Name of journal: World Journal of Gastroenterology

Manuscript NO.: 29492

Column: Basic Study

Title: Three-dimensional perfused human in vitro model of non-alcoholic fatty liver disease

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Reviewer code: 02485834

First decision: 2016-10-11 11:06

Scientific editor: Jing Yu

Scientific Research Process

This study describes the development of a novel in vitro model of non-alcoholic fatty liver disease (NAFLD). Using the organ-on-chip LiverChip® platform, primary human hepatocytes can be cultured in 3D microtissues on engineered scaffolds that recapitulate the liver capillary bed under perfusion. We cultured liver microtissues in the LiverChip® platform under fat and lean culture conditions to analyse the effects of continual triglyceride accumulation on primary human hepatocytes, mimicking the process that occurs in NAFLD patients.

Cryopreserved primary human hepatocytes were cultured in the fat and lean conditions and analysed for changes to their phenotype due to the fat loading. We analysed changes to the transcriptome of the cells, changes to the proteins they secrete and changes to their metabolic capacity. We also analysed whether the culture conditions developed caused any toxic effects to the cells and whether standard hepatic functions were maintained. Finally, the cells were treated with anti-steatotic drugs whilst they were cultured in high fat conditions, to see if the level of triglyceride accumulation could be modulated. All experiments were performed by CN Bio Innovations with some sample analysis being performed by contract research organisations, XenoGesis Ltd (Nottingham, UK) and Labstract Bioscience Support Services (Stevenage, UK). All experimental data was analysed by CN Bio Innovations using standard data analysis software.

Previous studies suggested that primary human hepatocytes could be cultured in the presence of free fatty acids for short periods of time (> 48 hours) without causing cytotoxicity. Using organ-on-chip culture technology was expected to enable for the first time the longer term culture of hepatocytes under high fat conditions. This study successfully demonstrated for the first time that this type of culture could be performed, which enables the molecular mechanisms the underlie fatty liver disease to be studied in more detail. The model developed in the study also provides an opportunity to screen drugs for anti-steatotic effects.