Gelatin-Based Hybrid Hydrogels as Matrices for Organoid Culture

Created on: 17-01-2024 - Last modified on: 22-01-2024

SCOPE OF THE METHOD

The Method relates to	Human health
The Method is situated in	Basic Research
Type of method	In vitro - Ex vivo
This method makes use of	Human derived cells / tissues / organs
Specify the type of cells/tissues/organs	Intrahepatic Cholangiocyte Organoids isolated from human liver tissue

DESCRIPTION

Method keywords

Gelatin

hydrogel

Polysaccharide

Biopolymer

liver
Tissue Engineering
Expansion
differentiation
Chemically defined

Scientific area keywords

Liver organoids
Hydrogels
Drug-induced liver injury (DILI)
In vitro model

Method description

The application of liver organoids is very promising in the field of liver tissue engineering; however, it is still facing some limitations. One of the current major limitations is the matrix in which they are cultured. The mainly undefined and murine-originated tumor matrices derived from Engelbreth−Holm−Swarm (EHS) sarcoma, such as Matrigel, are still the standard culturing matrices for expansion and differentiation of organoids toward hepatocyte-like cells, which will obstruct its future clinical application potential. In this study, we exploited the use of newly developed highly defined hydrogels as potential matrices for the culture of liver organoids and compared them to Matrigel and two hydrogels that were already researched in the field of organoid research [i.e., polyisocyanopeptides, enriched with laminin−entactin complex (PIC-LEC) and gelatin methacryloyl (GelMA)]. The newly developed hydrogels are materials that have a physicochemical resemblance with native liver tissue. Norbornene-modified dextran cross-linked with thiolated gelatin (DexNB-GelSH) has a swelling ratio and macro-and microscale properties that highly mimic liver tissue. Norbornene-modified chondroitin sulfate cross-linked with thiolated gelatin (CSNB-GelSH) contains chondroitin sulfate, which is a glycosaminoglycan (GAG) that is present in the liver ECM. Furthermore, CSNB-GelSH hydrogels with different

mechanical properties were evaluated. Bipotent intrahepatic cholangiocyte organoids (ICOs) were applied in this work and encapsulated in these materials. This research revealed that the newly developed materials outperformed Matrigel, PIC-LEC, and GelMA in the differentiation of ICOs toward hepatocyte-like cells. Furthermore, some trends indicate that an interplay of both the chemical composition and the mechanical properties has an influence on the relative expression of certain hepatocyte markers. Both DexNB-GelSH and CSNB-GelSH showed promising results for the expansion and differentiation of intrahepatic cholangiocyte organoids. The stiffest CSNB-GelSH hydrogel even significantly outperformed Matrigel based on ALB, BSEP, and CYP3A4 gene expression, being three important hepatocyte markers.

Lab equipment

- Standard cell culture equipment,
- UV-A light.

Method status

Published in peer reviewed journal

PROS, CONS & FUTURE POTENTIAL

Advantages

- Chemically defined material,
- Easy-to-use,
- Easy to tune for your needs (e.g. chemical composition, mechanical properties),
- Compatible with multiple biofabrication methods.

Challenges

- There are small adaptations needed to the current characterisation assay,

- Isolation of the cells from the matrices is a bit more challenging.

Modifications

Further optimization is currently under investigation in order to make the matrices suitable for the whole organoid culture process (expansion, differentiation and isolation).

Future & Other applications

They can be used for other organoids and cell culture in general. However, optimisation per cell type will be required.

REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION

References

https://doi.org/10.1021/acs.biomac.2c01496

Associated documents

carpentier-et-al-2024-gelatin-based-hybrid-hydrogels-as-matrices-for-organoid-culture.pdf

Links

Gelatin-Based Hybrid Hydrogels as Matrices for Organoid Culture

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