Long-term liver tissue cultivation

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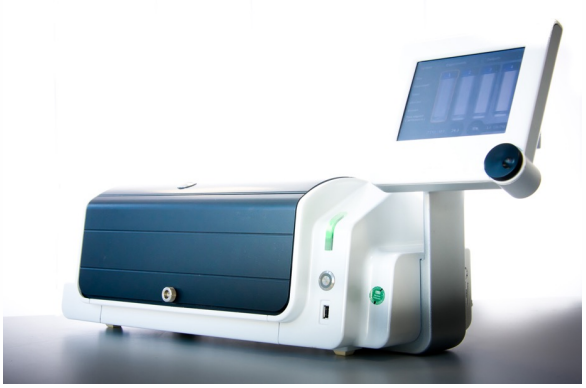
Enhance your research capabilities with our advanced CERO 3D Incubator & Bioreactor, designed for culturing human liver punch biopsies with unparalleled longevity, among other applications. Our cutting-edge technology departs from the traditional limitations of 2D hepatocyte cultivation, enabling you to maintain structural and functional viability for weeks.

Key Advantages:

- Possibility of extended Culture Viability:
  Increased the functional lifespan of liver biopsies, surpassing traditional cultivation timeframes and improving suitability for extended studies.
- Minimized Cell Death:
  Improved supply of nutrients into the tissue, which translates to a higher yield of viable cells, thus improving the efficiency of your tissue assays.
- Enhanced Assay Precision:
  Could improve drug metabolism studies thanks to maintaining the tissue structure and the participation of all hepatic cells for up to 21 days.

This innovation represents a significant step forward for tissue-based experimental designs. By providing a stable and representative environment, our technology could facilitate a more effective platform for both pharmacological studies and disease modeling.

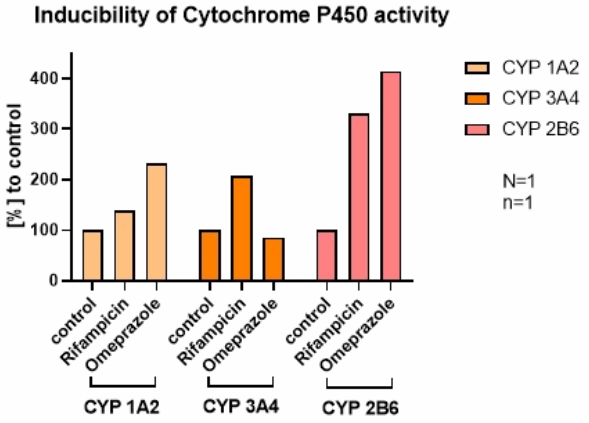
Boost the quality and reliability of your experiments with the CERO 3D Incubator & Bioreactor, where your experiments would benefit from longer-lasting cultures paired with conditions that closely reflects the cell's natural environment.



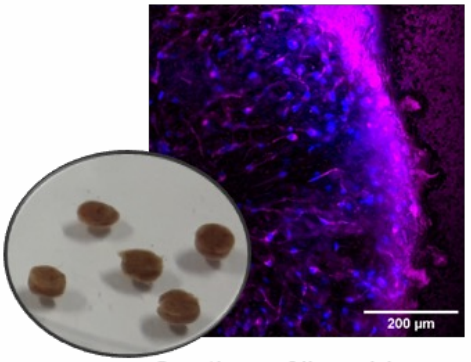
CERO 3D Incubator & Bioreactor for enhanced cell viability

Viability and Inducibility of human Liver Biopsy Punches

The integration of Cytochrome P450 enzyme activity in combination with MitoTracker imaging offers a comprehensive view of liver biopsy functionality. The preservation of basal CYP450 enzymes suggests the biopsies' maintain metabolic capabilities, essential for pharmacological studies. Moreover, preliminary studies suggest an inducible induction of some CYP450 by either rifampicin or omeprazole, two well-known CYP inducers. Simultaneously, MitoTracker imaging displays robust mitochondrial health, critical for cellular energy and metabolism. Taken together, this approach highlights the CERO 3D system's ability to maintain a physiologically relevant liver environment, emphasizing the model's utility for drug response and disease research.



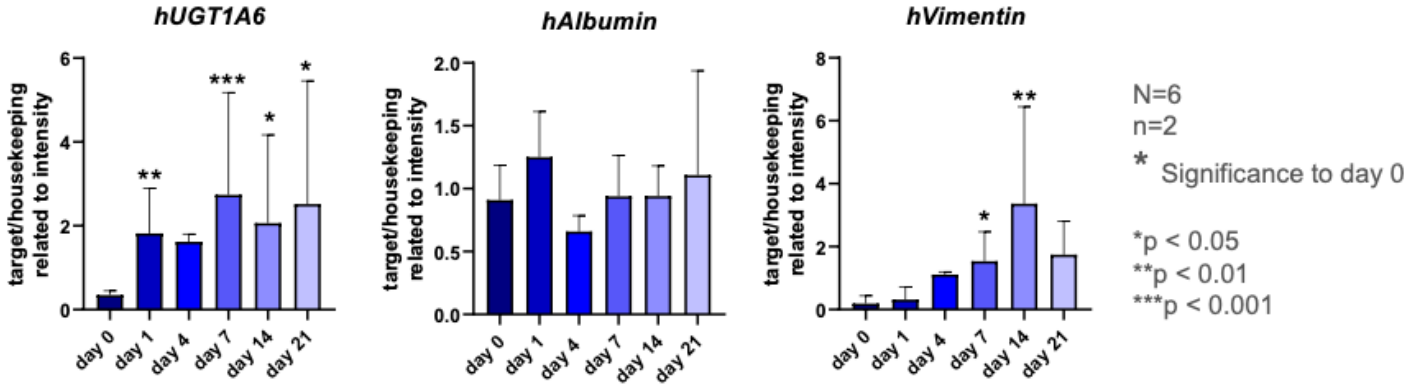
Cytochrome P450 activity increased with induction by Rifampicin or Omeprazole after a few weeks.



Section of liver biopsy after a few weeks
Blue: DAPI
Magenta: Mitotracker

Gene Expression in Liver Biopsy Punches up to 21 Days

Maintained gene expression in liver biopsies over three weeks suggests the preservation of specific liver functions, underlining the CERO system's efficacy in upholding both cell viability and functionality. Relative stable gene activity is vital for precise disease modeling and drug metabolism research, highlighting its importance in liver tissue research.



Gene expression showed preservation of functionality in human biopsy punches over 21 days.

Conclusion

- Recent scientific publications have highlighted the remarkable advancements in 3D liver modeling technologies, a trend that is further supported by findings presented in this application note. The CERO 3D Incubator and Bioreactor can maintain the viability and functionality of human liver biopsy punches for up to 21 days, offering a new promising tool for liver tissue research crucial for drug testing and disease modeling.
- Recent research by Klaas et al. [1] has partially corroborated similar data, demonstrating comparable induction of CYP enzymes in primary human hepatocytes when stimulated with rifampicin and omeprazole under similar culture conditions, utilizing the CERO 3D model.

Conclusion, ongoing

- The versatility of the CERO 3D extends beyond its utility in inducing CYP enzymes. It can also serve as a platform for cultivating and differentiating induced pluripotent stem cells (iPSCs) into hepatic organoids. A recently optimized protocol delineates the generation of hepatocyte-like cells (HLCs) from iPSCs in both 2D and 3D cultures, promising more reproducible and higher biomass organoids [2]. Moreover, the study identified a rapid recovery of CYP3A4 expression in frozen organoids, suggesting the feasibility of cryopreservation in maintaining functional organoid structures [2].
- The significance of 3D biomimetic liver models and culture systems lies in their ability to authentically replicate liver physiology and pathology [3,4]. Moreover, highlighting on how the bioprinting technology contributes to liver tissue reconstruction, aiding in research and potentially alleviating organ shortages was reported [5].
- The application note aligns with the above-mentioned publications, particularly with its demonstration of the consistent expression of liver-specific genes and the maintenance of mitochondrial function, as evidenced by Cytochrome P450 enzyme activity and MitoTracker imaging. This alignment indicates a crucial advancement in developing liver models that accurately reflect human physiology for medical research.

1. Klaas, M., Möll, K., Mäemets-Allas, K. et al. Long-term maintenance of functional primary human hepatocytes in 3D gelatin matrices produced by solution blow spinning. Sci Rep11, 20165 (2021). https://doi.org/10.1038/s41598-021-99659-1
2. Saskia Altmaier, Ina Meiser, Emilie Lemesre, Benjamin Chanrion, Rachel Steeg, Lidia Elena Leonte, Bjørn Holst, Boye Schnack Nielsen, Christian Clausen, Katharina Schmidt, Anne Marie Vinggaard, Heiko Zimmermann, Julia Christiane Neubauer, Mikkel Aabech Rasmussen. Human iPSC-derived hepatocytes in 2D and 3D suspension culture for cryopreservation and in vitro toxicity studies, Reproductive Toxicology, Volume 111, 2022, Pages 68-80,ISSN 0890-6238, https://doi.org/10.1016/j.reprotox.2022.05.005.
3. Sang Woo Lee, Da Jung Jung and Gi Seok Jeong. Gaining New Biological and Therapeutic Applications into the Liver with 3D In Vitro Liver Models. Tissie Eng Regen Med. 2020 Dec; 17(6): 731–745. doi: 10.1007/s13770-020-00245-9
4. Sarah Kammerer. Three-Dimensional Liver Culture Systems to Maintain Primary Hepatic Properties for Toxicological Analysis In Vitro. Int. J. Mol. Sci. 2021, 22(19), 10214; https://doi.org/10.3390/ijms221910214.
5. Changcan Li, Zhuoran Jiang and Huayu Yang. Advances in 3D bioprinting technology for liver regeneration. Hepatobiliary Surg Nutr. 2022 Dec; 11(6): 917–919. doi: 10.21037/hbsn-22-531.