



A high-throughput liver MPS capable of detecting small molecule and AAV-mediated hepatotoxicity

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Summary

The Organoplate® Graft provides a versatile platform for modeling liver physiology and drug-induced liver injury (DILI), supporting both small molecule tests and advanced therapies like AAV-based gene therapies. This scalable, immunocompetent 3D comprehensive liver model captures key liver features, including vascular structures and innate immune components, enabling more accurate toxicological evaluation and deeper insights into liver biology.

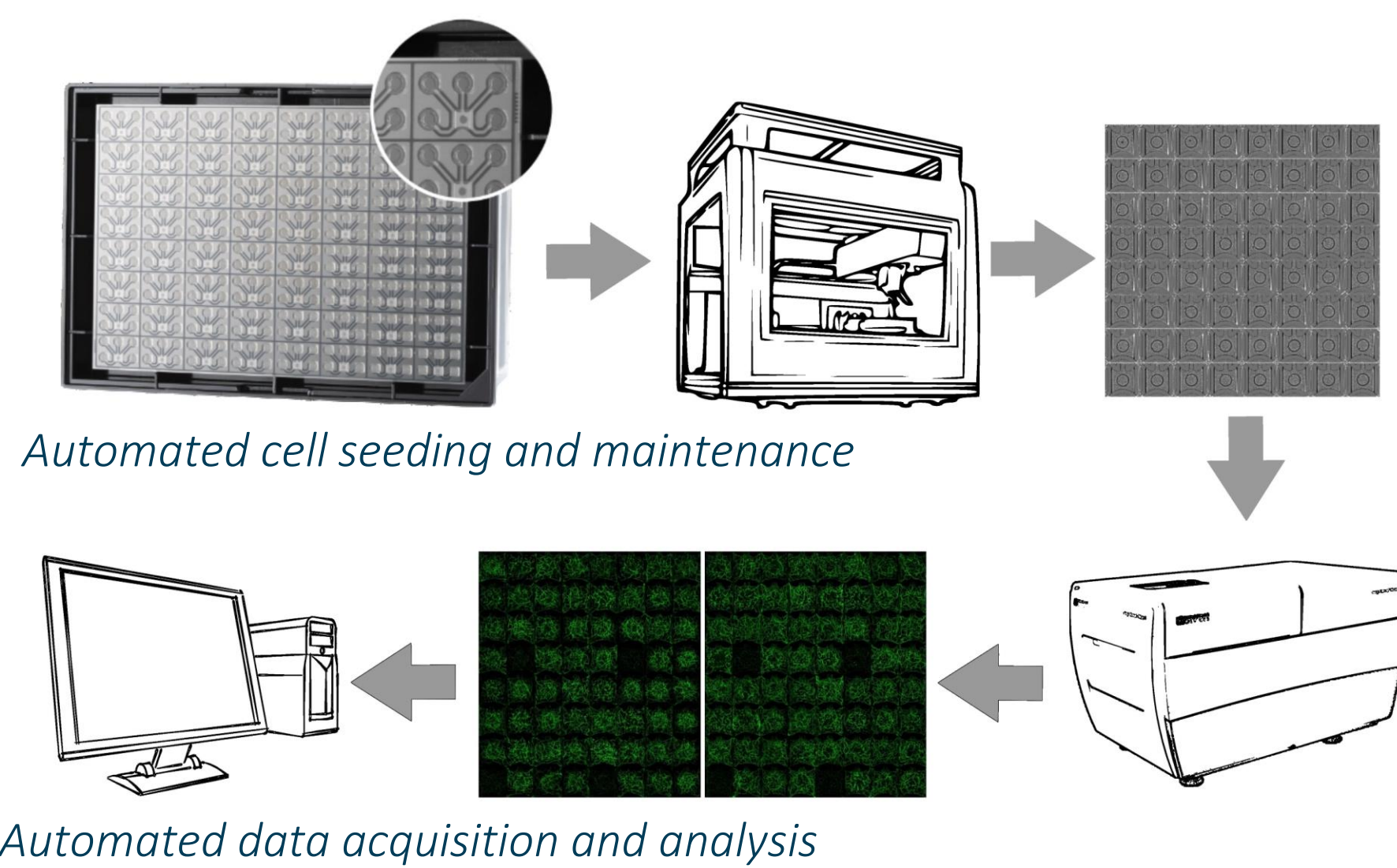
The Organoplate Graft and UniFlow Graft technology^{1, 2}



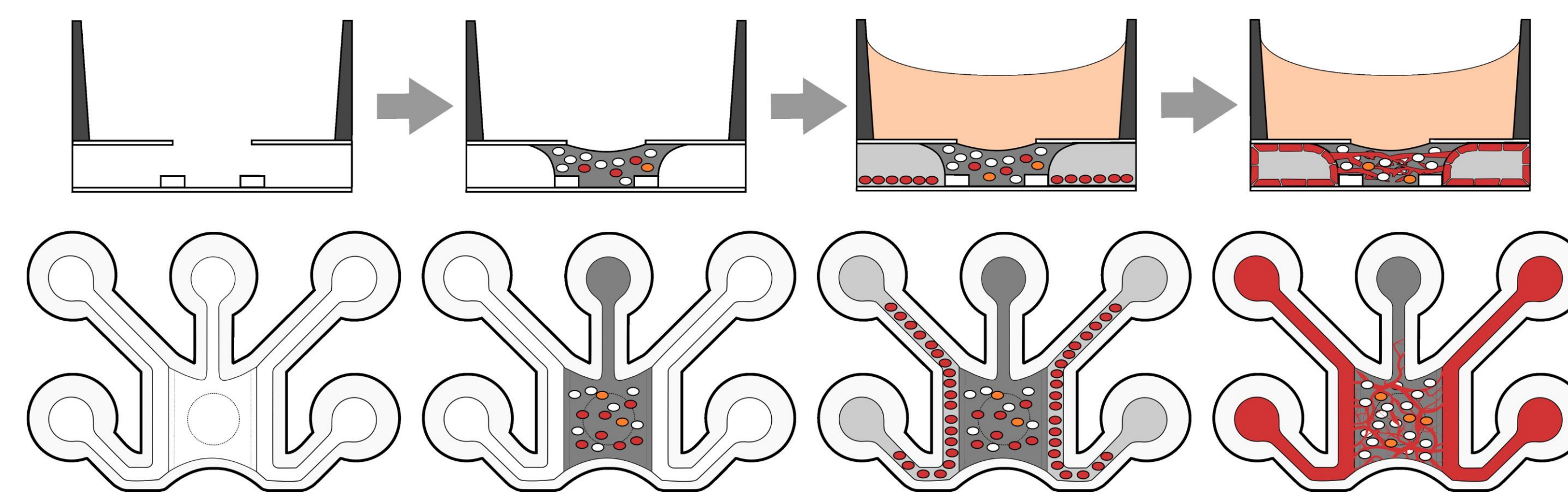
The Organoflow® provides continuous medium flow in the Organoplate with minimal settings required

- Based on standard 384 well-plate format – Easy to use
- No external pump – passive liquid control
- Membrane free – direct contact between cells and ECM

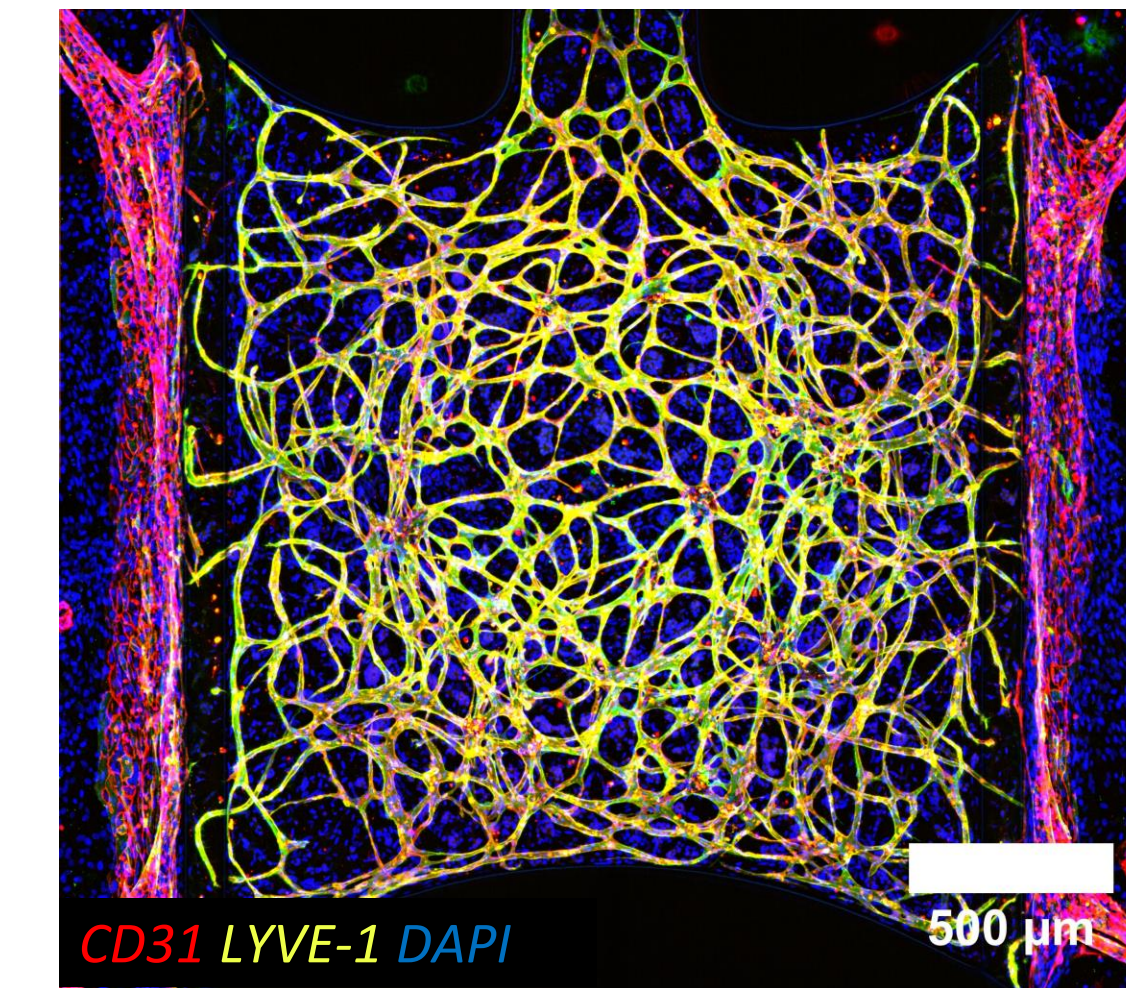
Automation compatible – High throughput (up to 64 chips per plate)



Comprehensive liver model in the Organoplate®

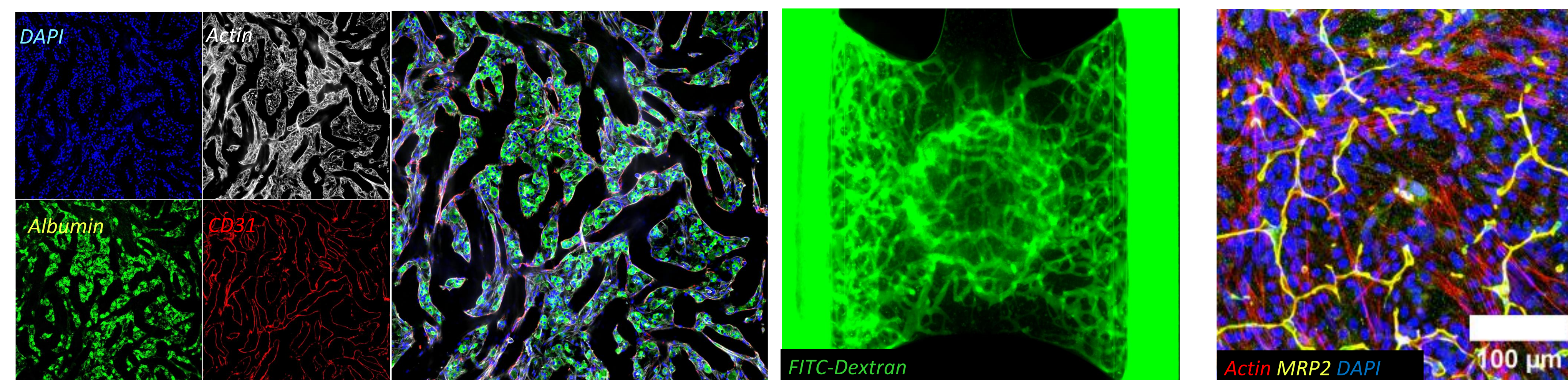


Seeding of hydrogel and liver cells (hepatocytes, stellate cells, liver-derived endothelial and Kupffer-like cells) and lateral endothelial vessels



Vascular network expresses LYVE-1 and connects lateral endothelial tubes

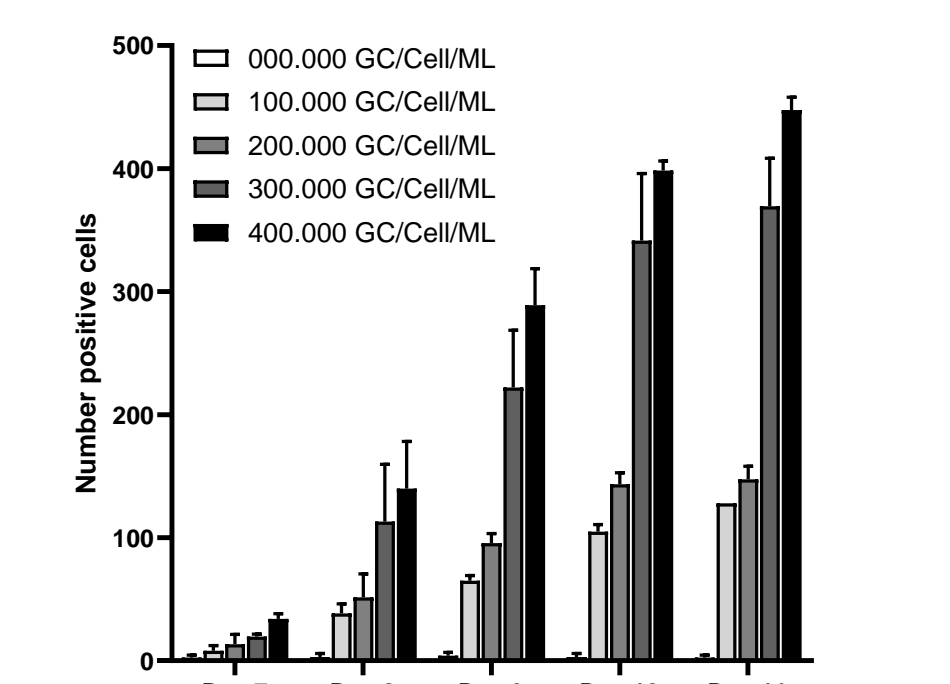
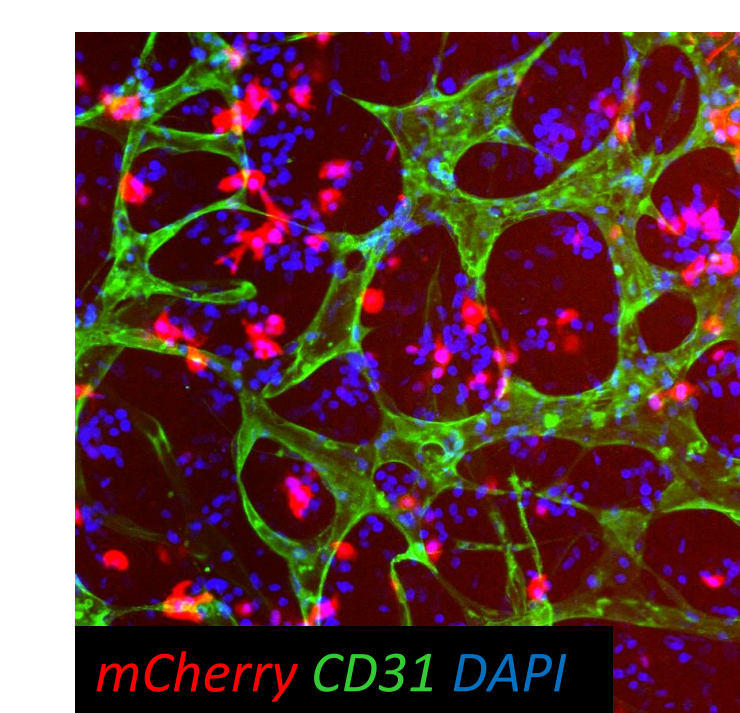
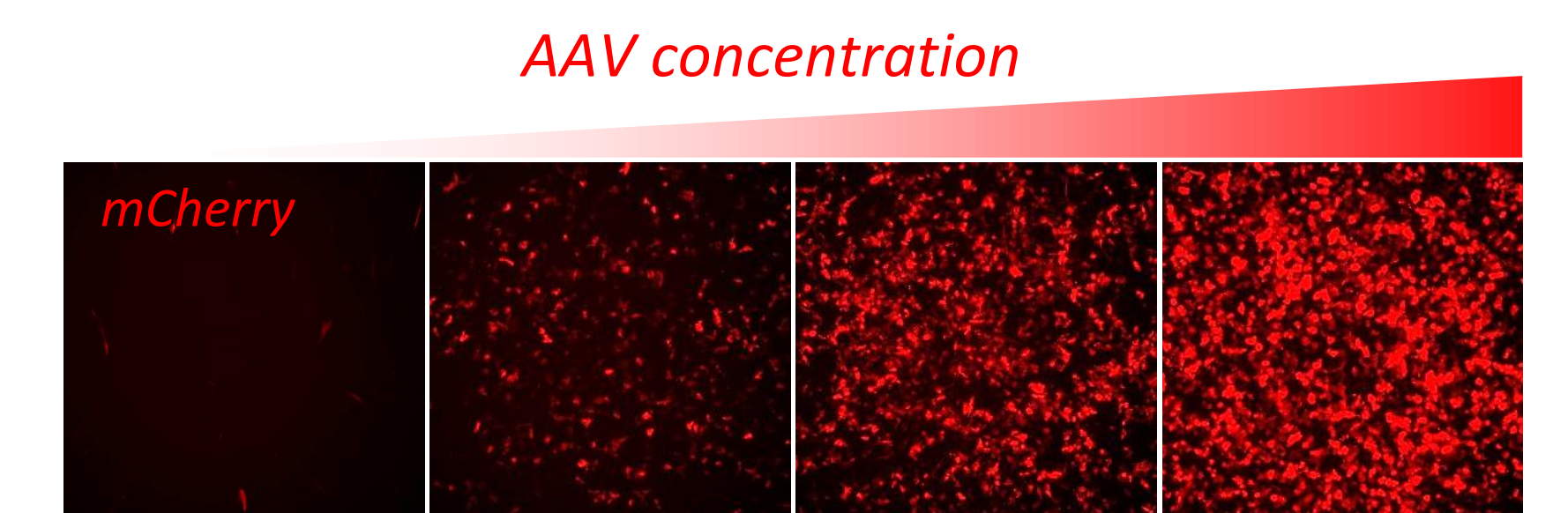
Organoplate liver model recapitulates the liver's architecture and supports comprehensive evaluation of hepatotoxicity.



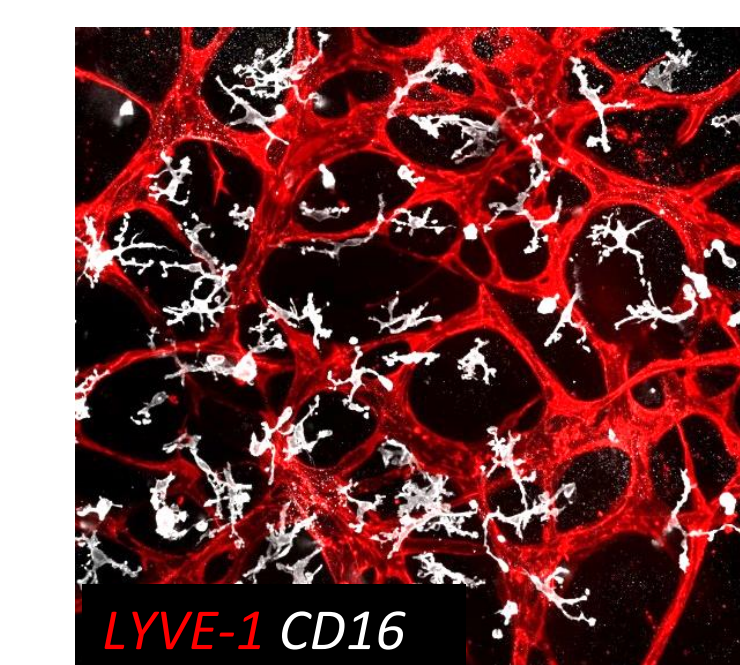
Complex architecture, with extensive vascular networks surrounding hepatocyte sheets. Perfusable vascular networks allow compounds and rAAVs to be introduced via the vasculature.

Liver tissue with 3D polarized hepatocytes.

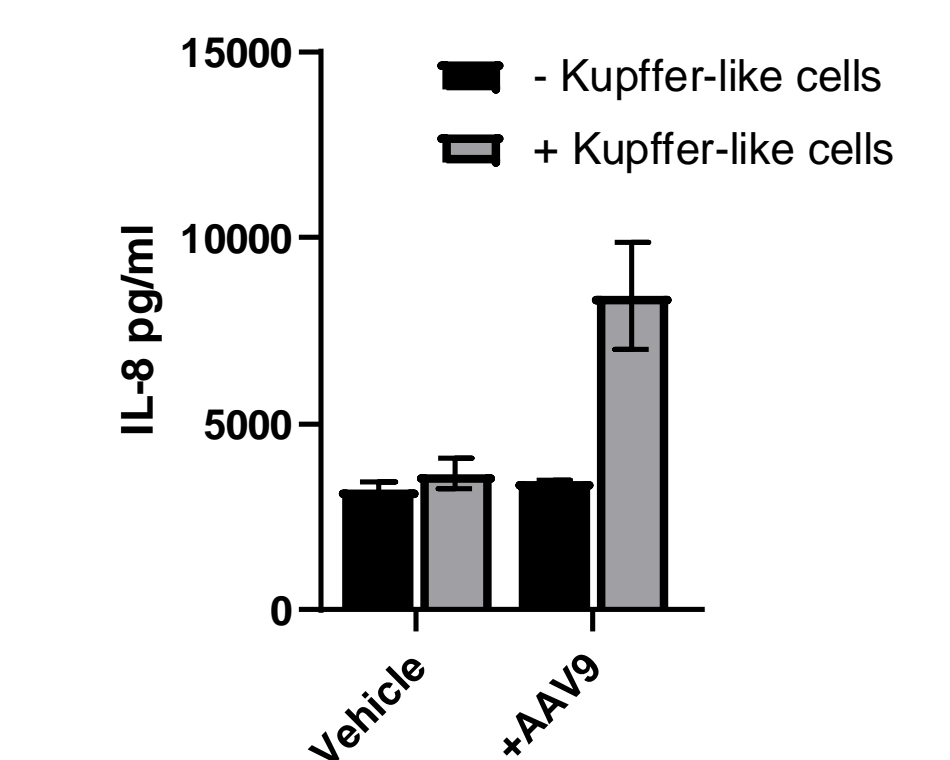
AAV-based therapy applications



AAV-mediated gene delivery of mCherry gene to hepatocytes

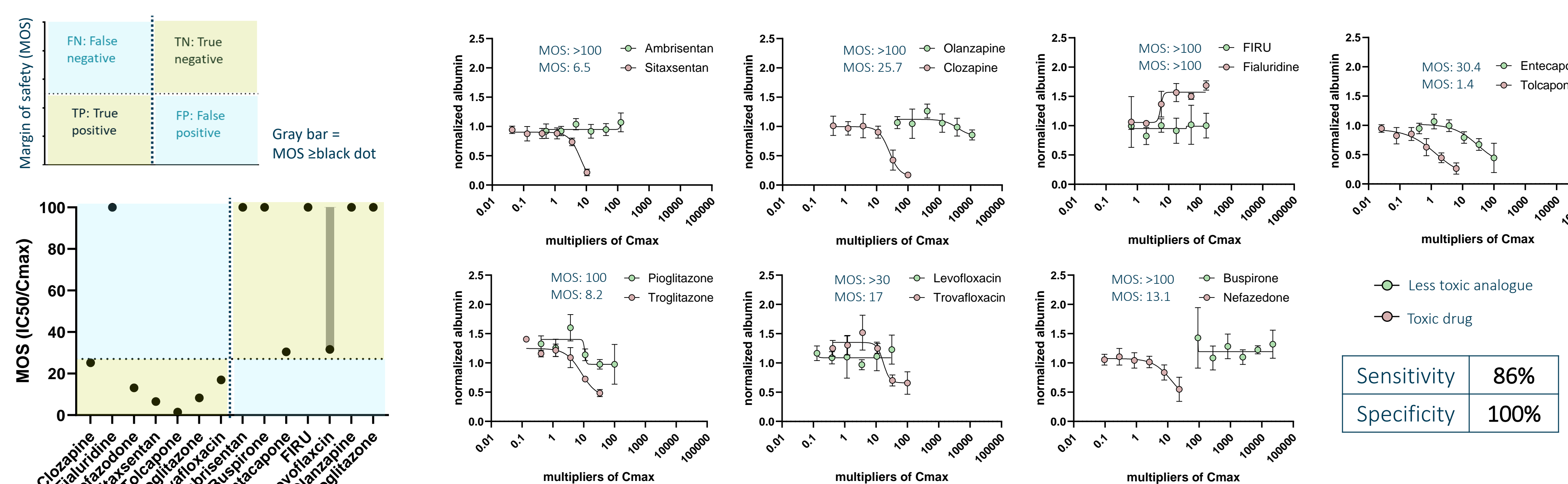


Liver tissue with inclusion of resident immune cells



AAV9-mCherry induce higher proinflammatory cytokine IL8 release in the presence of monocyte-derived macrophages

Assessing Drug Toxicity in the Comprehensive Liver Model



Margin of safety (MOS) for hepatotoxic and non-toxic drug pairs demonstrate the predictive accuracy and metabolic competence of the liver model.

Conclusion

In conclusion, we present a robust and automated complex liver model within the Organoplate Graft by embedding hepatocytes, liver-derived non-parenchymal cells in a hydrogel. This 3D liver holds the potential for groundbreaking progress in liver modelling which, besides including functional hepatic cells, also reflects the cellular organization and interactions found within the liver lobule. In conjunction with its high-throughput capability, this has the potential to revolutionize drug discovery and develop liver-safe therapies.

Literature

- [1] In vitro grafting of hepatic spheroids and organoids on a microfluidic vascular bed. Bonanini et al. *Angiogenesis*. 2022 Nov;25(4):455-470. doi: 10.1007/s10456-022-09842-9
 [2] A microvascularized in vitro liver model for disease modeling and drug discovery. Bonanini et al. *Biofabrication* 2024 Oct 24;17(1). doi: 10.1088/1758-5090/ad818a

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