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

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Organisation

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

Country Belgium

Geographical Area Brussels Region

SCOPE OF THE METHOD

The Method relates to	Human health
The Method is situated in	Basic Research
Type of method	In vitro - Ex vivo
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-foetoprotein (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 ± 1°C, 90 ± 5% humidity, 5.0 ± 1% CO2/air);

Type 2 laminar airflow HEK293T cells;

Ultracentrifuge Water bath (37 ± 1°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.