Establishment of sandwich cultures of primary human hepatocytes

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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

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	Primary human hepatocytes

DESCRIPTION

Method keywords

Sandwich cultures of hepatocytes

Scientific area keywords

Drug-induced cholestasis

Method description

This method describes a well-known optimised human *in vitro* model of drug-induced cholestasis. Cryopreserved primary human hepatocytes are cultured between two layers of extracellular matrix scaffold, which will delay dedifferentiation and allows to restore cell-extracellular matrix interactions. The sandwich culture method can be applied to both single cell culture dishes and multi-well plates, thus providing an opportune model for high-throughput screening.

Method status

Still in development

PROS, CONS & FUTURE POTENTIAL

Advantages

Suitable for long-term exposure;
Restored cell polarity;

Presence of cell-ECM interactions;
Formation of functional bile canalicular network;
Maintain functional expression levels of transport proteins and xenobiotic metabolization enzymes;
Applicable for quantifying and detecting cholestatic liabilities.

Challenges

Mass transfer barrier;
Difficult to culture in 96-well plates;
Require daily medium renewal due to accumulating toxic metabolites;
Hypoxic environment.

Modifications

The model is already modified by introducing a renewal of the collagen layer every 3-4 days. As a result, the model shows and extended cultivation regime up to 14 days (Parmentier et al. 2013).

Future & Other applications

The model could be used to assess the overall hepatotoxic potential of drugs, cosmetics, biocides or food additives.

REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION

References

Gijbels E., Vilas-Boas V., Deferm N. et al. (2019) Mechanisms and in vitro models of drug-induced cholestasis. Archives of Toxicology (submitted)
Gijbels E., Vanhaecke T., Vinken M. (2019) Establishment of sandwich cultures of primary human hepatocytes. Methods in Molecular Biology - Protocols in Experimental Cholestasis Research (accepted)
Other references you can find in attached document

Associated documents

Manuscript.docx

Links

IVTD - VUB
Prof. Mathieu Vinken - Team

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