Development and optimisation of complex liver models by 3D bio-printing.

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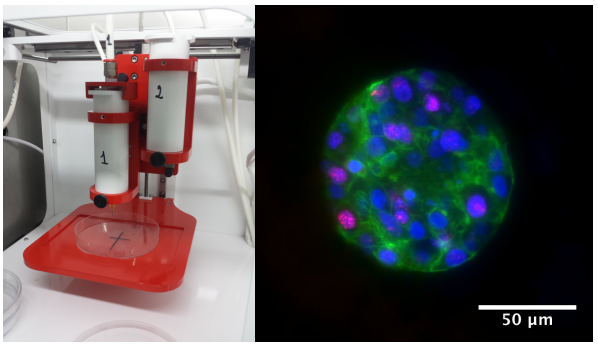
Abstract (300 word limit)

The use of conventional 2D in vitro culture models is increasingly questioned and their ability to accurately mimic the complete physiological function of the organs or tissues of interest can be limited. For a few times now, 3D models have been successfully developed by the team Dymec of IRSET, with improved function and phenotypes of many cells type, including primary and transformed hepatic cells.

The project aims to improve those 3D models by building a multicellular organoide-like liver model, with an organised architecture and in a reproducible and hight-throughput way. We relied on extrusion based bioprinting technology, which allows the precise and spatially controlled deposition of a biological material containing cells to form definite microarchitectures.

The first step of the work was to define the printing parameters: hydrogel concentration, step of cross linking, printing temperature, pressure and speed, have been optimised to obtain a printable structure which remained stable over the long term. Secondly, the long-term biocompatibility of these structures was tested by encapsulation of transformed hepatic cells. They preserved their long-term viability (> 30 days) and were able to proliferate in this biomatrix optimised for bioprinting. They organised themselves into spheroïds/*acini-like* structures and displayed an apico-basal polarity after 7 day of culture. The next step aim was to improve the liver function of the created structures, by bioprinting an architecturally organised cocultures with parenchymal cells, by adding to the currents bioprinted structures non-parenchymal cells.

Image



Recent Publications (minimum 5)

1. Bomo, J., Ezan, F., Tiaho, F., Bellamri, M., Langouët, S., Theret, N., and Baffet, G. (2016). Increasing 3D Matrix Rigidity Strengthens Proliferation and Spheroid Development of Human Liver Cells in a Constant Growth Factor Environment. J. Cell. Biochem. *117*, 708–720.
2. Lauschke, V.M., Hendriks, D.F.G., Bell, C.C., Andersson, T.B., and Ingelman-Sundberg, M. (2016). Novel 3D Culture Systems for Studies of Human Liver Function and Assessments of the Hepatotoxicity of Drugs and Drug Candidates. Chem. Res. Toxicol.
3. Murphy, S.V., and Atala, A. (2014). 3D bioprinting of tissues and organs. Nature Biotechnology *32*, 773–785.
4. Pampaloni, F., Reynaud, E.G., and Stelzer, E.H. (2007). The third dimension bridges the gap between cell culture and live tissue. Nature Reviews Molecular Cell Biology *8*, 839.
5. Ozbolat, I.T., and Hospodiuk, M. (2016). Current advances and future perspectives in extrusion-based bioprinting. Biomaterials *76*, 321–343.



Biography (150 word limit)

Marie Cuvellier started a PhD after completing her degree in Pharmaceutical Sciences at the Faculty of Pharmacy of Rennes I, and a MSc in Human Toxicology from the University of Paris Descartes. Her work at the IRSET focuses on the development of 3D multicellular liver models through 3D bioprinting, while working on the implementation of this technology at a larger scale within the institute.

Notes/Comments:

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