

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

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#### Organisation

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# 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  $(37 \pm 1^{\circ}C, 90 \pm 5\%$  humidity,  $5.0 \pm 1\%$  CO2/air); Type 2 laminar airflow HEK293T cells; Ultracentrifuge Water bath  $(37 \pm 1^{\circ}C)$ ; 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

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