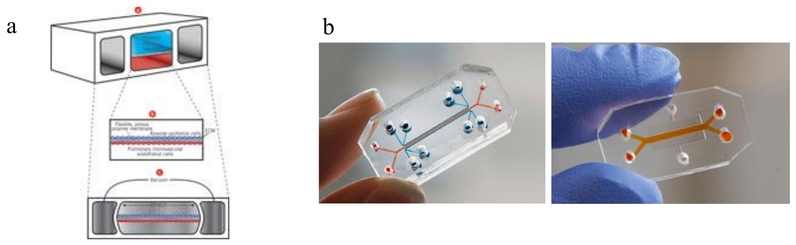

Fig. 1: a) cross section of the lung-on-a-chip, b) organ-on-a-chip devices with multiple inlets and outlets and multi-layered construction

Haas, Michael J. "Breathing Life into Lung Models." *Nature.com*. Nature Publishing Group, 22 July 2010. Web. 21 Apr. 2014.

"Organs-on-Chips." *: Wyss Institute at Harvard*. Harvard University, n.d. Web. 21 Apr. 2014.

Design Considerations

For cell environment, important factors to consider are temperature, pressure, and mechanical stress such as the flow rate or blood pressure. Regarding geometry, main considerations include whether or not the chip should be multi-layered, the dimensions, and which stage of gestation to emulate. Regarding cells, the thickness of cell layers, the source of the cells, and the cell maturation must be considered. For fluid medium, the use of blood or a substitute, and the viscosity must be considered. In addition, any supplements that are used, as well as the storage and how often the medium would need to be changed must be considered. For the testing, different teratogens and membrane compatability must be considered.

Fabrication

The PDMS base is fabricated with the use of a patterned slide, constructed from thin metal pieces (approximately 200 microns thick) glued to a glass slide. PDMS is mixed using a 10:1 ratio, poured over the molds, and sits until the molds are fully formed at an ambient temperature. The molds are then cleaned with ethanol, plasma cleaned, and layered with a membrane. All of the layers are subsequently pressed together, adhering the pieces and forming the final chip.

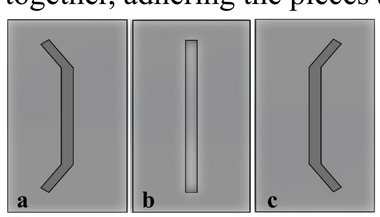

Figure 3

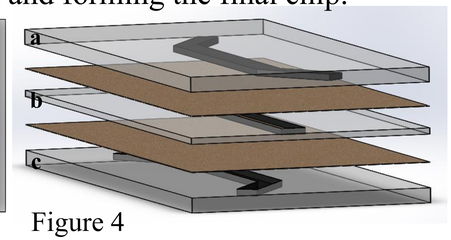

Figure 4

Fig. 3 shows the three different PDMS layers of the device side-by-side; Fig. 4 shows an expanded, “pre-bonded” model of the cotyledon-on-a-chip design highlighting the three layers of PDMS and the separating layers of Nafion.

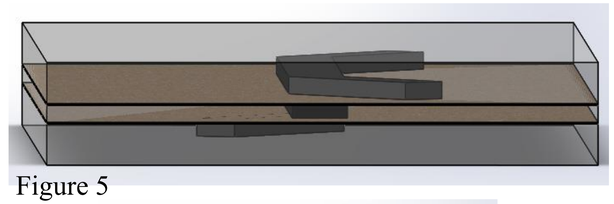

Figure 5

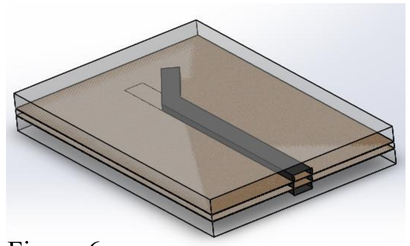

Figure 6

Fig. 5 shows a frontal view of the device after it has been compressed, aligned, and bonded; Fig. 6 is a cross section of the channel and demonstrates the three layers within the channel.

Future Work

Immediate future work with the cotyledon-on-a-chip device is centered around finding and implementing a more functional membrane to replace Nafion. Once this task is accomplished, experimentation with prototype microfluidic platforms will ensue to discover additional areas of the design that need alteration before creating a final product utilizing out-of-house lab fabrication methods.

References

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