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**Bioprinting functional hepatocyte organoids derived from human stem cells to treat liver failure**

**Li G, He J, Shi J, *et al.* Bioprinting functional hepatocyte organoids derived from human chemically induced pluripotent stem cells to treat liver failure. *Gut* 2025; 74(7): 1150-1164. doi: 10.1136/gutjnl-2024-333885.**

Regenerative medicine shows great potential as a therapeutic approach in liver failure. In this article, Li *et al.,* developed chemically re-programmed human induced pluripotent stem cells to generate 3D-bioprinted hydrogel-embedded hepatocyte organoids (3D-hCiPSCs-HOs), that lead to amelioration of disease parameters of when transplanted into in-vivo liver failure models.

Firstly, Li *et al.,* characterised and optimised the hCiPSC-hepatocyte differentiation process, spheroid/organoid formation and bioprinting of organoids. Using RT-qPCR, immunofluorescence, fluorescence-based assays, staining and simple microscopy, each of these steps were optimised based on cell viability, functionality and gene/protein expression. The final 3D-hCiPSC-HOs exhibited higher or equivalent hepatocyte-specific gene expression, with corresponding protein expression, albumin and urea synthesis and CYP3A4 (Cytochrome P450 3A4) activity, compared to pre-printed organoids and comparable to primary human hepatocytes.

Subsequently, 3D-hCiPSC-HOs transplanted into two mice models of liver failure (carbon tetrachloride (CCl4) and *Fah-/-*) lead to reduction of tissue inflammatory/fibrotic gene expression, improvement in serum liver function tests and albumin levels, histology and survival compared to sham procedure, 3D-printed A549 cells and blank transplant, at different time points. Extracted 3D-hCiPSC-HOs from *Fah*-/- mice showed maintained structural integrity and viability and angiogenesis coinciding with Dextran and CD31 staining, at day 60 post-transplant. Furthermore, hepatic gene expression was maintained along with presence of bile duct markers expression, suggesting tissue re-organisation, de-novo angiogenesis and bio-tolerance.

Li *et al.,* conclude that 3D-hCiPC-HOs are a feasible and effective approach in treatment of liver failure in their pre-clinical work, whereby future aspects should be focused on improving biocompatibility of hydrogels, mechanical integrity, scalability and ultimately, clinical translation.