Human liver spheroid co-cultures to investigate parenteral nutrition-induced hepatotoxicity

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Organisation

Name of the organisation Vrije Universiteit Brussel (VUB)
Department Department of Pharmaceutical and Pharmacological Sciences

Specific Research Group or Service
In Vitro Toxicology and Dermato-Cosmetology (IVTD)
Country Belgium
Geographical Area Brussels Region

SCOPE OF THE METHOD

The Method relates to	Human health
The Method is situated in	Basic Research, Translational - Applied Research
Type of method	In vitro - Ex vivo
Specify the type of cells/tissues/organs	C3A cells (clonal derivative of the human hepatoma HepG2 cell line), LX-2 cells (immortalized activated human hepatic stellate cell line)

DESCRIPTION

Method keywords

Liver spheroids
co-culture
RNA sequencing
Hepatotoxicity
spheroids
In vitro liver model
3D in vitro model
liver cells

Scientific area keywords

Total Parenteral Nutrition
Instestinal failure-associated liver disease
liver injury
in vitro toxicology
TPN
IFALD
nutrition

Method description

Total Parenteral Nutrition (TPN) can cause adverse effects, including metabolic disorders and liver injury. TPN-associated liver injury, known as intestinal failure-associated liver disease (IFALD), represents a significant problem affecting up to 90% of individuals receiving TPN. Despite numerous animal studies and clinical observations, the molecular mechanisms driving IFALD remain largely unknown. For this, a three-dimensional (3D) spheroid co-culture system consisting of both human parenchymal and non-parenchymal liver cells was used to elucidate the mechanisms of TPN-associated liver injury. Human liver spheroid co-cultures were set up using C3A cells, a clonal derivative of the human hepatoma HepG2 cell line, and LX-2 cells, an immortalized activated human hepatic stellate cell line.

Lab equipment

- Laminar air flow,
- Microscope,
- SpectraMax iD3 Multi-Mode Reader,
- Spectrophotometer,
- Attune Acoustic Focusing Cytometer.

Method status

Published in peer reviewed journal

PROS, CONS & FUTURE POTENTIAL

Advantages

The use of human-centered *in vitro* systems can overcome the limitations of clinical research and animal experimentation in the IFALD field, and allows in-depth investigation at the mechanistic level.

Challenges

Despite providing important molecular and cellular insights into mechanisms of liver injury secondary to TPN exposure, a limitation of the present study is the lack of direct clinical translation. This is particularly reflected in attempts to correlate the dosages of TPN used *in vitro* to those observed in clinics during a TPN regimen.

Future & Other applications

Computational toxicology methods that predict chemical toxicity and correlate *in vitro* and *in vivo* concentrations are available and could aid in the efforts needed to increase clinical relevance. In particular, physiologically based pharmacokinetic (PBPK) modeling can facilitate quantitative *in vitro* to *in vivo* extrapolation (QIVIVE) and allow to combine *in silico* and *in vitro* parameters and convert *in vitro* concentration–response curves into relevant *in vivo* exposures.
A combination of advanced heterotypic cell models, suitable *in vitro* and omics analysis, systems toxicology approaches, including AOPs and their networks and PBPK modeling holds great promise for advancing the translational research oriented toward unraveling further IFALD mechanisms and encouraging the safe use of TPN.

REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION

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Links

IVTD Research team (VUB)