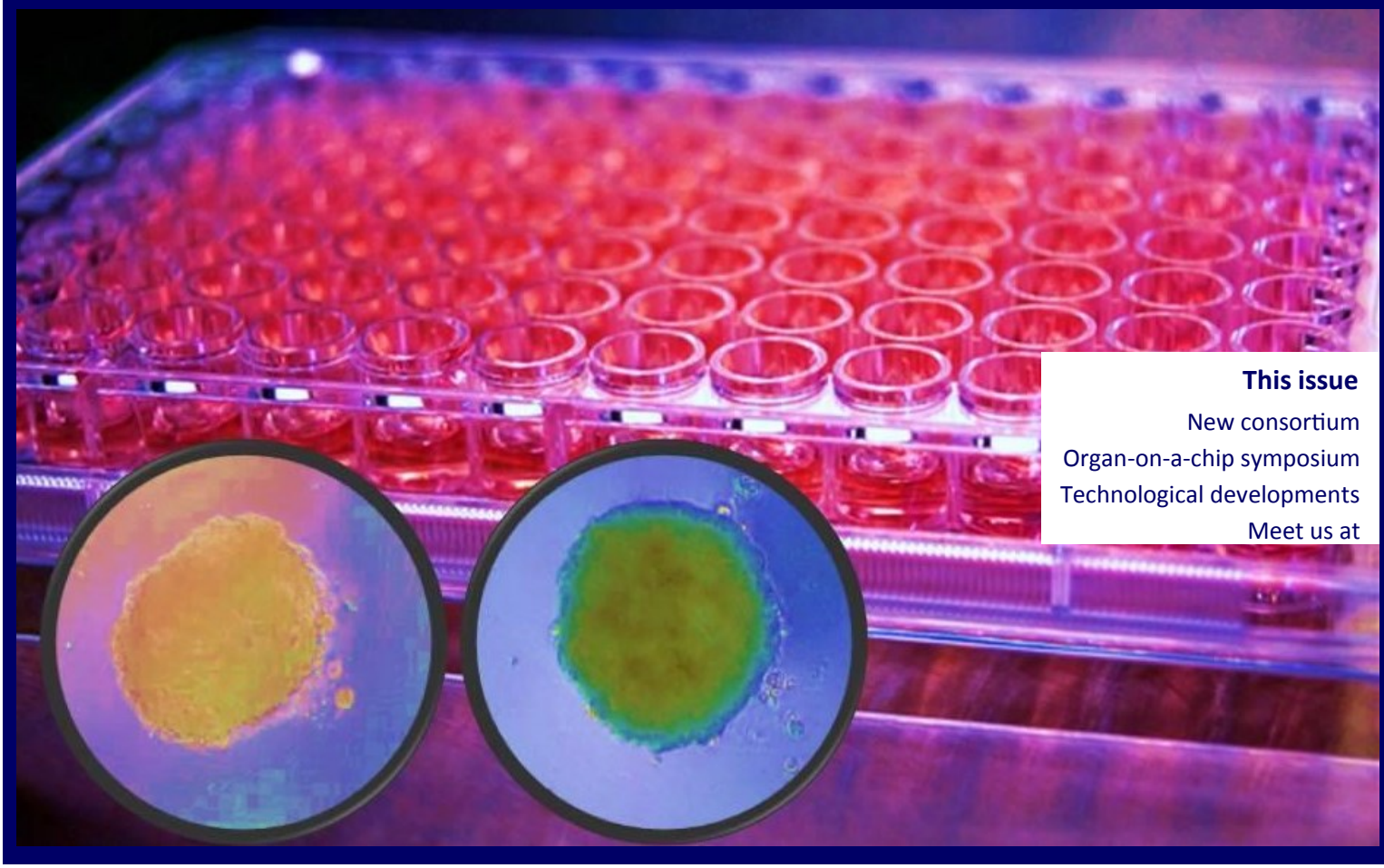
ERP Organ function-on-a-chip

Edition 4, February 2016



This issue

New consortium on the development of NASH organ function-on-a-chip model

15 February 2016. TNO (the Netherlands) recently signed an Agreement with InvitroCue Pte Ltd ("IVQ"; Singapore) and Takara Bio Europe AB (Sweden), under which they started a collaboration using different technologies to develop a model of non-alcoholic steatohepatitis (NASH). This collaborative project is part of TNO's Early Research Program 'Organ on-a-chip', for which it received funding from the Dutch Government.

NASH is a type of fatty liver disease, which mainly affects people with diabetes and obesity and is seen as one of the major societal and economic problems in healthcare. The number of NASH patients and committed healthcare costs increased four-fold in the last 15 years. Analysts now forecast that the market for NASH treatments could reach $35 to $40 Billion by Year 2025. Concomitant herewith, is an increasing demand for better predictive NASH preclinical model.

This two-year collaboration project aims to deliver a predictive translational *in vitro* model in which the effect of potential new medicines for NASH can be evaluated. The project perfectly fits within TNO's strategy to establish an ecosystem that has full potential of developing relevant organ function-on-a-chip systems for various human disease applications. Organ function on-a-chip models are advanced *in vitro* models that closely resemble the structural tissue arrangements and functional complexity of living organs and tissues by using human cells (co-)cultured in 3D environment and/or using microfluidic chips. Currently most of organ on-a-chip applications are used for testing toxicity of compounds. TNO's focus on efficacy and the introduction of human stem cells opens approaches toward precision medicine and population on-a-chip applications.

For more information about the ERP please contact

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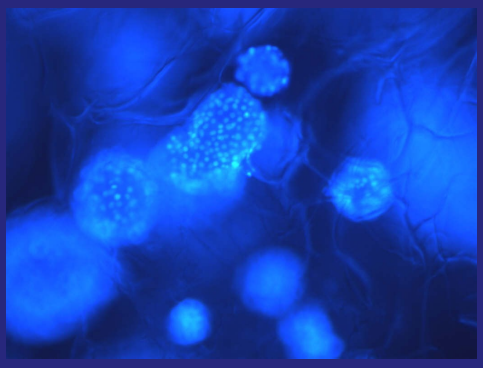
TNO provides unique knowledge and expertise regarding *in vivo* models of NASH, pathways and the etiology of disease. TNO's system biology approach and the data integration from *in vivo* models as well as human data will contribute to the translation to human disease development and effect of NASH treatments.

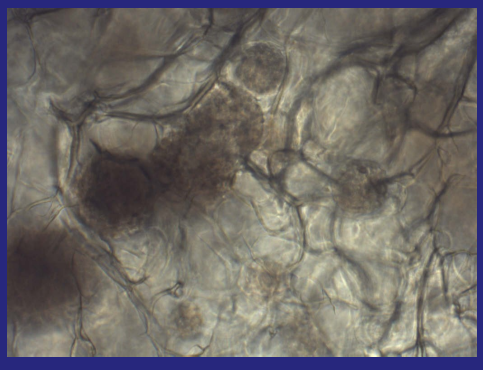
IVQ has a notable track record in 3D-scaffolds through its participation with pharmaceutical and development projects, as well as DMPK *in vitro* analysis on liver drug compounds. IVQ will use its extensive know-how gained through its considerable experience in the 3D-scaffold models and its track record in preclinical pharmaceutical drug screening to contribute to the successful development and operation of consortium. The *in vitro* preclinical models represent one of the primary focuses of IVQ's business, and IVQ will continue to strive to develop predictive preclinical models and assays in this area.

Takara Bio Europe will contribute with their unique knowledge and expertise on 3D-culture systems and application/differentiation of human pluripotent stem cells into hepatocytes. Together we will have a worldwide partnership that employs three different companies sharing their technologies and expertise, which will deliver novel applicable models for testing potential new medicines in liver disease and liver toxicity issues. The project contributes to the aim of replacement, reduction and refinement of animal studies.

Hepatocyte spheroids in a 3D scaffold

The goal of liver disease-on-a-chip program is to develop tools for better translational / predictive testing of efficacy in the liver. As a part of our step-wise approach, we cultured hepatic cells from the Hua7 cell line in 3D scaffolds, which enabled them to grow in spheroids as depicted in the pictures below (blue: DAPI staining, 100x). This 3D structure creates a more human in vivo-like environment, mimicking not only the structural architecture of the cells, but also the cell-cell interactions, which cannot be achieved with conventional 2D cell culture techniques.





Meet us at the:

- **International Organ On A Chip Symposium 2016. 9-10 March, University of Twente, Enschede, The Netherlands**
- **SOT. March 13-17, New Orleans, USA**
- **BIO-Europe Spring. April 4-6 2016, Stockholm, Sweden**

Invitation to join

The TNO Early Research Program 'Organ on-a-chip', is an open innovation network in which TNO works on liver-, gut- and lung-function-on-a-chip applications. Potential end users of these technologies such as Pharma and Biotech companies and also university medical centers, diagnostic companies, (read-out) technology providers and regulatory bodies are invited to join this open innovation network to tap their research plans into these programs. If of interest please contact Dr. Robert Ostendorf (robert.ostendorf@tno.nl).

Organ function-on-a-chip mini-symposium @ TNO

On October 7th 2015, the mini-symposium Organ function-on-a-chip took place at TNO Zeist.

This event brought together researchers and business developers with the goal of discussing the roadmap of TNO's Early Research Program "Organ function-on-a-chip". Two external speakers from the department of Applied Stem Cell Technologies of the MIRA Institute for Biomedical Technology and Technical Medicine, TU Twente, were invited to present their view on this rapidly evolving technology.

Andries van der Meer, Assistant professor and coordinator for strategic research orientation 'Organs-on-Chips' at the institute, presented his view on the technology development and implementation. Organs-on-chips have a right to play in the biometric and outcome data, collection of the data and monitoring the outcome as a surrogate for patient outcome. In addition, organs-on-chips can be personalized by the implementation of stem cell technology and can then be applied for precision medicine, finding the right therapy for each patient.

Robert Passier, head of department, emphasized on new, innovative models and technologies that are required not only for drug development, but also for the understanding of disease mechanisms, such as CVD and for regenerative medicine.

During the discussion of the ERP Roadmaps for liver disease-on-a-chip, gut function-on-a-chip and lung function-on-a-chip, TNO's right to play within these fields and potential markets was fine-tuned. In addition, the standardization and validation of this rapidly evolving technology, and the need thereof, was heavily debated, resulting in an informative and successful symposium with food for thought!