In vitro model for drug-induced phospholipidosis

Commonly used acronym: *drug-induced phospholipidosis (DIPL)*
Created on: 22-10-2018 - Last modified on: 06-11-2018

SCOPE OF THE METHOD

Alternative method relates to	Human health
Alternative method is situated in	Basic Research, Translational - Applied Research
Type of alternative method	In vitro - Ex vivo
This method makes use of	Human derived cells / tissues / organs
Specify the type of cells/tissues/organs	liver

DESCRIPTION

Method keywords

Human skin stem cells-derived hepatic cells
liver embryogenesisin vitro
drug screening
drug-induced liver injury

Scientific area keywords

liver

Method desription

Human skin stem cells-derived hepatic cells (hSKP-HPC) have already shown to be a good human in vitro tool to screen for compounds that can induce hepatic steatosis

and acute liver failure. Another important liver disorder that is often reason of discontinuation of chemicals in drug discovery is drug-induced phospholipidosis. Phospholipidosis is a metabolic disorder characterized by an excessive intracellular accumulation of phospholipids. The objective of my research is the application of hSKP-HPC to investigate liver phospholipidosis and the elucidation of the mechanisms leading to this pathological condition in vitro. Hereby, hSKP-HPC are cultured in a standard two dimensional (2D) setup. Data show that hSKP-HPC exposed to amiodarone, which is known to induce PL in vivo, accumulate phospholipids and neutral lipids intracellularly. Typical lamellar inclusions can also be identified by transmission electron microscopy. Significant upregulation of genes involved in lysosomal activity and biosynthesis of new phospholipids is found in our cell model.

Lab equipment

Method status

Validated by an external party (e.g. OECD, EURL ECVAM,...)

PROS, CONS & FUTURE POTENTIAL

Advantages

Strenghts are represented by inter-donor variability reflecting the human situation

Future & Other applications

Potential application of this cell model in related to drug toxicity screening platform

REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION

References

Rodrigues RM, Heymans A, De Boe V, Sachinidis A, Chaudhari U, Govaere O, Roskams T, Vanhaecke T, Rogiers V, De Kock J. ,Toxicol Lett. 2016 Jan 5;240(1):50-9. doi: 10.1016/j.toxlet.2015.10.014. Epub 2015 Oct 20 Rodrigues RM, De Kock J, Branson S, Vinken M, Meganathan K, Chaudhari U, Sachinidis A, Govaere O, Roskams T, De Boe V, Vanhaecke T, Rogiers V., Stem Cells Dev. 2014 Jan 1;23(1):44-55. doi: 10.1089/scd.2013.0157. Epub 2013 Sep 21.

Associated documents

Other remarks

Experimental design: 1- Human skin stem cells are differentiated towards hepatic cells for 24 days 2- Differentiated cells are exposed to the drug of interest (amiodarone, in this case) 3- Quantification of lipids is performed using flow cytometry 4- Modulation of gene expression under drug exposure is evaluated by qPCR Controls: cells non-exposed to the drug represent the control group Data interpretation and acceptance criteria: stastisticel analysis Performance: yes Applicability domain: amiodarone(in my study) , valproic acid and acetaminophen were already tested in this cell model. I am not aware of compounds that cannot be used on the cell model since they were not tested yet.

PARTNERS AND COLLABORATIONS

Organisation

Name of the organisation Sciensano

Department Chemical and physical health risks

Country Belgium

Name of the organisation VUB

Department IVTD

Country Belgium