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Hepatic differentiation of human induced pluripotent stem cells in a perfused 3d porous polymer scaffold for liver tissue engineering

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A huge shortage of organs for transplantation has motivated the research field of tissue engineering to develop bio-artificial liver tissue and even a whole liver. Due to limitations of primary hepatocytes regarding availability and maintenance of functionality, stem cells and especially human induced pluripotent stem cells (hIPS cells) are an attractive cell source for liver tissue engineering.

Our approach for engineering liver tissue is to culture and differentiate hIPS cells in a 3D porous polymer scaffold built-in a perfusable bioreactor to ensure supply of oxygen and nutrients and removal of waste. To investigate the hepatic differentiation at flow conditions, IPS-derived definitive endoderm cells were seeded into the scaffold and differentiated according to a protocol developed by our collaborator Cellectis AB. Compared to conventional batch cultures, a similar hepatocyte-like cell morphology and gene expression of the hepatocyte nuclear transcription factor 4α was observed, whereas a decreased expression was for seen for the transcription factor CAR and the CYP enzymes CYP3A5 and CYP3A7. Furthermore, expression of albumin and α-fetoprotein was almost knocked down. However, expression of all markers was increased by the use of conditioned medium or medium with a two times lower concentration of the signalling factors than those optimized for conventional batch cultures.

Thus, our results suggest that the flow conditions affect paracrine cell signalling necessary for liver differentiation and/or functionality, as well as the concentration of signalling factors in the differentiation medium has to be adapted to the different environment at flow with constant renewal of the culture medium.

Biography

Mette Hemmingsen has completed her PhD about culture and differentiation of cells in microfluidic array systems and is currently doing postdoctoral studies in liver tissue engineering from The Technical University of Denmark, Department of Micro- and Nanotechnologies.

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