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LIVER

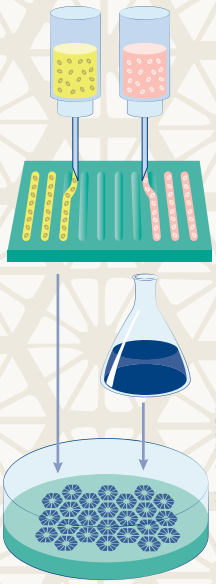
Bioprinted liver lobules

A 3D triculture hepatic model has been described in a new study. The model involves patterned bioprinting of multiple physiologically relevant cell types in a system that recapitulates the complex biology and morphology of the liver.

The liver is a unique organ comprising hepatocytes assembled into 3D hexagonal lobule units, supported by cell types with both endodermal and mesodermal origins. This microstructure organization has an important role in hepatic function, and conventional culture methods that rely upon 2D monolayers are considered inadequate for accurately mimicking the 3D microenvironment. Now, building on their previous work with bioprinting technology, Ma *et al.* have produced a hexagonal 3D hydrogel-based model incorporating not only human induced pluripotent stem cell (hiPSC)-derived hepatic progenitor cells, but also human endothelial cells and adipose-derived stem cells.

The investigators printed the predefined liver tissue in two parts. "First, a honeycomb pattern of 900 μm-sized hexagons is printed, each containing liver cells derived from hiPSCs," report corresponding authors Shaochen Chen and Shu Chien. "[Then] endothelial and mesenchymal supporting cells are printed in the spaces between the stem-cell-containing hexagons," they add. This new model has several distinct advantages over other 2D and 3D liver models, including generation time (the entire 200 μm thick, 3 × 3mm square construct takes only seconds to print), as well as phenotypic and functional enhancements to morphological organization, liver-specific gene expression, metabolic product secretion and cytochrome P450 induction.

As the model contains appropriate cell combinations in a biomimetic microstructure, it has the potential for applications such as disease modelling and drug screening, in addition to personalized medicine, as the hiPSCs are sourced from a patient's own skin cells. The liver is also characterized by a dual blood supply from both the hepatic artery and portal vein, as well as biliary ducts for bile secretion. "We will incorporate this unique portal triad system in our future work to make an even more realistic *ex vivo* model of the liver," says Chien.



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"We hope this work will open the door to printing other functional tissues such as heart, kidney, cancer and neuron that require complex tissue architecture, multiple cell types and vasculature support," concludes Chen.

Iain Dickson

ORIGINAL ARTICLE Ma, X. *et al.* Deterministically patterned biomimetic human iPSC-derived hepatic model via rapid 3D bioprinting. *Proc. Natl Acad. Sci. USA* http://dx.doi.org/10.1073/pnas.1524510113