In vitro human stem cell-based model of non-alcoholic steatohepatitis

Commonly used acronym: *NASH model*

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Organisation

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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
Specify the type of cells/tissues/organs	Human skin-derived adult stem cells

DESCRIPTION

Method keywords

Stem cells

Genetics

Lipids

in vitro

hepatic differentiation

inflammation

Scientific area keywords

NAFLD

NASH

Drug discovery

drug screening

preclinical

hepatology

metabolic syndrome

insulin resistance

Method description

Non-alcoholic fatty liver disease (NAFLD) ranges from simple steatosis to severe, life-threatening non-alcoholic steatohepatitis (NASH). Steatosis is mostly asymptomatic and does not cause health complications. However, in 5-10% of the cases it proceeds to NASH in which hepatic inflammation occurs and for which no therapy or drugs currently exist. Today's investigation of NAFLD and NASH relies mainly on animal models, which are not representative for the human situation. Therefore, we developed a predictive, human-based *in vitro* model that could be used to investigate molecular mechanisms that drive NASH, identify druggable targets and evaluate potential anti-NASH compounds. The model is based on the exposure (24h) of human skin-derived stem cells (hSKP)

differentiated towards hepatic cells (hSKP-HPC) (R. M. Rodrigues et al., Stem Cells Dev. 23, 44–55 (2014)) to factors involved in the metabolic syndrome and hepatic inflammation. The model has proven to be able to detect the anti-NASH properties of a potential anti-NASH drug currently being evaluated in a phase III clinical trial.

Lab equipment

Biosafety cabinet;

Flow-cytometer;

RT-qPCR (+ evt. microarray/RNA-sec facility);

Fluorescence microscope.

Method status

Still in development

PROS, CONS & FUTURE POTENTIAL

Advantages

Resuts within 24 hours;

Sensitive;

Multiple donors can be tested.

Challenges

The proliferation and hepatic differentiation takes among one month.

Future & Other applications

The primary application potential of this method is testing potential anti-NASH drugs.

REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION

References

R. M. Rodrigues et al., Stem Cells Dev. 23, 44–55 (2014)

R. M. Rodrigues et al., Arch. Toxicol. 90, 677–689 (2016). The manuscript for this method has been submitted to Pharmacological Research: Boeckmans, J., Buyl, K., Natale, A., Vandenbempt, V., Rogiers, V., De Kock, J., Marcelino Marcelino Rodrigues, R.* & Vanhaecke, T.* (*Equally contributing senior authors). Elafibranor restricts lipogenic and inflammatory responses in a human skin stem cell-derived model of NASH (Submitted)

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