

ORGANTRANS

Controlled Organoids Transplantation as Enabler for Regenerative Medicine Translation

Liver disease

- 2 million deaths per year worldwide
- Transplantation is the only effective treatment for various liver diseases
- Only 10% of global transplantation needs are met
- Demand for livers is projected to increase by 23% in the next 20 years

ORGANTRANS target patients

- Chronic end-stage liver diseases
- Residual healthy tissues



Liver cancer



Cirrhosis



Fatty liver

Overview



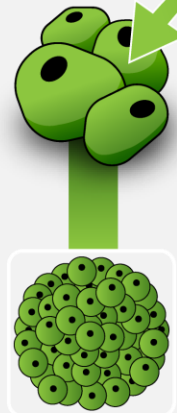
OrganTrans

Process for organoids transplantation

Autonomous self-assembly

Stem cells-derived organoids

Standardized organoids & automation



New regenerative therapy

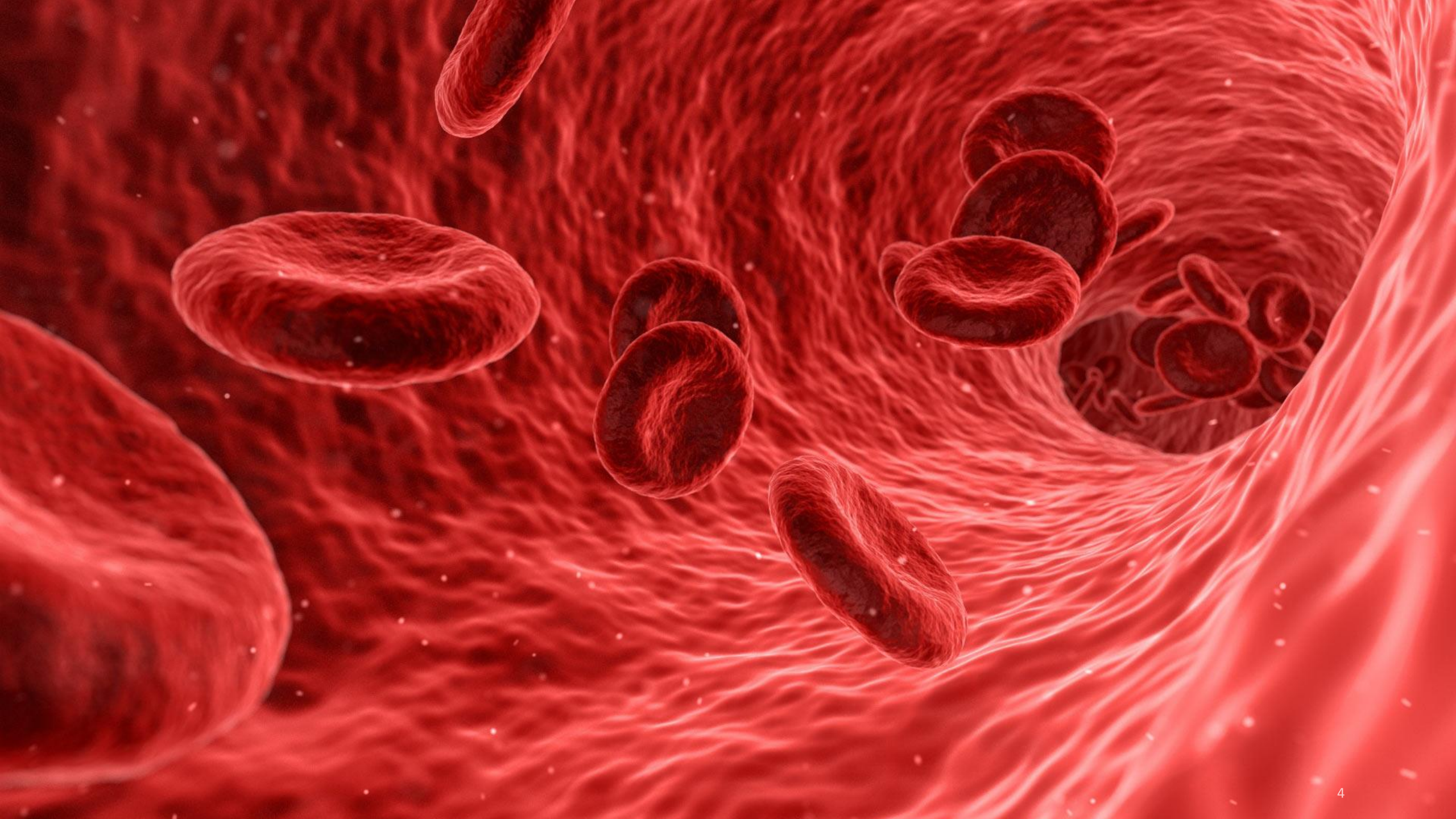


Biomimicry

FDA-approved materials

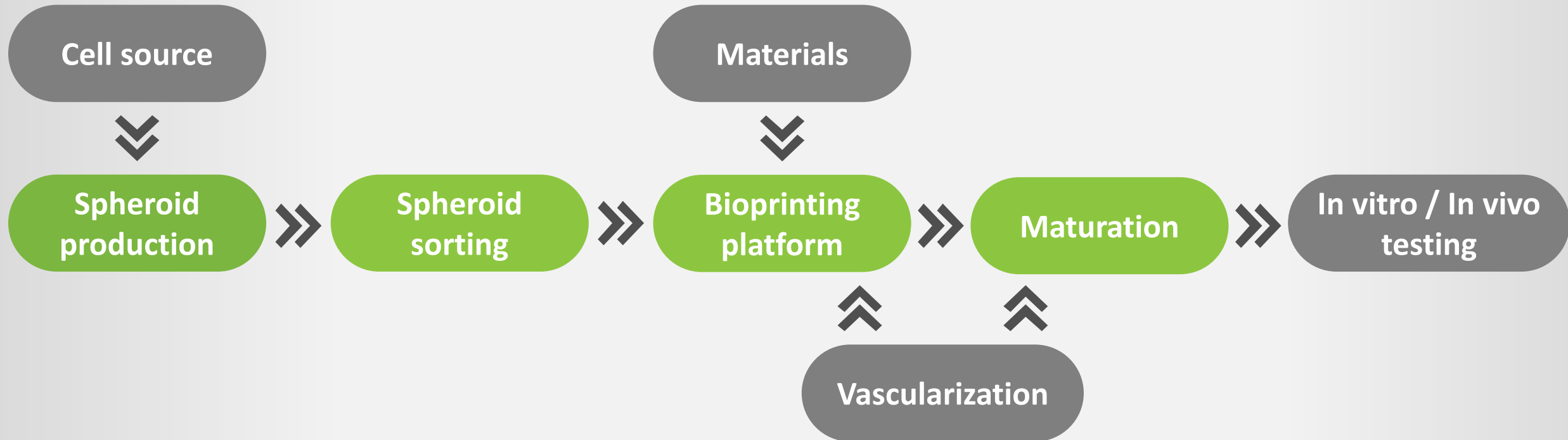
Vascularization





Enabling technologies & processes

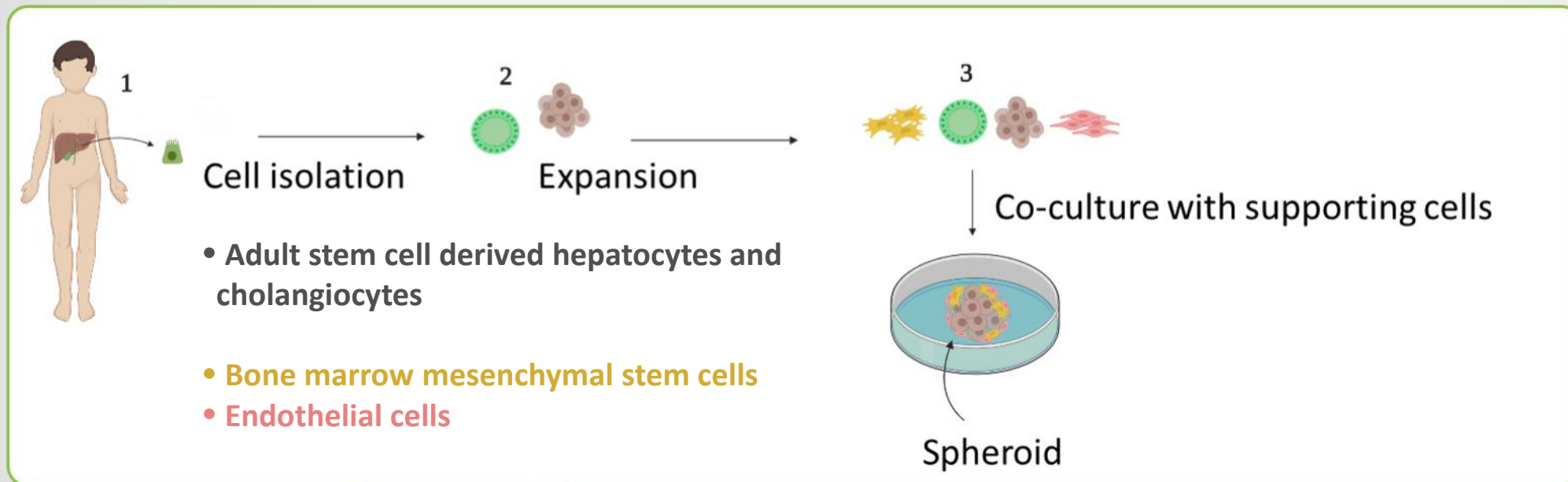
✦ **Technologies**
✦ **Processes** } Standardization workflow



Cell source

Production of liver organoids in large scale

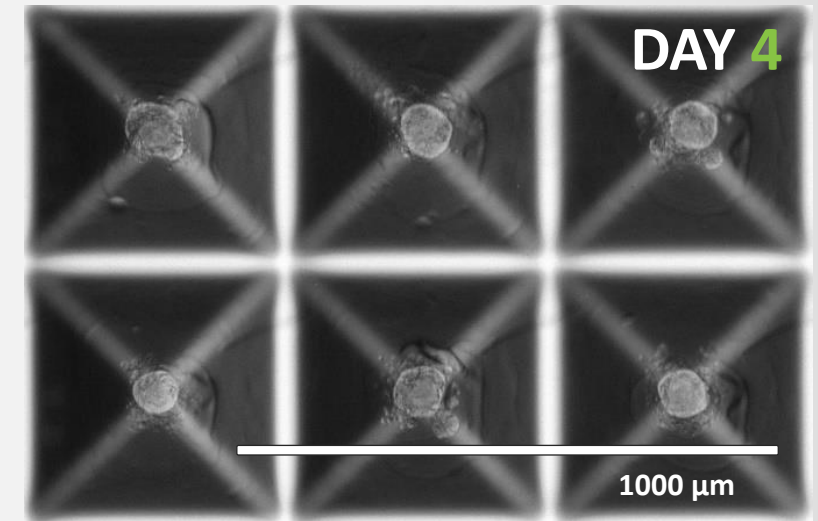
- Optimization of co-cultures and universal media
- Supporting cells: mesenchymal stem cells and endothelial cells



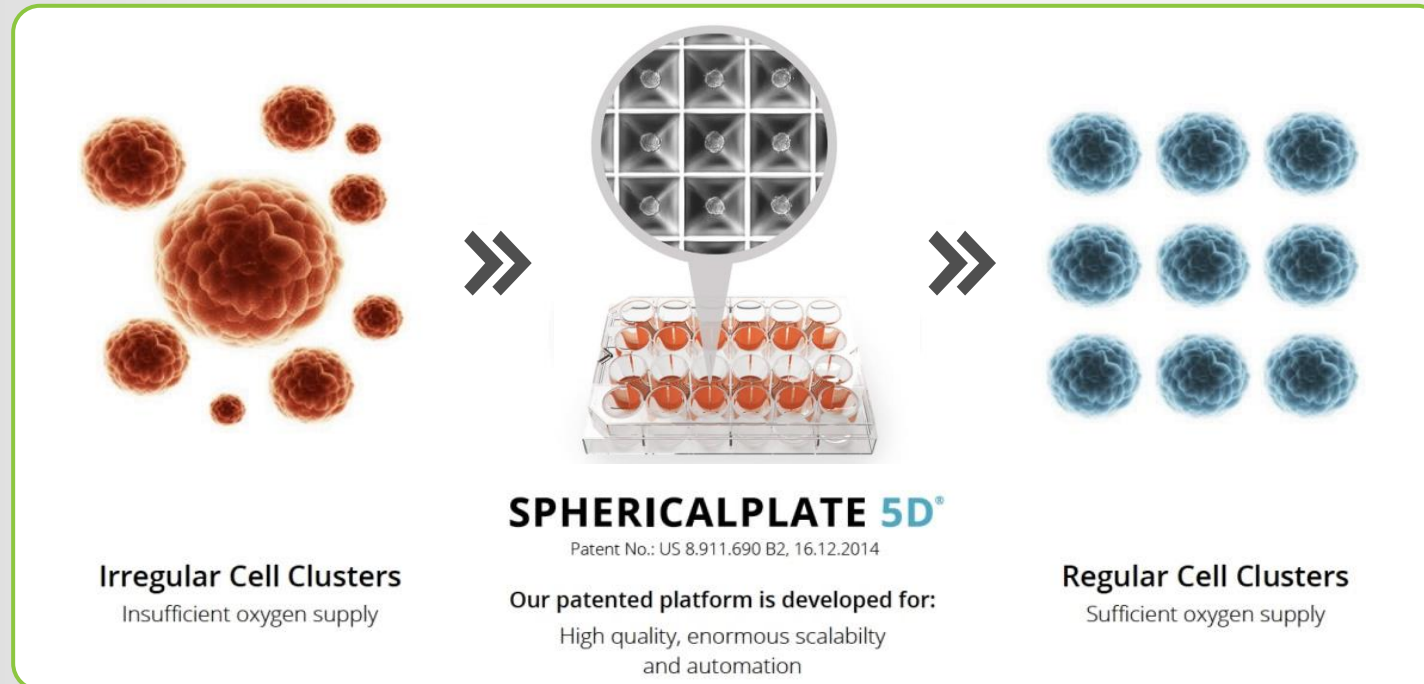
Production of hepatic spheroid

Sphericalplate 5D[®] - Upscaling without loss of spheroid quality

- Self-assembling of hepatic cells into standardized spheroids
- Establishing Roadmap for technical cGMP implementation

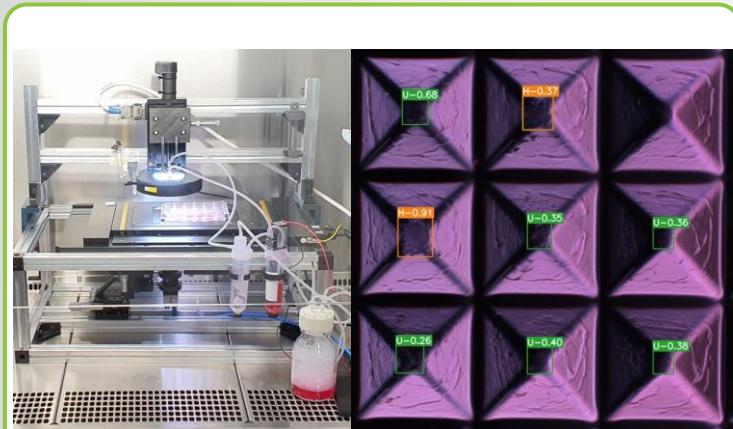
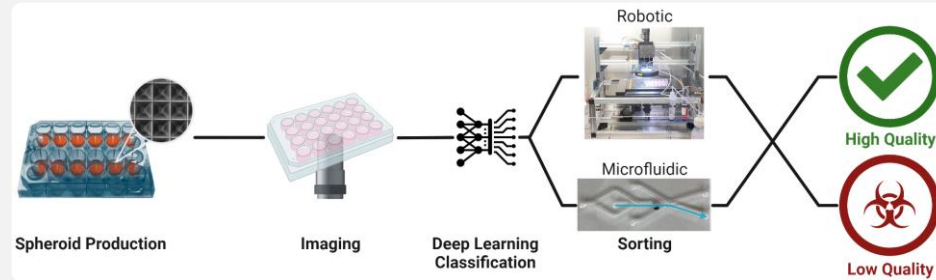


- Intrahepatic Cholangiocyte Organoids
- Stem cells
- Endothelial cells



Sorting of hepatic spheroids

Quality control and safety



1. Imaging & Classification



2. Individual extraction of **LOW QUALITY** spheroids

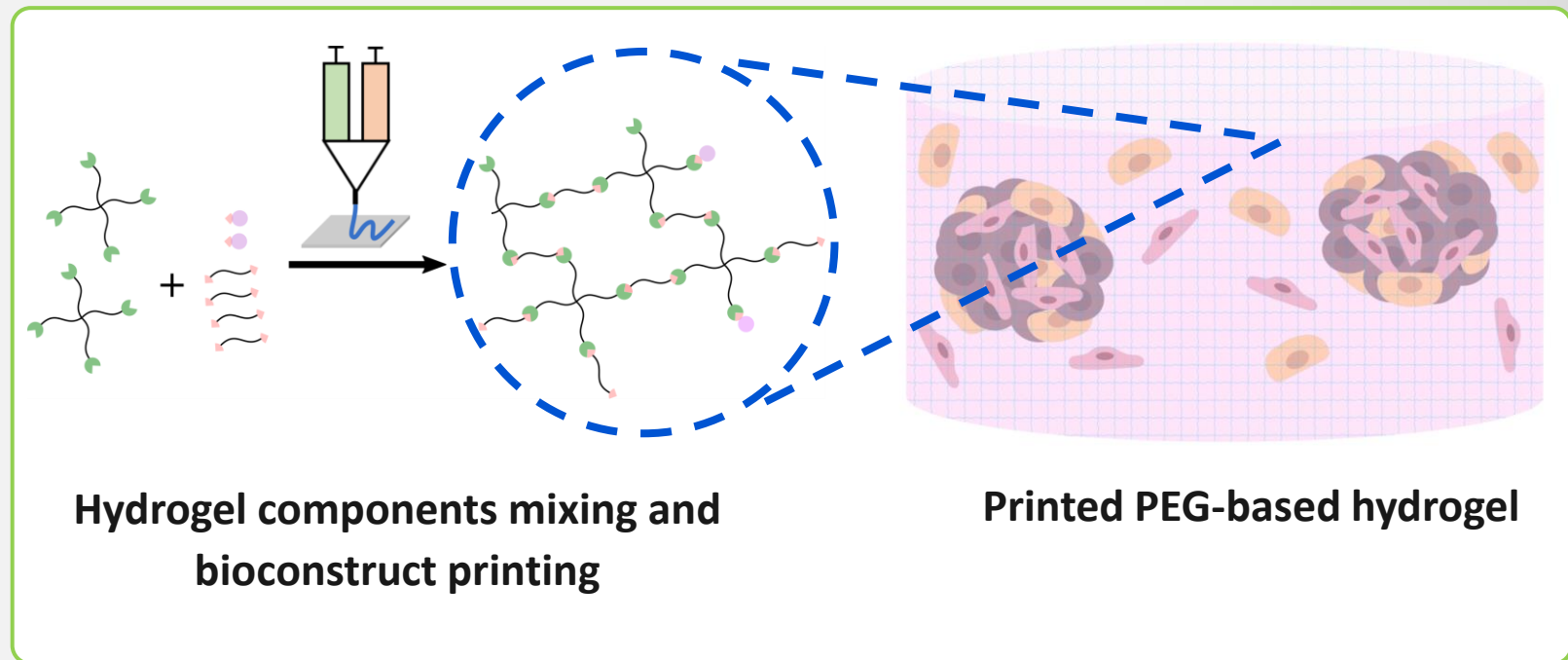


3. Bulk harvesting of **HIGH QUALITY** spheroids

Materials

PEG-based hydrogel

- Biofunctional
- Custom architecture
- Tunable porosity
- Cell spheroid protection
- Printability
- Controlled degradation
- Tunable stiffness



Bioprinting platform

Controlled mixing of hydrogel precursors and assembly of spheroids

- Combination of biodegradable bioinks with sacrificial scaffolds
- Integrated stirring
- Temperature and humidity control

User- and bio-friendly preparation
CARTRIDGE

Organoid printing technologies
PRINT-HEADS

Multi-materials management
MICROFLUIDICS

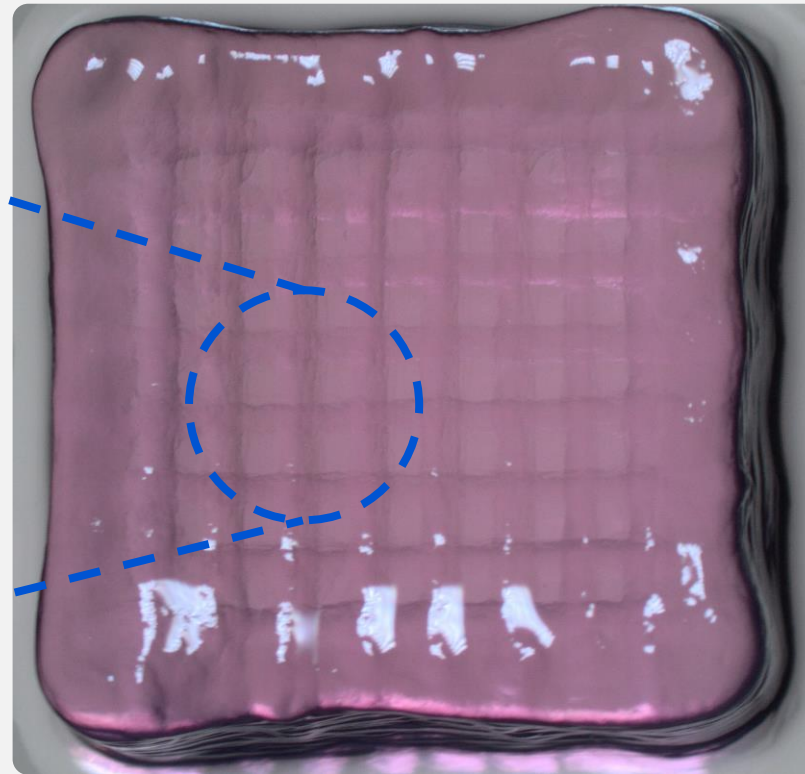
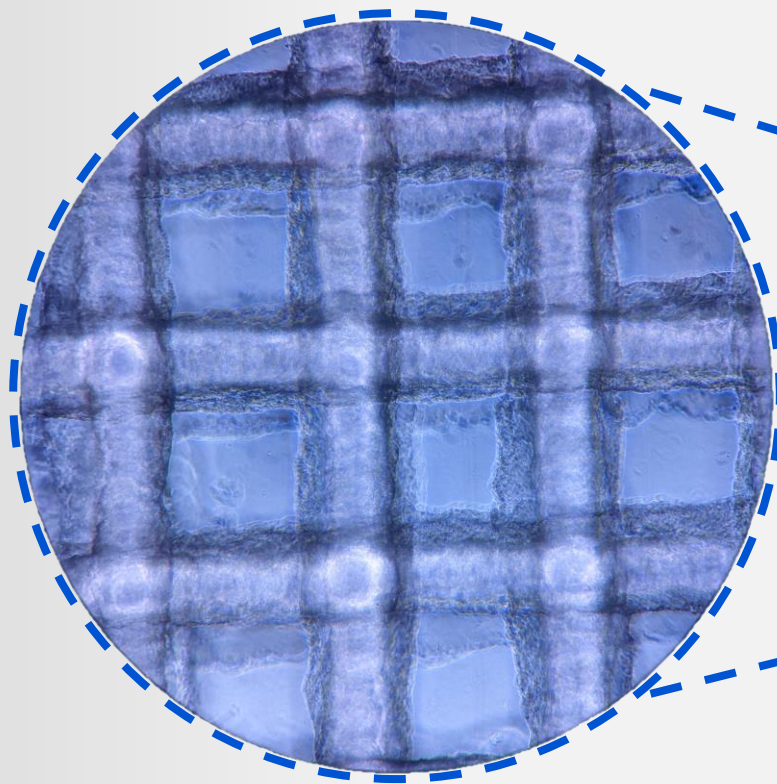
Assisted algorithmic design
SOFTWARE

Key components



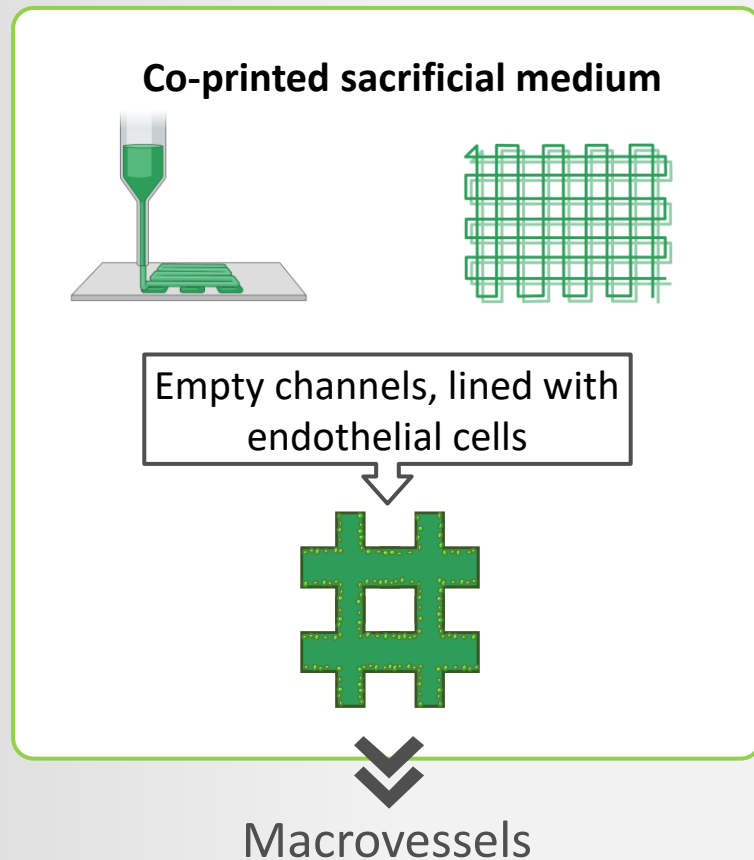
3D printed liver bioconstruct

Sacrificial material for perfusion and maturation

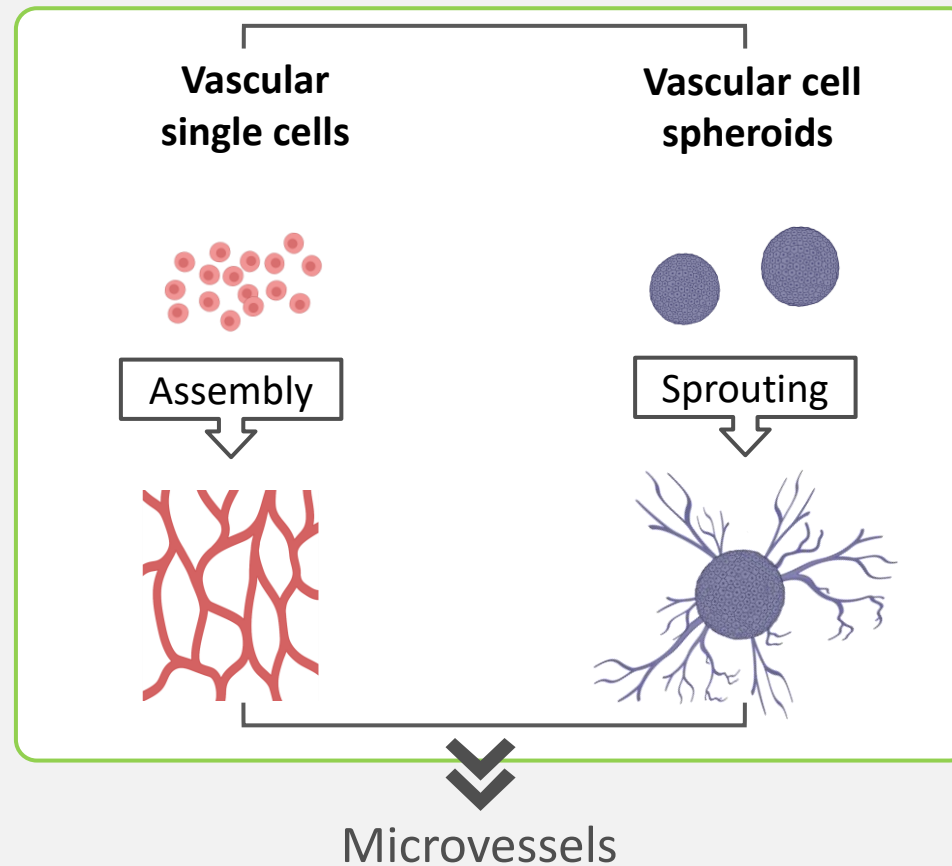


Vascularization strategy

Infusion



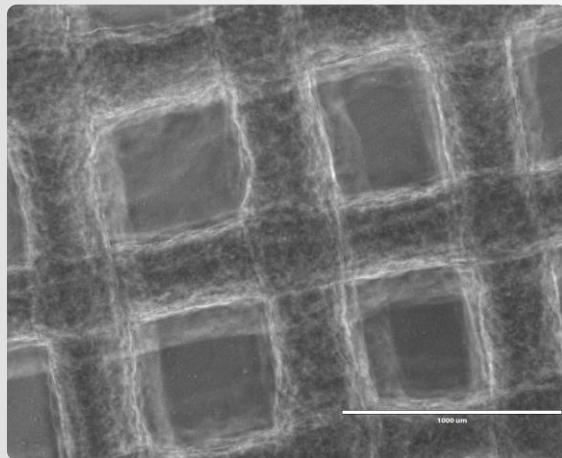
Inclusion



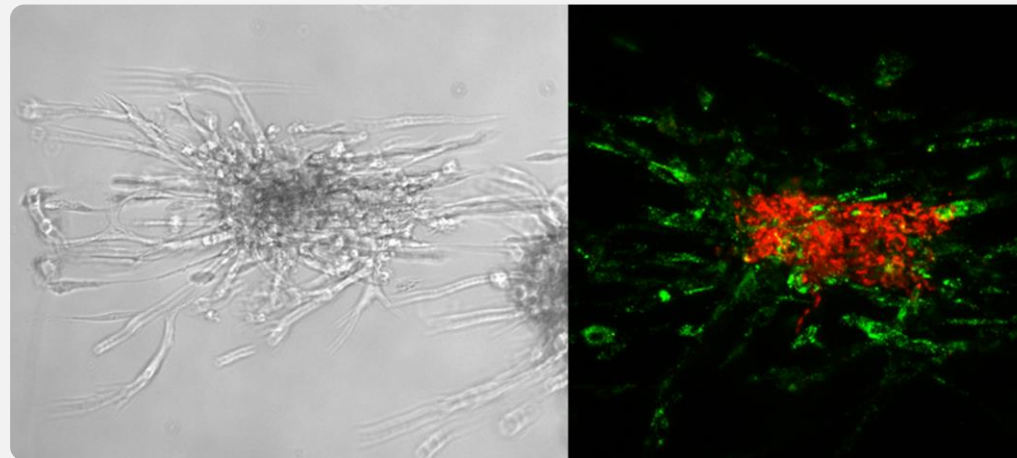
Vascularization

Macrovessels + Microvessels

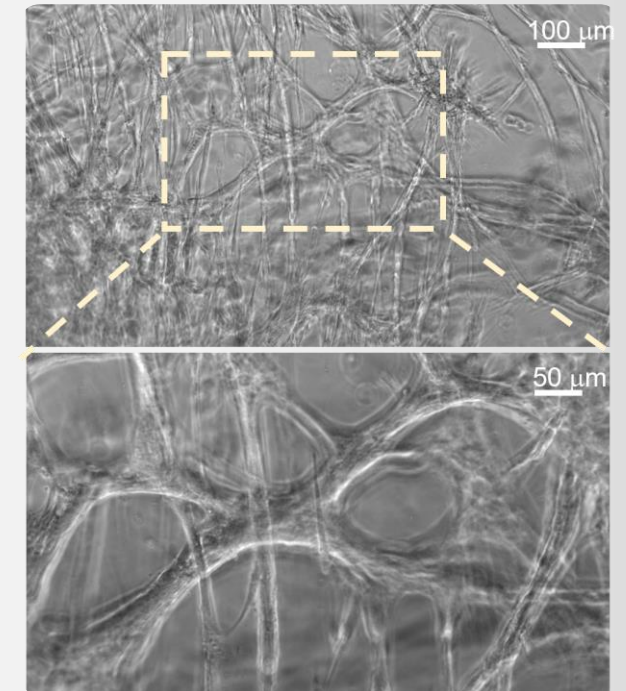
- A. Sacrificial channels with endothelial cells for perfusion (macrovessels)
- B. Vascular cell spheroids to generate microvessels by sprouting
- C. Single vascular cells to generate microvessels by assembly in networks and secondary sprouting



A.



B.

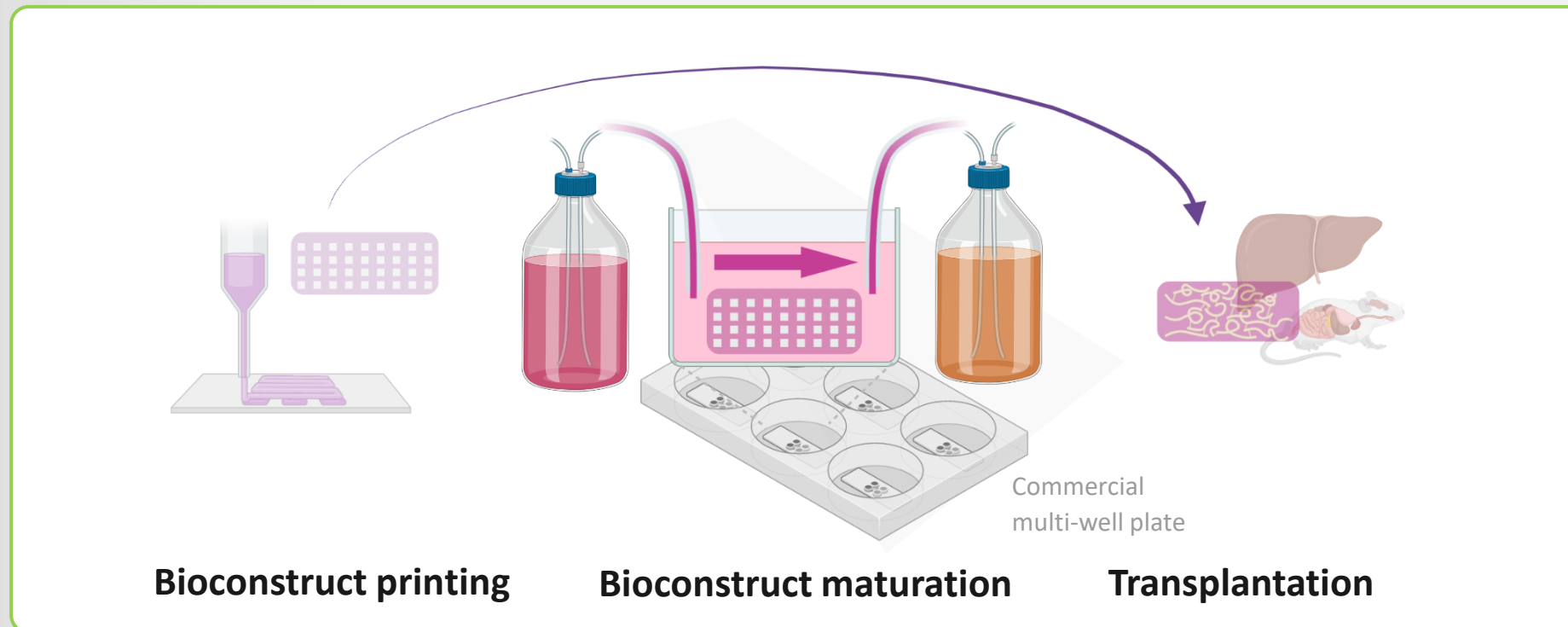


C.

Maturation

Perfusion in closed system

- Continuous and unidirectional flow through chamber

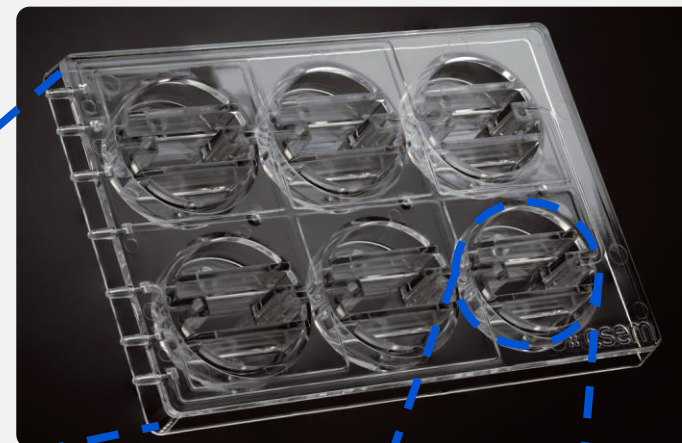


Perfusion of liver bioconstruct

Perfusion platform



Microfluidic based lid for closed perfusion

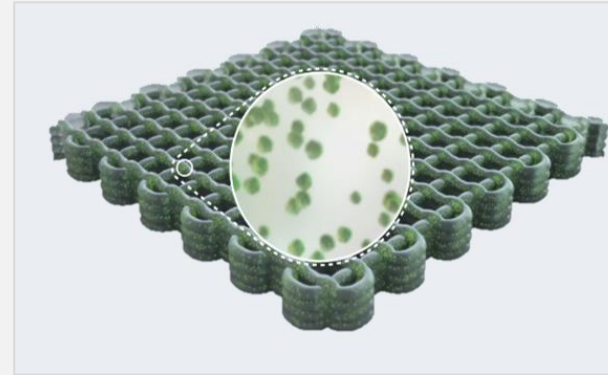


Insert for bioprinting

Testing of liver bioconstruct

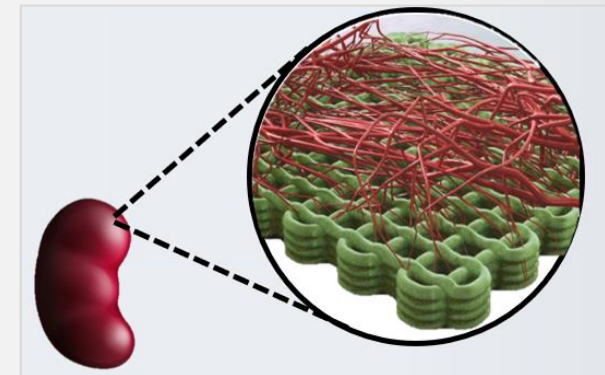
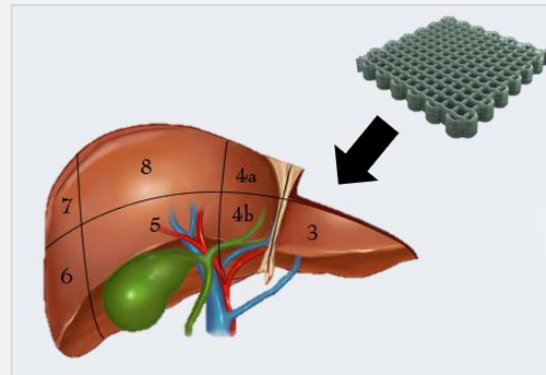
In vitro

- Gene expression profiling
- Viability
- Functionality



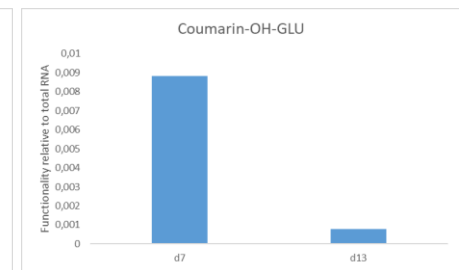
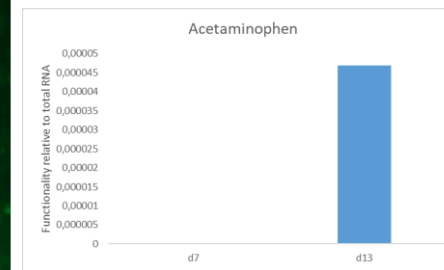
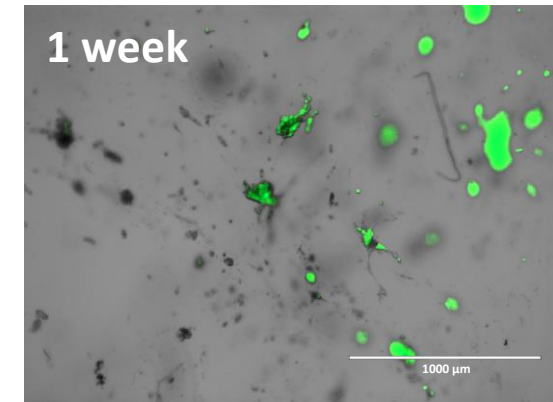
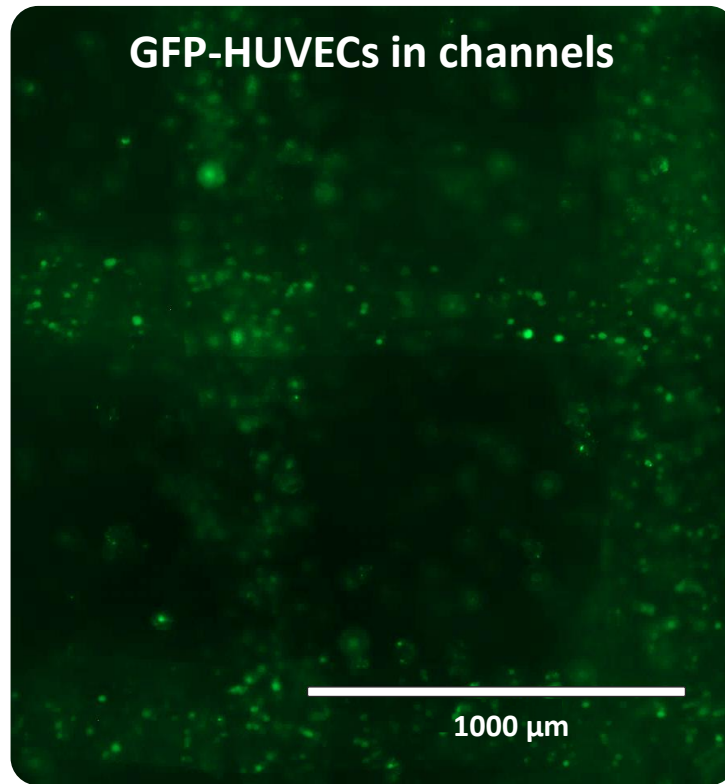
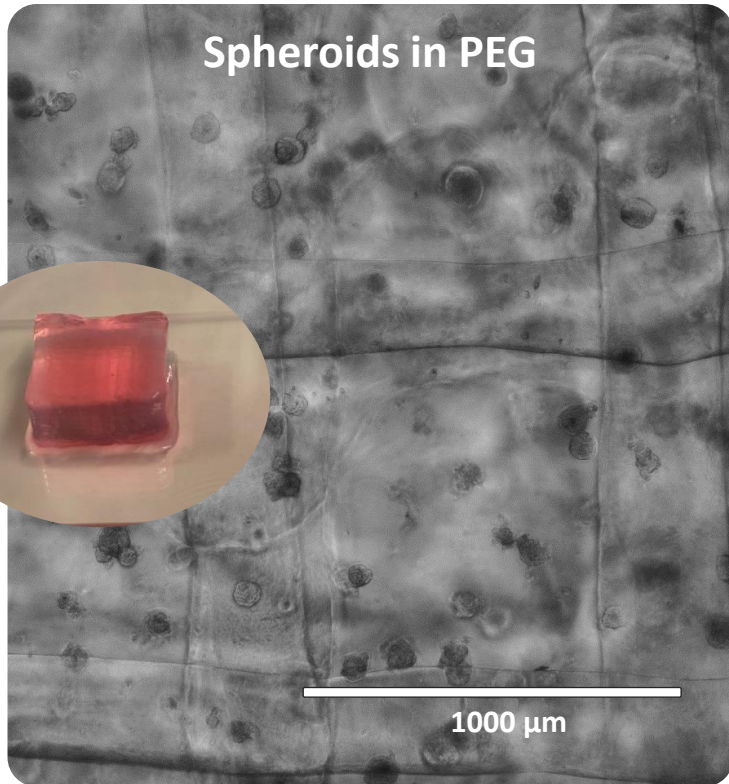
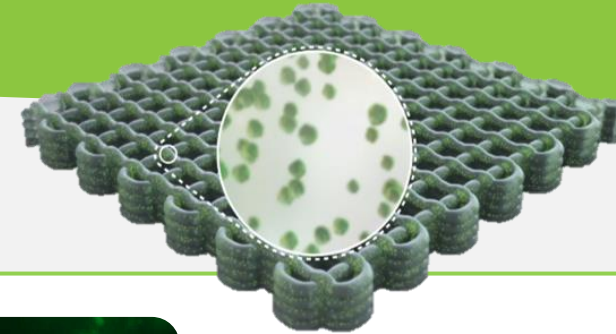
In vivo

- Vascularization under kidney capsule
- Orthotopic transplantation



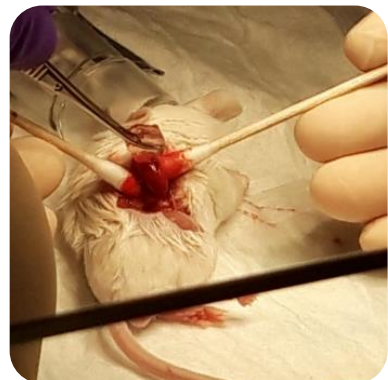
Liver tissue engineering

Tissue viability & functionality

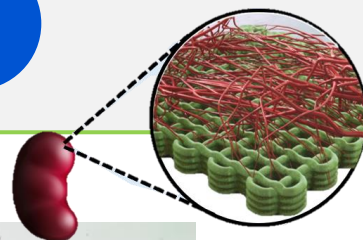


Transplantation

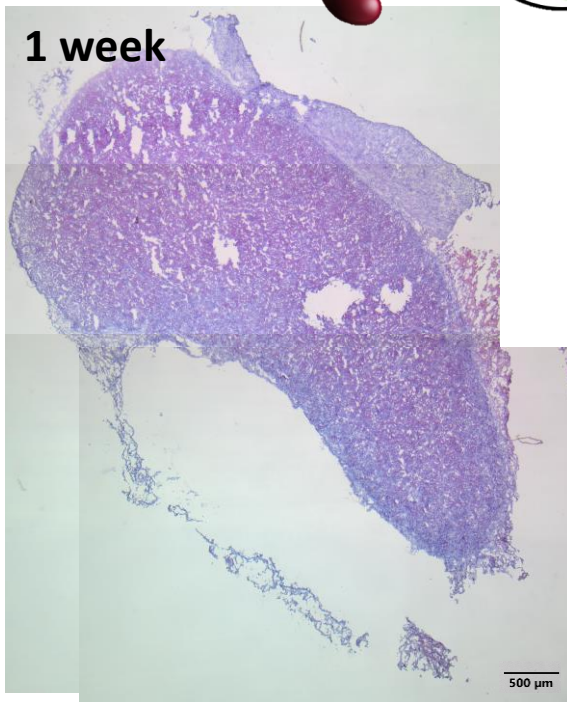
Kidney capsule



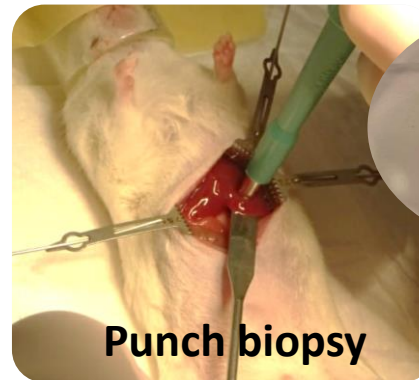
After harvesting



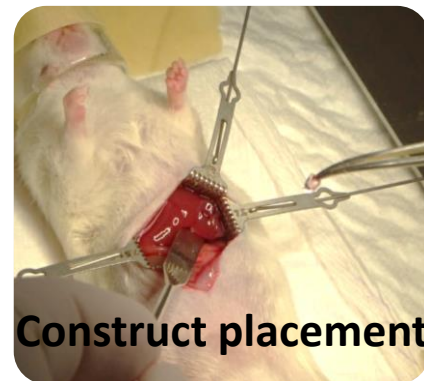
1 week



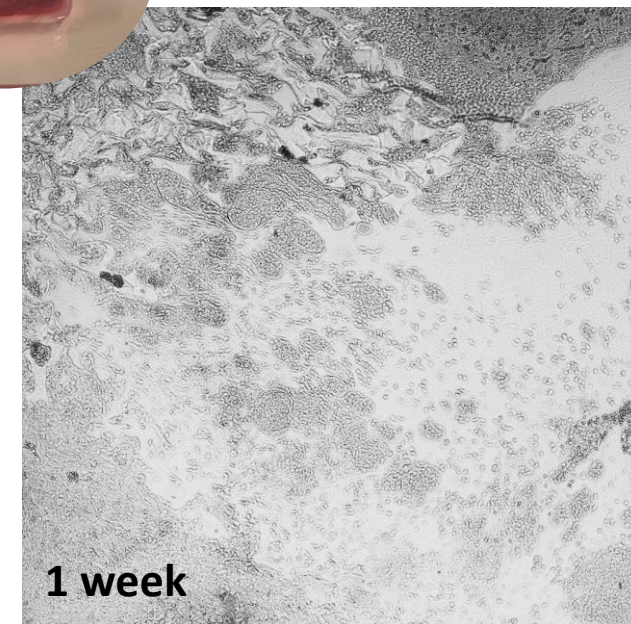
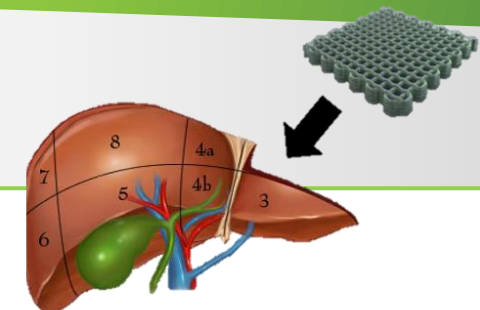
Orthotopic transplantation



Punch biopsy



Construct placement



1 week

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