Journal of
Electrical Engineering and Electronic Technology

Abstract

Development of a diet-induced model for non-alcoholic steatohepatitis (NASH) and fibrosis in an organotypic spheroid-based liver-on-chip model

Haysam Ahmed1,2, Karin Toet1, Hossein Eslami Amirabadi1, Bob van de Water2, Roeland Hanemaaijer1, Geurt Stokman1

1TNO Healthy Living, Leiden, The Netherlands
2Leiden Academic Centre for Drug Research, Leiden, The Netherlands

Abstract:
Non-alcoholic fatty liver disease (NAFLD) is currently the most common form of chronic liver disease and may progress towards NASH associated with liver fibrosis, cirrhosis, and hepatocellular carcinoma. Despite ongoing efforts, there is no effective therapeutic treatment available for NAFLD-NASH. This is partly due to an incomplete understanding of disease mechanisms, relevant biomarkers and predictive preclinical models for drug screening. We therefore developed a disease-mimicking in vitro model which closely resembles the pathophysiology of liver fibrosis induced by lifestyle. In addition, we introduced microfluidic flow to our cell model to investigate the effect of homeostatic tissue perfusion versus conventional static culture conditions.

Primary human hepatocytes, Kupffer cells, and stellate cells were cultured in a matrix-free environment, resulting in formation of multiple uniformly-sized spheroids. Fatty acids, carbohydrates, inflammatory and immunomodulatory factors were used at physiological concentrations to faithfully recapitulate disease development and progression of NAFLD-NASH. Development of steatosis and fibrosis was characterized. Transcription and protein analyses confirmed expression of different collagen isoforms upon full disease induction. Different drugs and drug combinations were tested to determine their effect on inflammation and more importantly fibrosis.

A novel, customized liver-on-chip was developed in-house. The chip was 3D-printed using proprietary material that has very low drug adsorption to circumvent the shortcomings of the widely used polydimethylsiloxane (PDMS). Spheroids were subjected to continuous pump-driven flow for 2 weeks. Exposure

to fatty acids and carbohydrates under flow conditions resulted in a more homogenous distribution and size of lipid droplets, as compared to static culture conditions.

We will further investigate the effect of microfluidic flow in our model on the therapeutic efficacy of reference compounds and compounds currently in clinical trials, using steatosis, inflammation, and deposition of collagen as read-outs.

Biography:
Haysam Ahmed is an experienced biomedical researcher with an ultimate goal of assisting the development of more effective and safer drug/cellular therapies that can be used to treat patients. Throughout his career, Haysam has worked on various projects all aimed at addressing issues with dire need for innovative solutions such as skin grafts for burn patients, a bio-aritificial liver for liver failure patients, and most recently a non-alcoholic fatty liver disease model that faithfully recapitulated key aspects of the disease and helped identify a drug combination that can potentially treat that disease which affect millions globally.

Webinar on Organ on Chip; November 15, 2020

Citation: Haysam Ahmed; Development of a diet-induced model for non-alcoholic steatohepatitis (NASH) and fibrosis in an organotypic spheroid-based liver-on-chip model; Webinar on Lab-on-Chip; November 15, 2020.