

Lentiviral reprogramming of human umbilical cord-derived mesenchymal stromal cells towards hepatocyte-like cells

Created on: 20-03-2019 - Last modified on: 28-02-2022

SCOPE OF THE METHOD

The Method relates to	Human health
The Method is situated in	Basic Research
Type of method	In vitro - Ex vivo
This method makes use of	Human derived cells / tissues / organs
Specify the type of cells/tissues/organs	umbilical cord

DESCRIPTION

Method keywords

human adult stem cells

hepatocyte-like cells

lentiviral reprogramming

umbilical cord

Scientific area keywords

in vitro liver model

Drug-induced liver injury (DILI)

human hepatocyte-like cells

liver enriched transcription factor

human adult stem cells

Method description

Human umbilical cord-derived mesenchymal stromal cells (hUC-MSCs) express several key liver-specific transcription factors as well as hepatic progenitor markers. However, they still lack the hepatocyte nuclear factors 1-alpha (HNF1a) and 4-alpha (HNF4a), indispensable for their reprogramming towards hepatocyte-like cells. This method comprises the reprogramming of hUC-MSCs towards hepatocyte-like cells through HNF1a lentiviral over-expression. Whole genome microarray analysis revealed that the expression of the nuclear receptor retinoid X receptor (RXR) gamma and the nuclear transcription factor HNF4a, in HNF1a-transduced hUC-MSCs, was significantly upregulated compared to the control conditions. This expression was even higher than found in human hepatocytes. The same was observed for the uridine 5'-diphospho-glucuronosyltransferase (UGT) 1A family. Further, a significant upregulation was observed for alpha-fetoprotein (AFP), alpha1-antitrypsin (A1-AT), the phase I biotransformation enzymes cytochrome P450 (CYP) 1A2 and CYP2A6 and the drug transporter multidrug resistance protein (MDR) 1.

Lab equipment

Incubator ($37 \pm 1^\circ\text{C}$, $90 \pm 5\%$ humidity, $5.0 \pm 1\%$ CO_2/air);

Type 2 laminar airflow HEK293T cells;

Ultracentrifuge Water bath ($37 \pm 1^\circ\text{C}$);

Inverse-phase contrast microscope;
Pipettes;
Pipettors;
Colorimetric reverse transcriptase assay;
Human hepatocytes;
Affymetrix microarray technologies;
Partek Genomics Suite Software.

Method status

Still in development

PROS, CONS & FUTURE POTENTIAL

Advantages

Persistent expression of HNF1a transcription factor in hUC-MSCs;
Endogenous induction of HNF4a expression.

Challenges

Genomic integration of the lentiviral vector.

Modifications

Usage of a non-integrative reprogramming method e.g. mRNA transfection.

Future & Other applications

Generation of hepatocyte-like cells for the development of functional human liver-based *in vitro* models for pharmaco-toxicological purposes.

REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION

Associated documents

PARTNERS AND COLLABORATIONS

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

Geographical Area Brussels Region

Coordinated by



Financed by

