Drug-induced phospholipidosis in hepatic cells derived from human skin-derived precursors

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Organisation

Name of the organisation Vrije Universiteit Brussel (VUB)

Department Pharmaceutical and Pharmacological Sciences

Specific Research Group or Service In Vitro Toxicology and Dermato-Cosmetology

Country Belgium

SCOPE OF THE METHOD

The Method relates to	Human health
The Method is situated in	Translational - Applied Research
Type of method	In vitro - Ex vivo

DESCRIPTION

Method keywords

toxicology

in vitro

drug testing

Intracellular lipids

phospholipids

Phospholipidosis

amiodarone

Scientific area keywords

hepatic differentiation

Hepatotoxicity

skin-derived precursors

skin stem cells

Method description

Drug-induced phospholipidosis (DIPL) is a metabolic disorder characterized by an excessive intracellular accumulation of phospholipids caused by cationic drugs. Hepatic cells derived from human skin are evaluated as an *in vitro* model to investigate DIPL and its mechanisms. Human skin stem cells (hSKP) are isolated, under informed consent, from human circumcised foreskin samples of young boys and hSKP are differentiated for 24 days to obtain hepatic-like cells (hSKP-HPC), as previously described. hSKP-HPC are exposed to amiodarone, a drug known to induce phospholipidosis in humans. Upon exposure to amiodarone for 24, 48, 72h, hSKP-HPC retain intracellular phospholipids, form lamellar bodies and show alterations at the gene expression level. Overall, these findings prove that hSKP-HPC might contribute to setting up an accurate *in vitro* platform for hepatotoxicity testing.

Lab equipment

Laminar air flow;

Flow cytometry;

Transmission electron microscopy;

Reverse transcriptase-polymerase chain reaction (qPCR) reagents.

Method status

History of use

PROS, CONS & FUTURE POTENTIAL

Advantages

Applicability of hSKP-HPC for the quick assessment of drug-induced phospholipidosis *in vitro*;

Different human donors can be tested to assess toxicity.

Future & Other applications

In vitro toxicity testing in the drug development process

REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION

References

W. H. Halliwell, “Amphiphilic Drug-Induced Phospholipidosis,” Toxicol. Pathol., vol. 25, no. 1, pp. 53–60, 1997. [2] R. M. Rodrigues et al., “Human skin-derived stem cells as a novel cell source for in vitro hepatotoxicity screening of pharmaceuticals.,” Stem Cells Dev., vol. 23, no. 1, pp. 44–55, 2014

Associated documents

Article A Natale 2017.pdf

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