Differentiation of human-induced pluripotent stem cell under flow conditions to mature hepatocytes for liver tissue engineering - DTU Orbit (24/12/2018)

Differentiation of human-induced pluripotent stem cell under flow conditions to mature hepatocytes for liver tissue engineering

Hepatic differentiation of human-induced pluripotent stem cells (hiPSCs) under flow conditions in a 3D scaffold is expected to be a major step forward for construction of bioartificial livers. The aims of this study were to induce hepatic differentiation of hiPSCs under perfusion conditions and to perform functional comparisons with fresh human precision-cut liver slices (hPCLS), an excellent benchmark for the human liver in vivo. The majority of the mRNA expression of CYP isoenzymes and transporters and the tested CYP activities, Phase II metabolism, and albumin, urea, and bile acid synthesis in the hiPSC-derived cells reached values that overlap those of hPCLS, which indicates a higher degree of hepatic differentiation than observed until now. Differentiation under flow compared with static conditions had a strong inducing effect on Phase II metabolism and suppressed AFP expression but resulted in slightly lower activity of some of the Phase I metabolism enzymes. Gene expression data indicate that hiPSCs differentiated into both hepatic and biliary directions. In conclusion, the hiPSC differentiated under flow conditions towards hepatocytes express a wide spectrum of liver functions at levels comparable with hPCLS indicating excellent future perspectives for the development of a bioartificial liver system for toxicity testing or as liver support device for patients.

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