

ERP Organ on a chip

Edition 2

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Caco2-cells on 3D-printed scaffolds for the 'Gut on a chip'

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For the gut-on a chip, a surface mimicking the villi of the gut can help to improve the cell differentiation.¹

SECOND NEWSLETTER

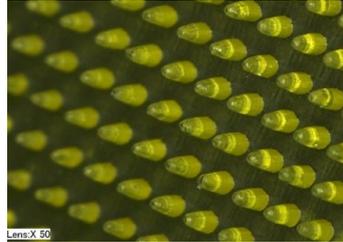
Here we present the second newsletter of the ERP organ on a chip.

We want to use this form of communication as an additional means to inform those involved and those interested about the progress of the ERP:

- Scientific development
- Building of the ecosystem

By using additive manufacturing or '3D printing' in popular words, at TNO EfAM in Eindhoven, scaffolds were fabricated which mimic the surface structure of the gut, see figure. The 3D-printed scaffold consists of an array of cones with a rounded top.

Shown before is that Caco2-cells can actually survive on the by TNO-developed 3D-printed material *BI-OC*. The next step was to investigate whether the Caco2-cells are also viable on these scaffolds and to see whether the cells actually migrate to-



wards the top of the 'villi'. Currently cell culturing has been taken place for 4 weeks on these scaffolds and the cells are still viable.

After the first two weeks of cell-culturing, 4 samples were taken and H&E stained to visualize the Caco2-cells. This week, the samples were analyzed. The picture on the right shows that the cells are actually on the top the villi-structures! This indicates that the cells actually migrate upwards. If this is indeed the case we can investigate if this also has an influence on the cell differentiation... and therefore their function! Exciting times are coming up!

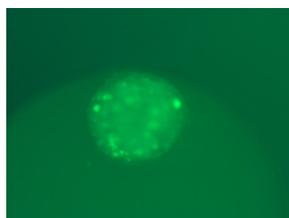
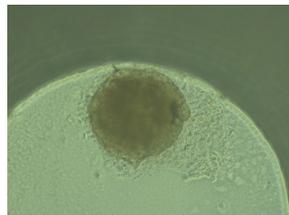
1. Costello et al., *Synthetic Small Intestinal Scaffolds for Improved Studies of Intestinal Differentiation*, 2014

Development of bile canaliculi in 3D cultured liver micro-tissues

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3D cultivation of primary hepatocytes and stem-cell derived cells has a huge advantage over conventional 2D monolayer culture by mimicking the tissue-like environment resulting in a more physiological organization of the cells.

Here we show that the stem-cell derived HepaRG cells readily form 3D spheroids using the hanging drop method. Moreover, we demonstrate the formation of functional bile canaliculi by exposing the micro-



tissues to CDFDA (Carboxy-Dichloro-Fluorescein DiAcetate), a fluorescent probe that is actively secreted into the bile.

We have met important first steps towards real liver function-on-chip, which will be implemented in future metabolic, pharmacokinetic and efficacy studies. Current developments are focusing on generation of a 3D disease mimicking in vitro model of NASH (nonalcoholic steatohepatitis), for which co-culture with stellate cells is needed.