GravityFLOW™ – Microfluidic Multi-Tissue Culturing Platform for 3D InSight™ Microtissues

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Introduction

Three-dimensional cell cultures in microfluidic devices have been considered to address the limitations of 2D cell cultures in mimicking in vivo-like environments. Especially perfused multi-tissue networks promise more systemic insight on how compounds act in the human body. So-called "body-on-a-chip" systems receive more and more interest to improve the drug development process.

Combining 3D cell cultures and microfluidic technology poses several challenges. Cells and tissue structures have to preserve their native functionality over time, while the systems need to be simple and robust to set up and operate. Ease of use and standardization towards SLAS standards are further important factors for wider acceptance and for automation with existing methods.

Platform Concept

3D InSight™ Microtissues

- Reliable and standardized off-chip 3D InSight™ microtissue production
- Identical process for multiple cell types
- Quality controlled
- Available on-demand

GravityFLOW™ plate

- Microfluidic channel network with custom-designed 3D InSight™ Microtissue compartments
- In vivo-like conditions: liquid-to-cell ratios, fluid residence times, dynamic mechanical forces (shear)
- Adjustable and robust closed-loop medium perfusion

Transfer with modular and highly flexible microtissue arrangement

Design and Operation of the GravityFLOW™ Platform

Parallel microtissue loading using multi-channel pipet

Microtissue configuration for pro-drug activation studies

- Optimized flow around the microtissue
- 10 parallel multi-tissue experiments per plate

Continuous medium perfusion through periodic tilting

- Up to 60 experiments through stacking
- Tubing-less, pump-less and bubble-free setup

Bioactivation of Cyclophosphamide

Direct effect of Cyclophosphamide (CP) on tumor

Effect of metabolized Cyclophosphamide (CP) on tumor

Conclusions

The GravityFLOW™ microfluidic platform allows highly flexible combination of 3D InSight™ Microtissues in a microfluidic format and studying their interaction over time. The simple and reliable setup, including loading of microtissues, media sampling and operation, as well as the SBS plate format enables its routine use for parallelized substance testing. The results indicate the utility and multi-tissue functionality of this platform as well as the importance of continuous medium circulation to assess liver-mediated pro-drug activation of Cyclophosphamide.

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