ERP Organ on a chip

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TNO and Organ on a chip

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Better predictive preclinical models that represent the human situation are needed for better selection of success or failure of compounds in the clinical drug development phase. These predictive models are a high unmet need of pharmaceutical industry, and would be also be of great use to nutritional industry, which increasingly uses pharmaceutical research models for testing compounds and ingredients. Organ function on-a-chip models provide a promising animal-free approach to solve this issue.

FIRST NEWSLETTER

Here we present the first 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

TNO has unique knowledge and technologies in house to significantly improve and speed up the model development, validation and application of "organ-on-a-chip" technology. By combining these technologies we will unlock the full potential of the somewhat scattered expertise present at TNO and generate a potential new growth area.

As TNO we aim to achieve this by generating, optimizing and validating sophisticated generations of human *in vitro* models in a step-by-step approach according to the market demand.

Our **breakthrough technology** will be better predictive and time reducing screening platforms, which will improve and shorten the preclinical drug development process. TNO chose to focus on lung, liver and gut function on a chip.

In all three cases the first step will be to generate relatively simple, cell-based medium throughput in vitro models with relevant readouts, which can as such already be used by industrial partners.

Liver function on a chip

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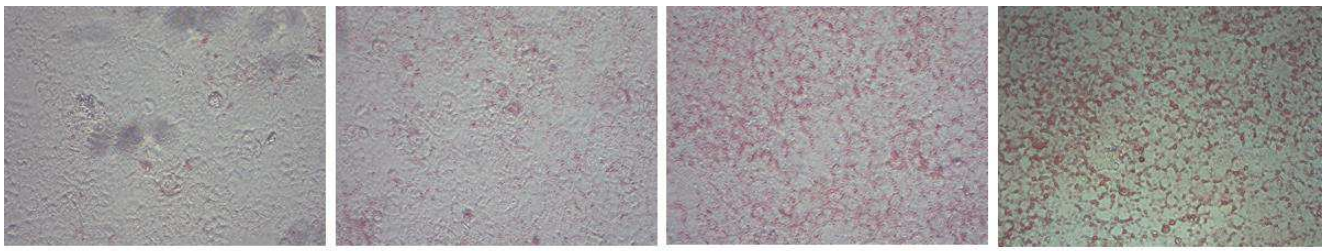

A: Contr/DMSO/BSA | **B: Contr/DMSO/ 0.1 mM oleate/BSA** | **C: Contr/DMSO/ 0.3mM oleate/BSA** | **D: Contr/DMSO/ 1 mM oleate/BSA**

Induction of steatosis (fatty liver cells) in HuH7 cells (human hepatocyte cell line) by exposure to fatty acids (oleate). Concentrations of 0.3 mM (C) and 1mM oleate (D) clearly induced steatosis in the HuH7 cells. The oleate (fatty acid) is mainly accumulated in the cell membrane. Similar results were obtained using HepaRG cells (iPSC derived hepatocytes). We are curenly focussing on intervention studies using this cellular model and on the induction of steatosis in a 3D cultured cell model (hanging drop) with the aim to generate a more physiological relevant and sophisticated disease mimicking model .

Additive manufacturing for the 'Gut on a chip'

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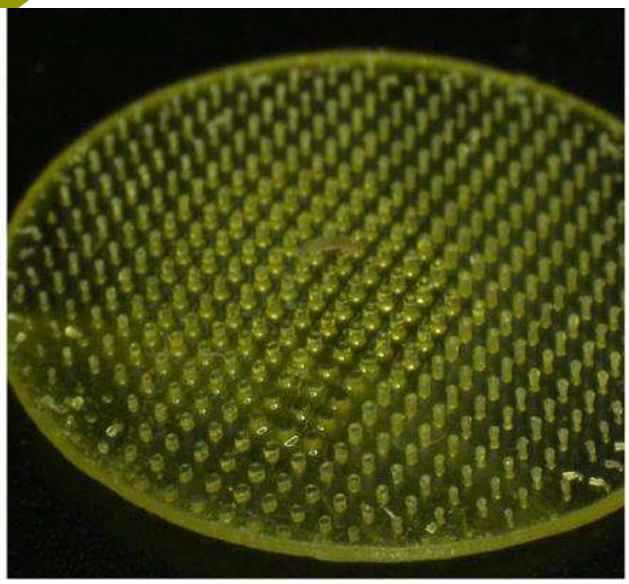
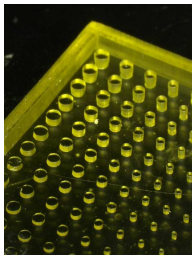


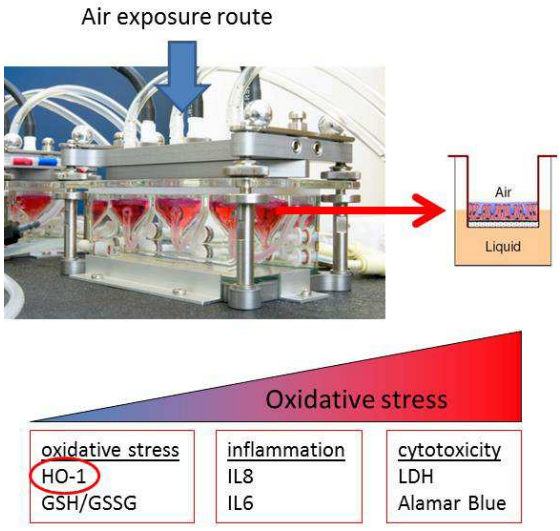
For the gut-on a chip, a surface mimicking the villi of the gut can help to improve the cell differentiation.[1] By using additive manufacturing at TNO EfAM in Eindhoven, a project has started to fabricate these villi-like structures. First a material has been developed suitable for cell adhesion and growth which was successfully tested with Caco2-cells. With this material, micron size features up to ~150µm can be made which is in the order of the villi-size (see pictures). The actual scaffolds are now being designed and soon will be tested for their effect on the intestinal cell differentiation. Will this lead to the next intestine model? To be continued…



Monitoring induction of oxidative stress on a chip

Contact: Paula Amaral Santos, TNO MHR in collaboration with van 't Hoff program, Paula.AmaralSantos@tno.nl, +31 88 866 6533

How to monitor the induction of oxidative stress (OS) in real-time in a lung-on-a-chip system? In the early stages of the OS process, carbon monoxide (CO) is produced by the enzyme HO-1 and released into the culture medium and into the air phase. Measuring the quantity of CO over time can be an indirect way of assessing the activity of HO-1 and, therefore, of the induction of OS. For that, three possibilities are being explored: photo-acoustics spectroscopy, turn-on fluorescent probes and reaction with hemoglobin followed by spectrophotometric analysis. The first experiments are planned and preliminary results are expected soon.



Companies and potential collaborators that have been contacted in the past few weeks

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The number of technology providers on 3D culture systems is increasing rapidly. At the BioEurope Spring meeting, recently held in Paris, the ones we met are all looking for applications of their technology in the field of organ on-a-chip. Our decision to focus on organ *function* on a chip applications perfectly fits in the thoughts of the big pharma companies with whom we discussed our program.

For more information about the ERP please contact:

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