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PhD Research Activities

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Bioartificial liver device using progenitor cells or induced pluripotent stem cells

My PhD project is mainly concerned with developing a prototype bioartificial liver to act as a temporary support for liver failure patient until liver transplantation, which is currently the only treatment for liver failure.

When designing a bioartificial liver, special attention should be paid to reconstructing a proper cellular microenvironment that ensures highest and prolonged functional activity of the liver cells.

Global workplan overview:

The appropriate cellular polarization and paracrine cellular communication found in 3D liver cultures have been associated with improved longevity of function in culture. In order to achieve that, hollow fiber membrane bioreactors would be utilized. Into those bioreactors, human primary liver cells (either parenchymal cells alone or in co-culture with non-parenchymal cells) would be cultured either as single cells or spheroids in order to mimic the in vivo situation as closely as possible. Moreover, differentiation protocols would be examined using stem cells of different types (mesenchymal and induced pluripotent stem cells) in order to try to differentiate them into hepatocyte-like cells.

What has been done do far:

Over the past few months, liver micro-tissues were obtained via realization and culturing of hepatocyte spheroids into crossed hollow-fiber membrane bioreactors (batch and continuous) made up of polyethersulfone (PES). The hepatocyte spheroids fused together forming liver micro-tissues as confirmed by scanning electron microscope images. In the continuous bioreactor, the liver-specific functions in terms of urea synthesis and diazepam biotransformation were much higher than in the case of the batch bioreactors. In the batch bioreactors, the micro-tissues were maintained viable for 16 days.

What next?

These promising results pave the way for further experimentation utilizing different hollow-fiber membranes in the bioreactor and/or the use of heterotypic spheroids made up of co-cultures of hepatocytes and non-parenchymal cells in order to further optimize this in-vitro liver model.