OOACT Network Sabbatical Funding/ Round 1/Initial report: Lay summary of findings

Next-Generation Material for high-volume production of Sustainable, Biocompatible Organ-On-Chip devices

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An Organ on a chip (OOC) device is a powerful and emerging tool that hosts the living tissues constituting an organ and enables scientists, researchers and clinicians to study organs without using expensive, complex, and ethically-questionable animal models. Since the emergence of the first OOC device in 2007, complex functionalities have been added to a simple structure, leading to the so-called body-on-a-chip field. The translation from research to the market has happened relatively fast. To this date, at least 28 companies are proposing body and tissue on-a chip devices. The material of choice in most commercial organ-on-a-chip platform is an elastomer (PDMS, a type of silicone) commonly used in R&D. Although this material is biocompatible, transparent, flexible, and relatively easy to manufacture at small scale, a variety of issues have been encountered by consumers while using it, including deformation, unwanted evaporation, release of unwanted additives, leading to unpredictable results. This, and the fact that this elastomer moulding is difficult to automate, are the biggest drawbacks of PDMS as a substrate material for OOC application.

Our vision is to develop the use of Polylactic acid (PLA), a biocompatible thermoplastic material from renewable resources for the field of organ-on-chip. We have recently proposed PLA as new substrate material for the production of environmentally sustainable, single-use, devices for medical research, which circumvent the traditional problems encountered with the elastomer PDMS. We have optimised PLA workability in conjunction with a layered laser-based prototyping technique and demonstrated optimal transparency and surface roughness suitable for most basic biological applications. We are now embarking on a new phase of research to demonstrate the utility of these PLA microdevices in the field of Organ-On-A-Chip.

The aim of this proof-of-concept project was to investigate the suitability of Polylactic Acid (PLA) as new substrate material for Organ-on-a-Chip applications.

The partner *Rome Tor Vergata* evaluated cell motility and cell-cell interaction on polystyrene versus PLA substrates, starting from the automatic analysis of videos of cells moving under the microscope in the microfluidic microenvironment. The kinematic descriptors of PC-3 prostate cancer cells between the PLA substrate and the PS substrates were very similar despite slight difference on the surface topology. In *Leeds,* Human umbilical vein endothelial cells (HUVECs) primary cells for 7 days on PLA, PDMS, COC substrates. Pristine and functionalised PLA substrates performed as the control PS (no statistical difference). Combined with additional data obtained at Heriot-Watt University and in the literature, the toxicity data indicates that PLA is a suitable material for cell culture. Translating from a polystyrene substrate to a PLA substrate should be feasible for all types of cell culture. Our findings are described in https://www.biorxiv.org/content/10.1101/647347v1

The work at *Micronit* focused on the direct micromilling of PLA sheets. Micronit investigations showed that micromilling on PLA is feasible. *Microfluidic Chip Shop* molded 300 devices of the 737 model from their catalogue (interaction chips). This operation showed that it is possible to mold microfeatures, typical for organ-on-chip with PLA. The PLA molded chips have been closed by Heriot-Watt University and we are now seeking further funding to test these chips.

This pilot study has established that PLA has a strong potential to be the next-generation substrate for OOC applications. PLA devices can satisfy both end-users (mechanical, optical, biocompatible properties) and industrials, who could produce them at scale.