

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

*Commonly used acronym: NASH model*

*Created on: 13-03-2019 - Last modified on: 28-02-2022*

## SCOPE OF THE METHOD

<b>The Method relates to</b>	Human health
<b>The Method is situated in</b>	Translational - Applied Research
<b>Type of method</b>	In vitro - Ex vivo
<b>This method makes use of</b>	Human derived cells / tissues / organs
<b>Specify the type of cells/tissues/organs</b>	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-seq facility);  
Fluorescence microscope.

### **Method status**

Still in development

### **PROS, CONS & FUTURE POTENTIAL**

#### **Advantages**

Results 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)

## 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

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