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Poster: strategies to reduce animal numbers for testing biological

## **A new human hepatocyte cell line as a vantage point for a new generation of organoid liver test systems?**

*Anke Hoppensack, Lisa Kaschel, Johanna Schanz, Kirstin Linke, Heike Mertsching*

Fraunhofer Institute for Interfacial Engineering and Biotechnology (Stuttgart) (DE)

e-mail: anke.hoppensack@igb.fhg.de

The human liver is the main organ of drug biotransformation. To analyze substance activity or the generation of toxic by-products can be generated animal experimentation is routinely applied. These experiments are ethically critical and the results cannot be exactly transferred to the human organism because of significant differences in drug metabolism. Thus, a model has to be developed that meets the requirement of being comparable to the complexity and functionality of the human liver. At the same time such a model has to be applicable and reproducible.

At the Fraunhofer IGB a liver module based on an acellularised porcine jejunal segment with a maintained vascular system has been established (Schanz et al., 2007). This module allows a physiological co-culture of endothelial cells and hepatocytes. Initially, because of their better availability porcine hepatocytes were used for system development and now a possible human cell source has to be evaluated. Furthermore, the liver module has to be compared with established hepatocyte culture systems like sandwich and monolayer culture.

Primary human hepatocytes cannot be obtained in an adequate quantity and reproducible quality. Most hepatocyte cell lines are dedifferentiated and thus do not exert liver-specific functions. We compared a new human hepatocyte cell line in sandwich and monolayer culture with primary human and porcine hepatocytes.

Immunohistological experiments showed that the cell line does not feature all hepatocyte specific markers although its morphology is similar to primary hepatocytes. Nevertheless, the cell line performs liver-specific functions as urea and albumin synthesis as well as biotransformation. These functional results indicate that this cell line could be used as a human hepatocyte source.

Further functional testing will show if the cell line integrated in the vascularized liver module could be a vantage point for a new generation of organoid liver test systems, which could minimize animal experiments in terms of the 3R principles.

### **References**

Schanz, J., Linke, K., Mertsching, H. (2007). A vascularised liver cell module as an alternative to animal experiments. *ALTEX* 24, 223.

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