OrganTrans
Process for organoids transplantation

ORGANTRANS

Controlled Organoids Transplantation as Enabler for Regenerative Medicine Translation

www.organtrans.eu

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 874586, project ORGANTRANS.

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

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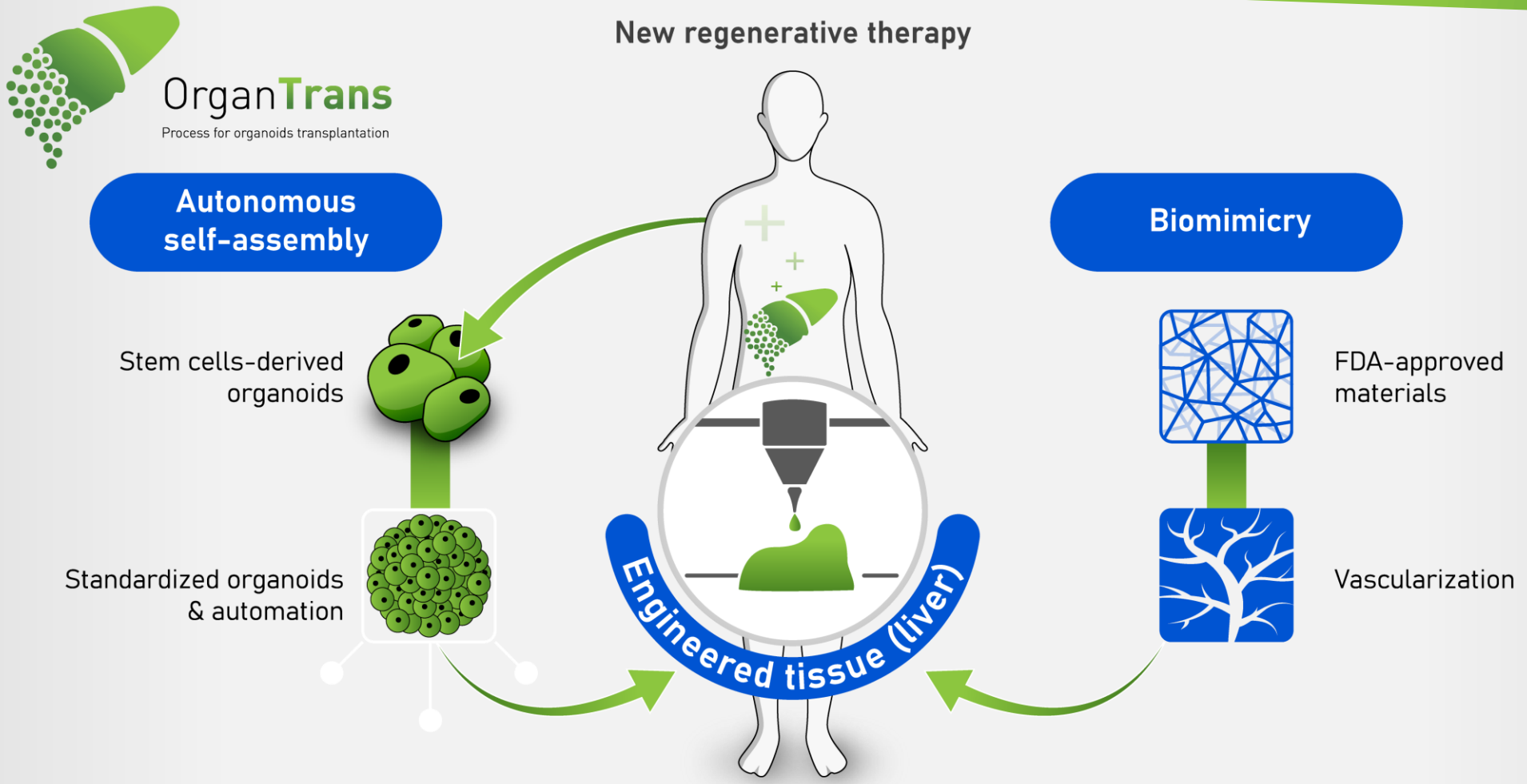
Overview



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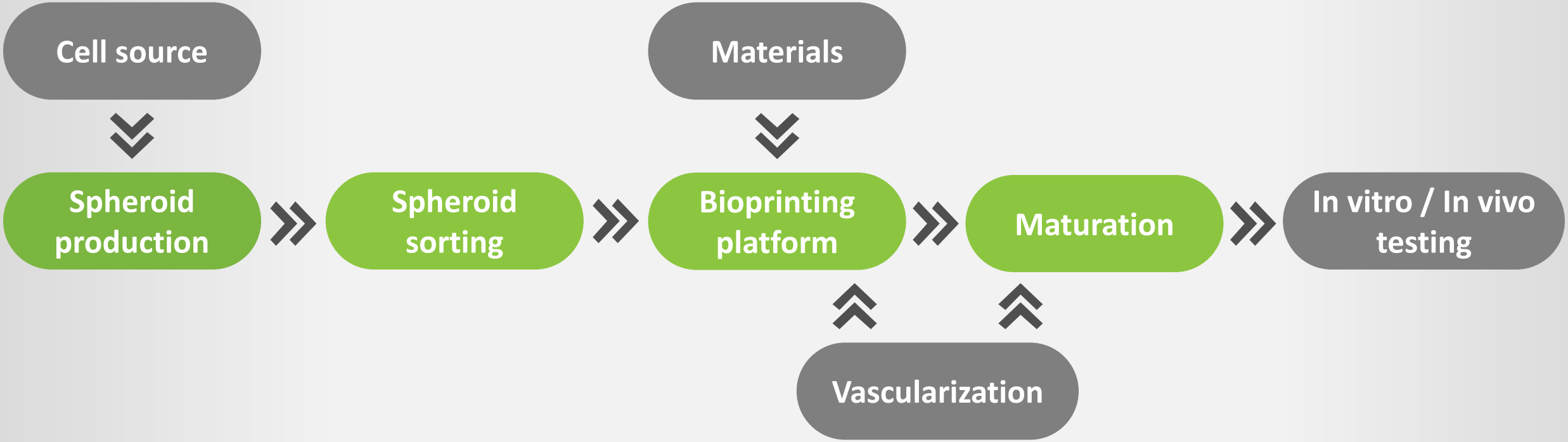
Enabling technologies & processes

- **Technologies**
- **Processes**



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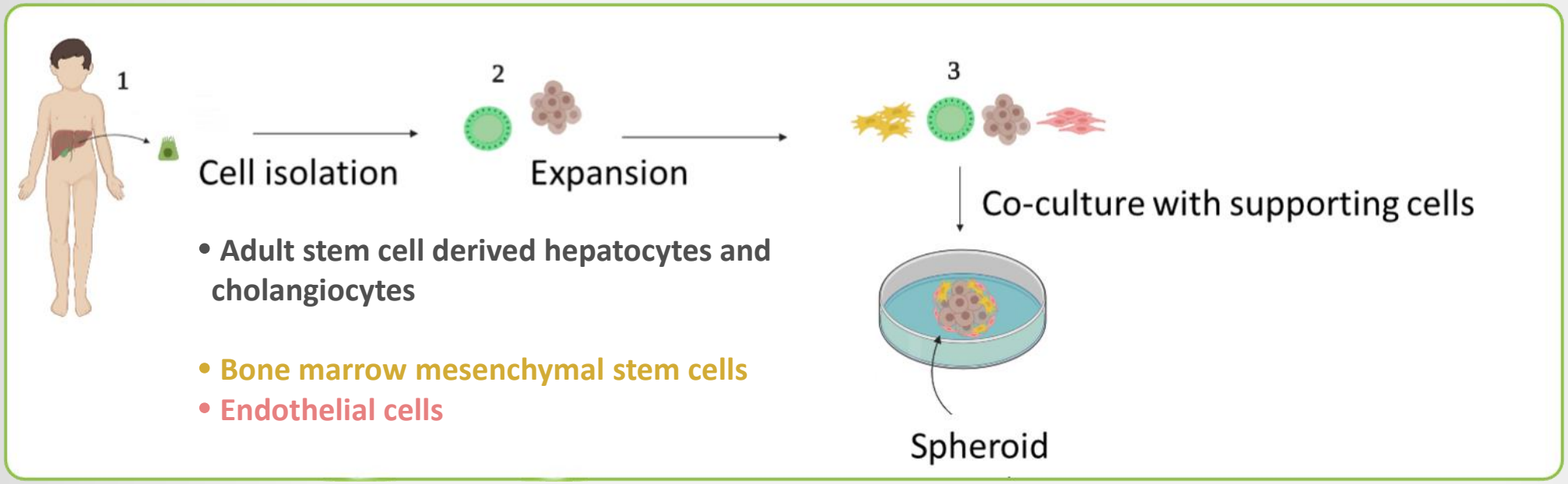
Cell source

Production of liver organoids in large scale

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



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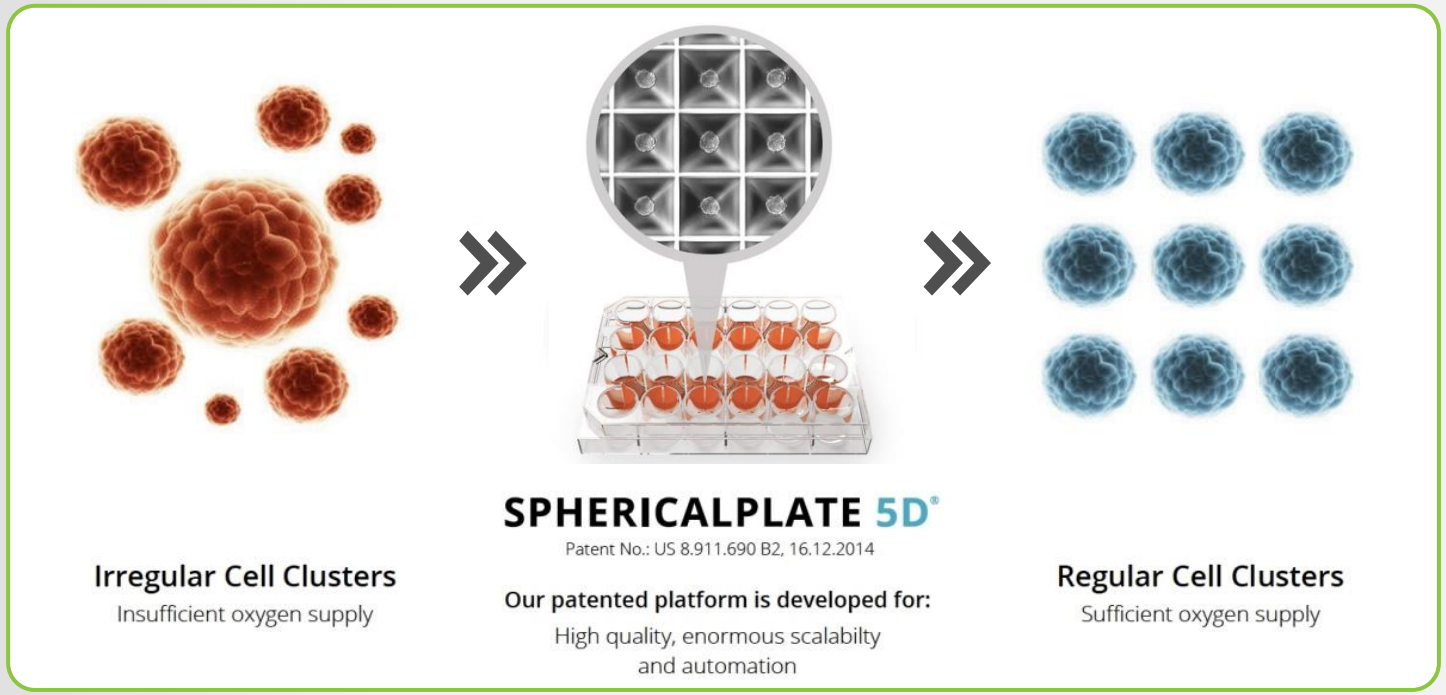
Spheroid production

Sphericalplate 5D®

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



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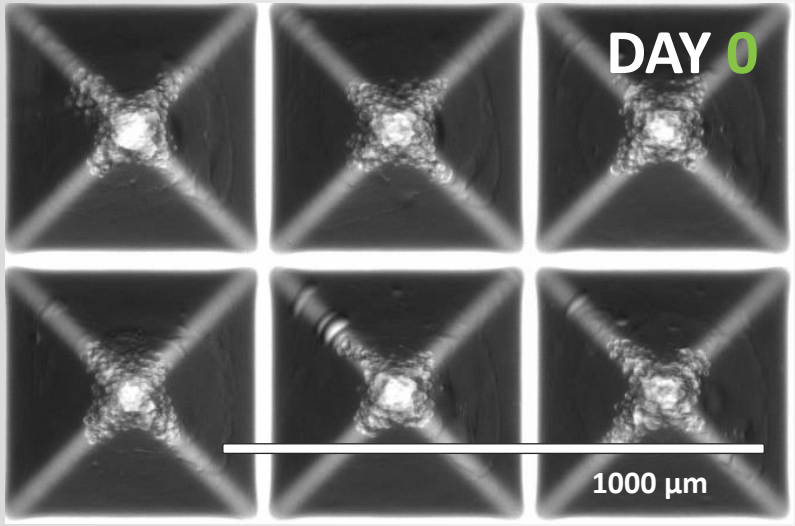
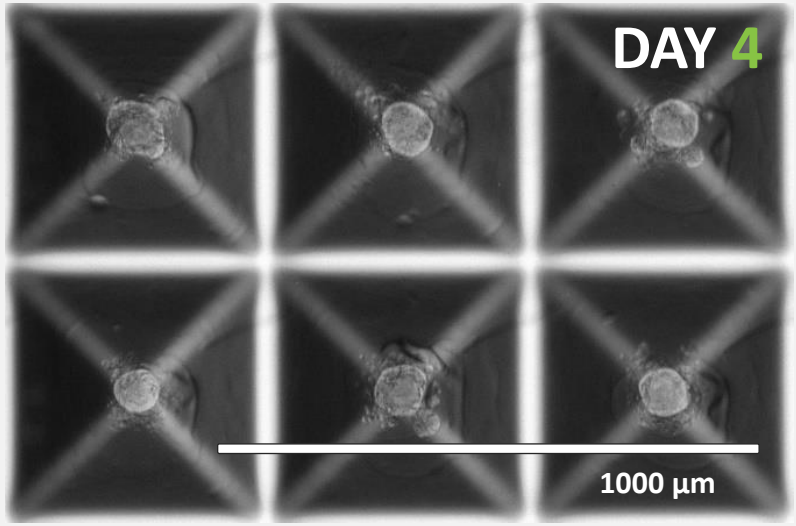
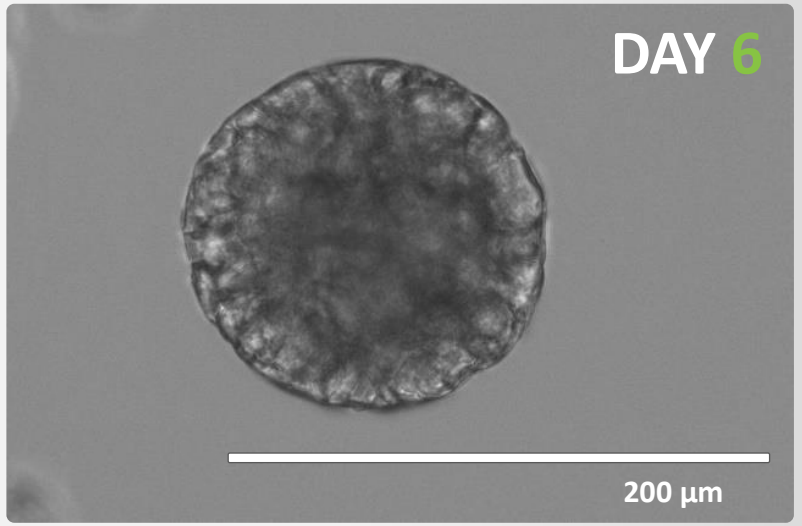
Production of hepatic spheroids

Upscaling without loss of spheroid quality

- Intrahepatic Cholangiocyte Organoids (ICOs)
- Stem cells
- Endothelial cells







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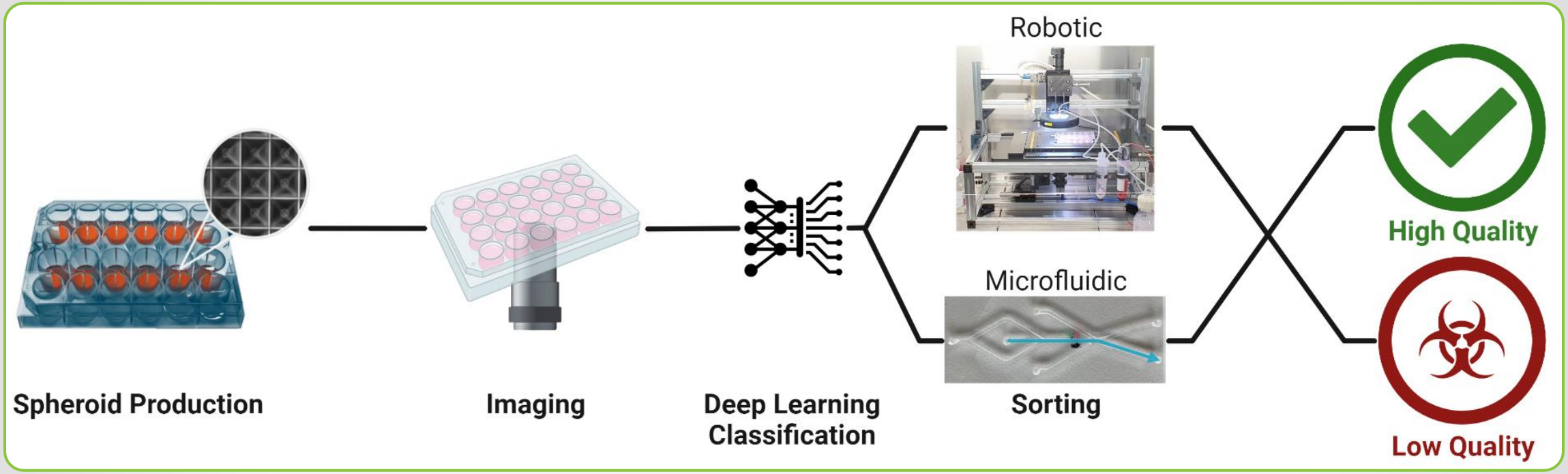
Spheroid sorting

Quality control and safety



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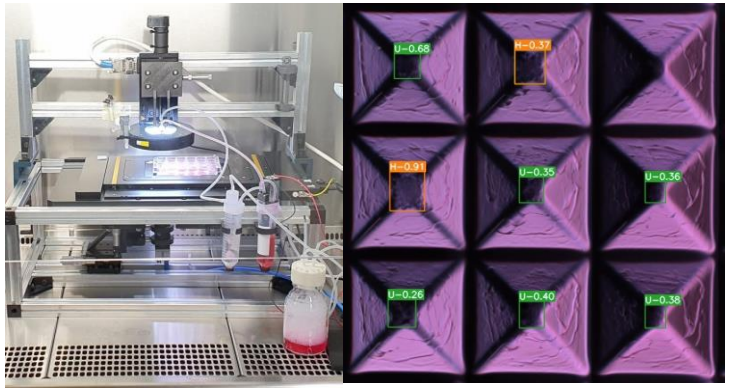
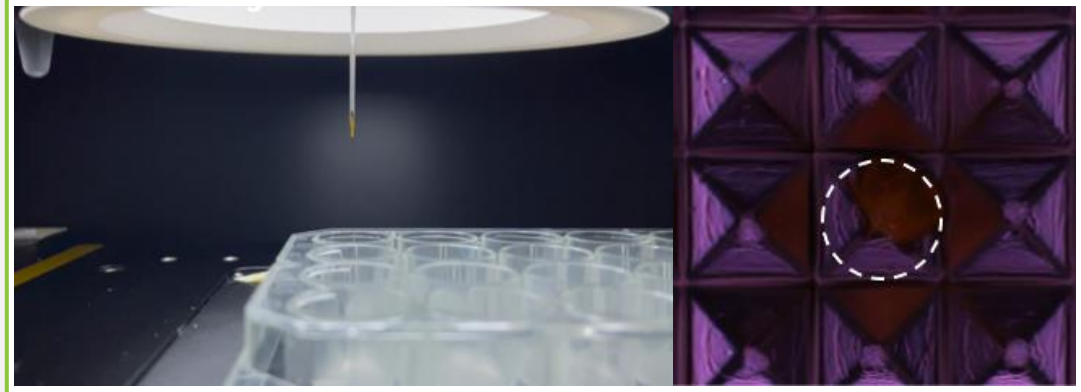
Robotic sorting of hepatic spheroids

Strategy in 3 steps



1. Imaging & Classification



2. Individual extraction of low-quality spheroids

3. Bulk harvesting of high-quality spheroids

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Materials

PEG-based hydrogel

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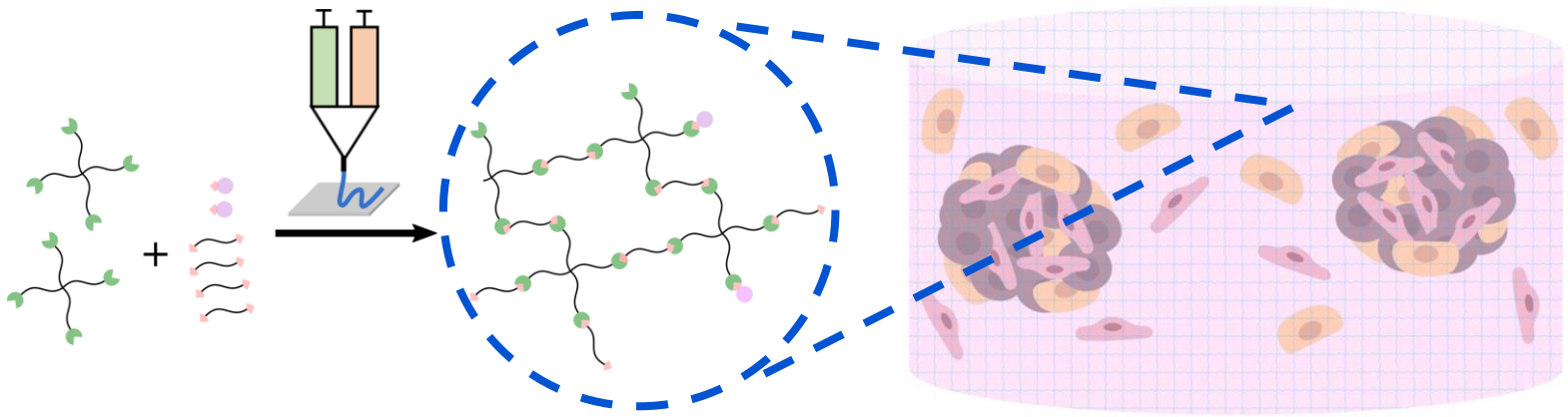
- Biofunctional
- Custom architecture
- Tunable porosity
- Cell spheroid protection
- Printability
- Controlled degradation
- Tunable stiffness



Hydrogel components mixing and bioconstruct printing

Printed PEG-based hydrogel

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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

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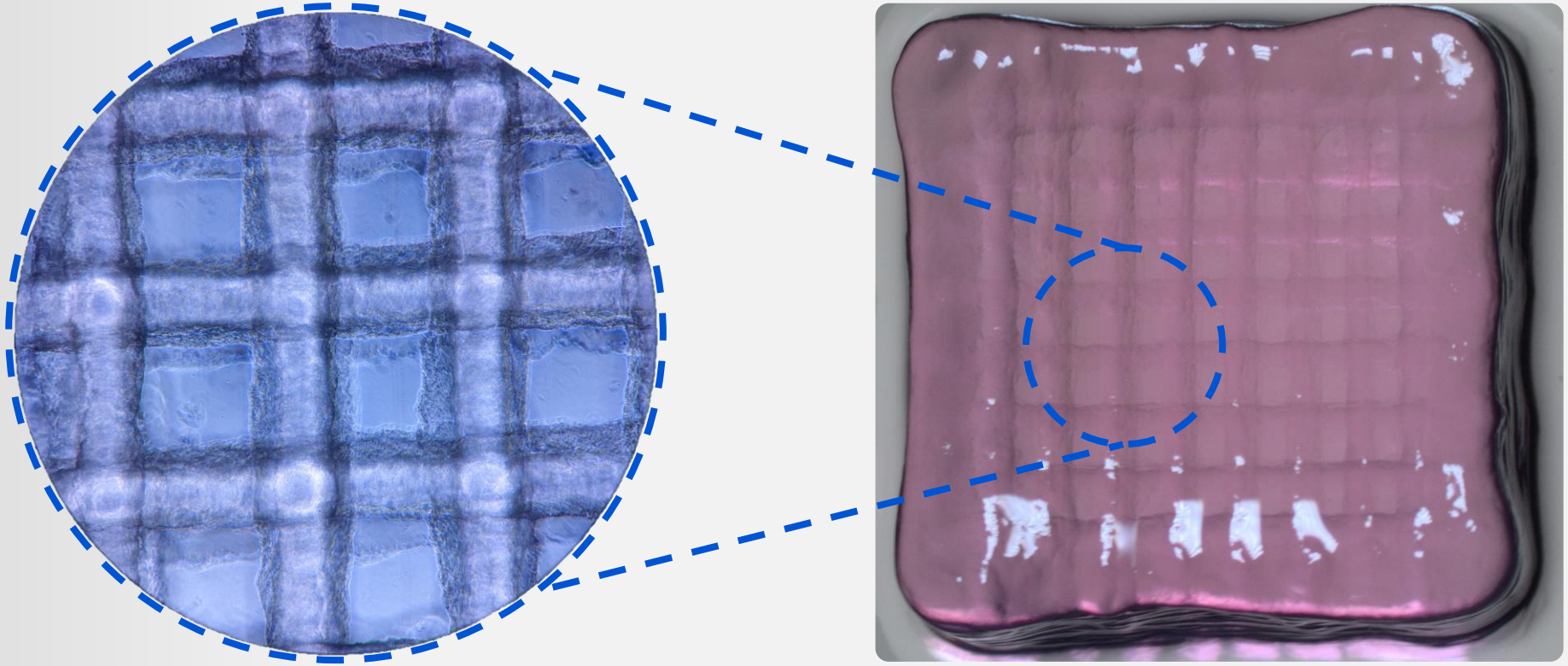
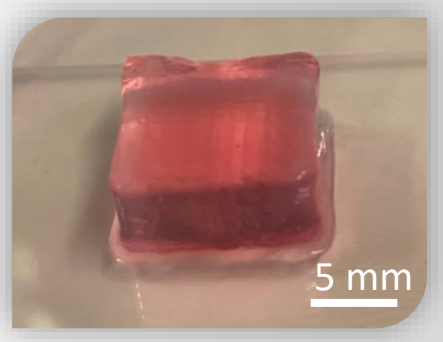
3D printed liver bioconstruct

Sacrificial material for perfusion and maturation





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Vascularization

APPROACH

CONCEPT

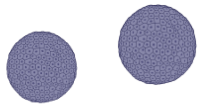
AIM

Inclusion model

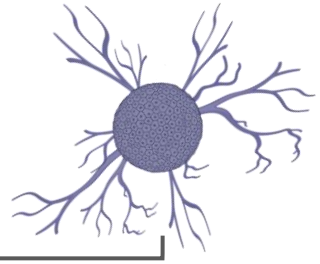
Vascular single cells

Assembly

Vascular cell spheroids



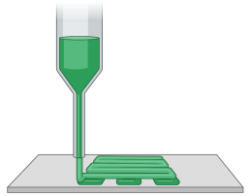
Sprouting

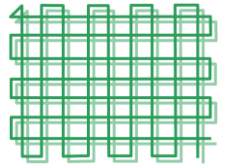


Microvessels

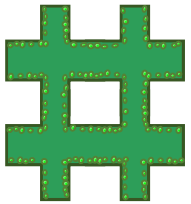
Infusion model

Co-printed sacrificial medium





Empty channels, lined with endothelial cells



Macrovessels

VIB

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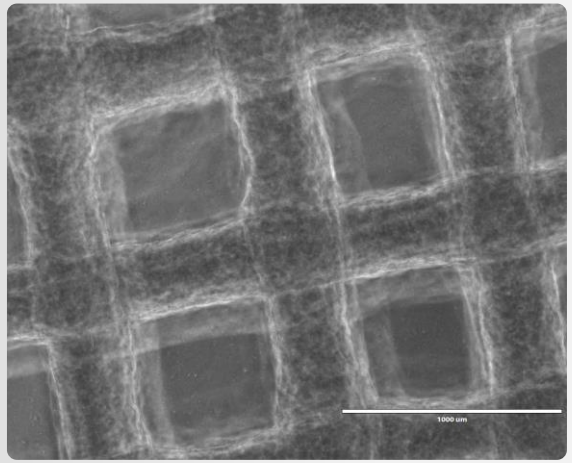
Vascularization

Macro- and microvessels

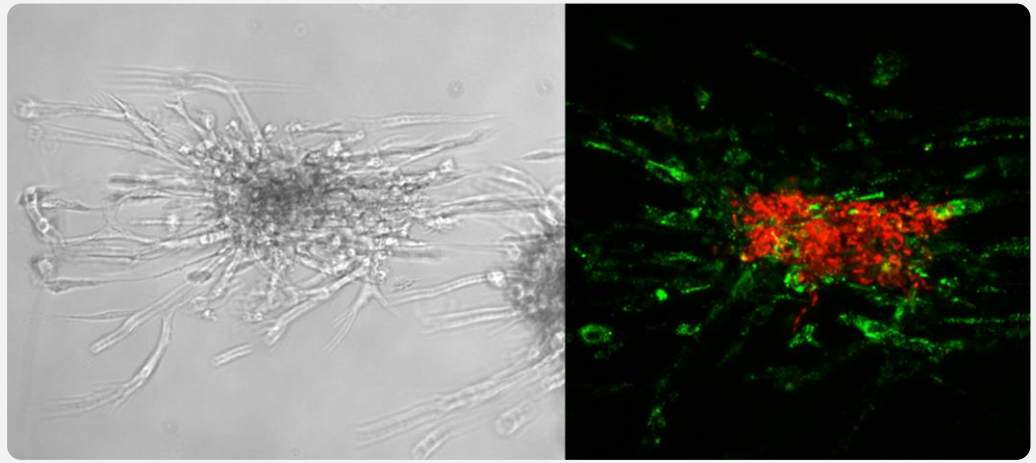
A. Sacrificial channels with endothelial cells for perfusion (macrovessels)

B. Vascular cell spheroids to generate microvessels by sprouting

C. Single vascular cells to generate microvessels by assembly in networks and secondary sprouting



A.



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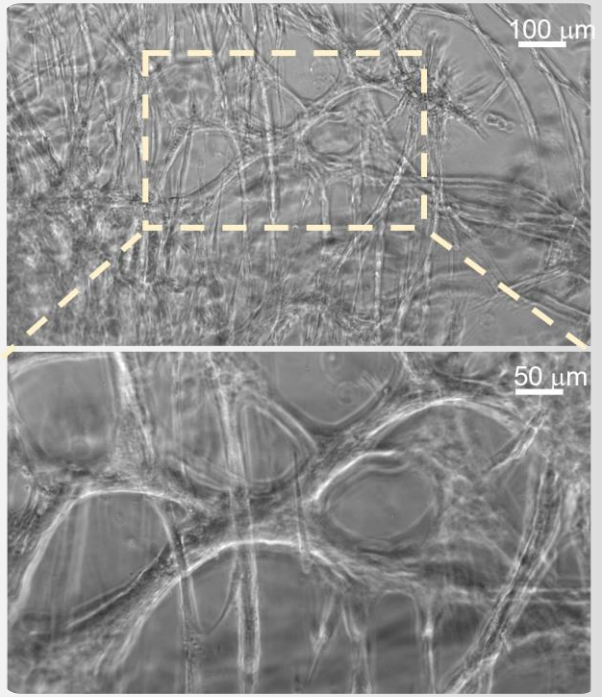

C.

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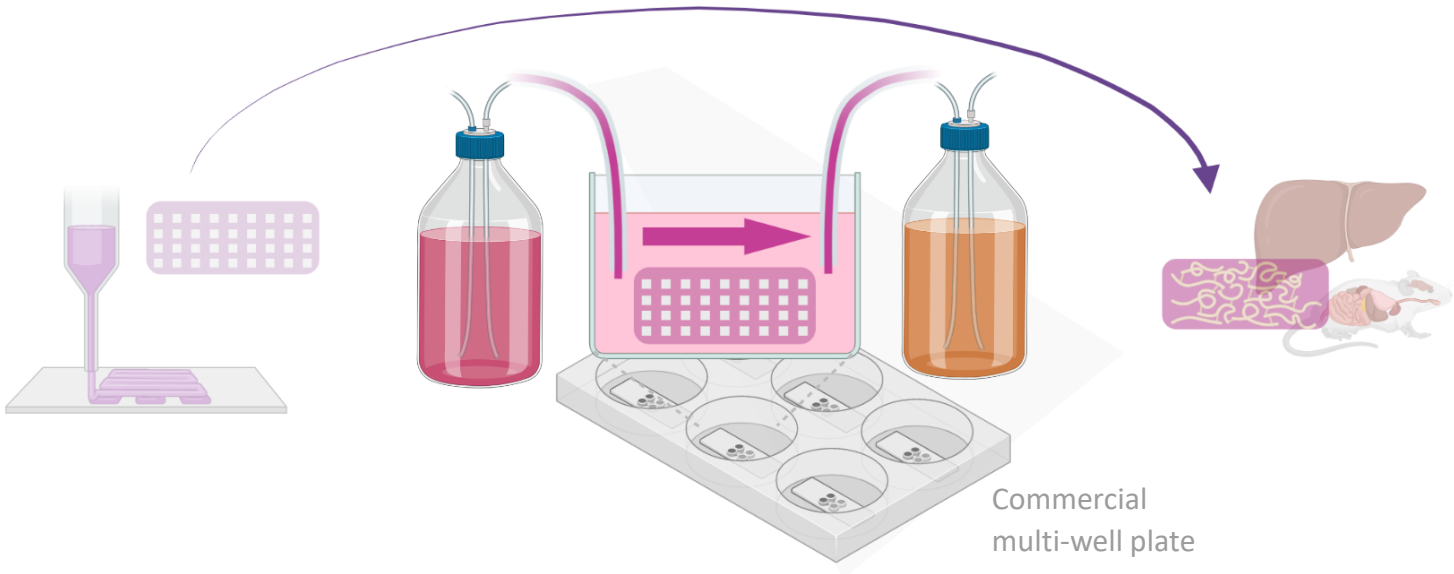
Maturation

Perfusion in closed system

- Continuous and unidirectional flow through chamber



Bioconstruct printing **Bioconstruct maturation** **Transplantation**

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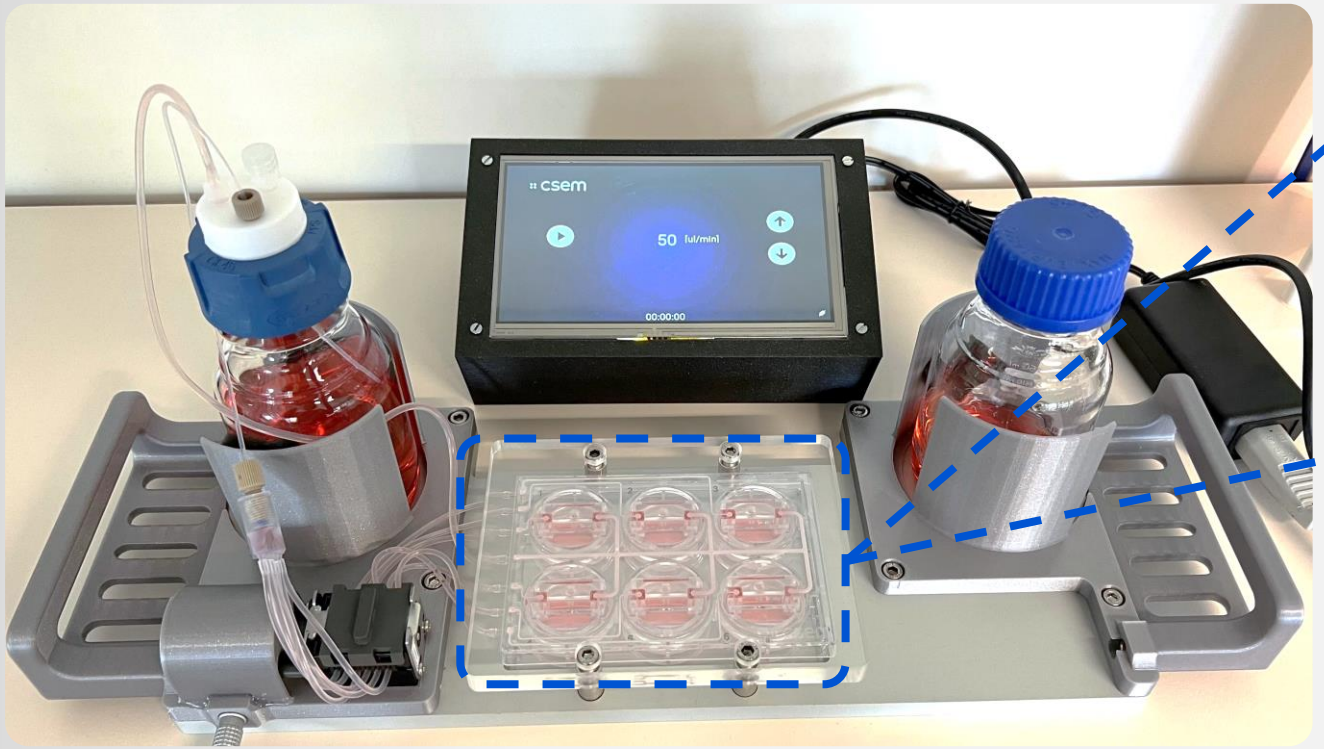
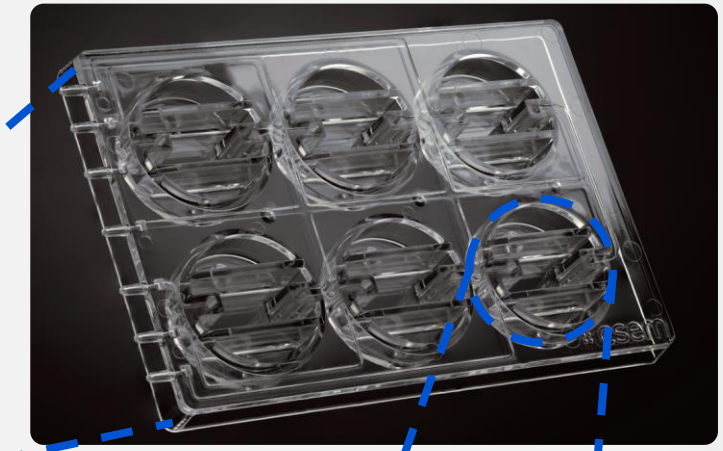
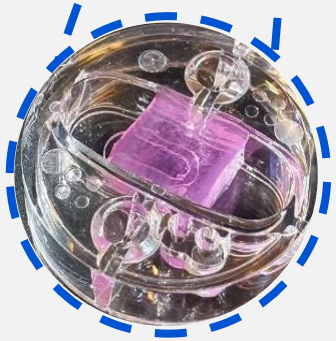
Perfusion of liver bioconstruct

Perfusion platform



Microfluidic based lid for closed perfusion





Insert for bioprinting

csem

Utrecht University

REGENHU

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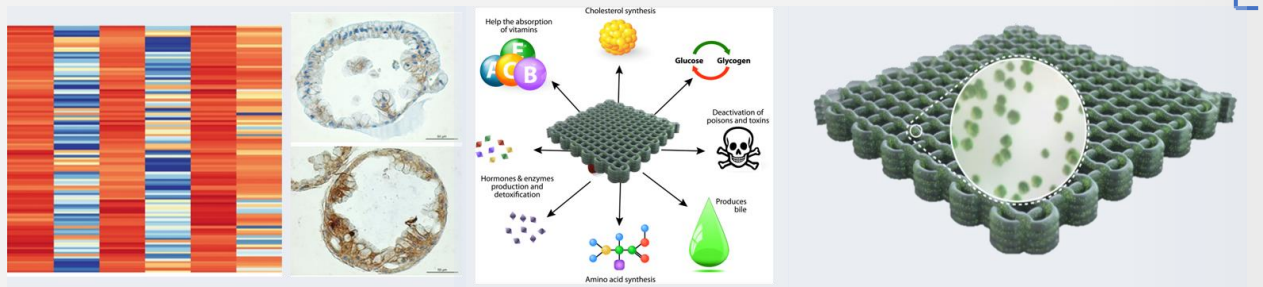
In vitro / in vivo testing

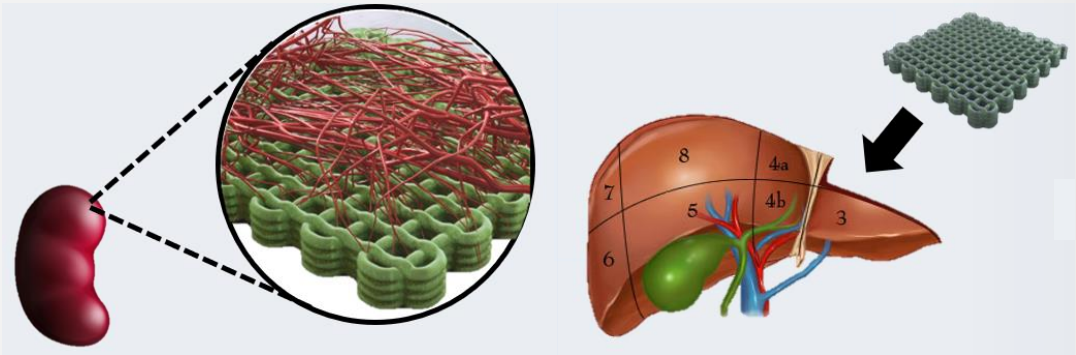
In vitro

- Expression profile and histology
- Functionality
- Functional in vitro liver constructs



In vivo

- Vascularization under kidney capsule
- Orthotopic transplantation
- Functional liver rescue in vivo



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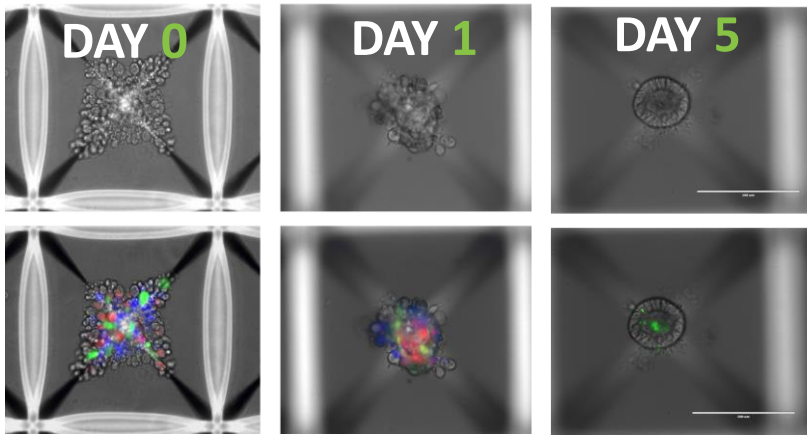
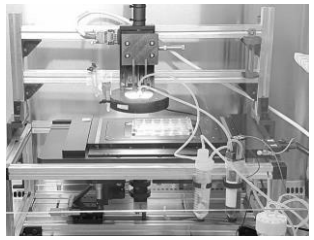
Liver tissue engineering

Viable liver construct



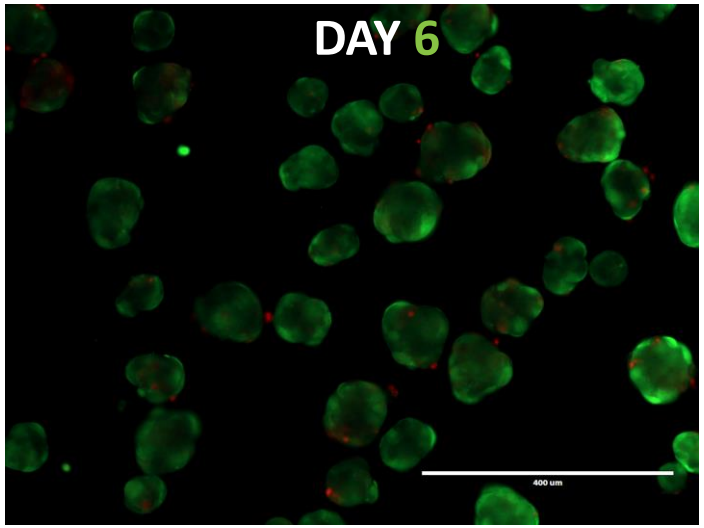
ICOs + CellTracker™ Blue
MSCs + CellTracker™ Red
HUVEC-GFP

Sorting



Bioprinting

Perfusion



Live / Dead staining

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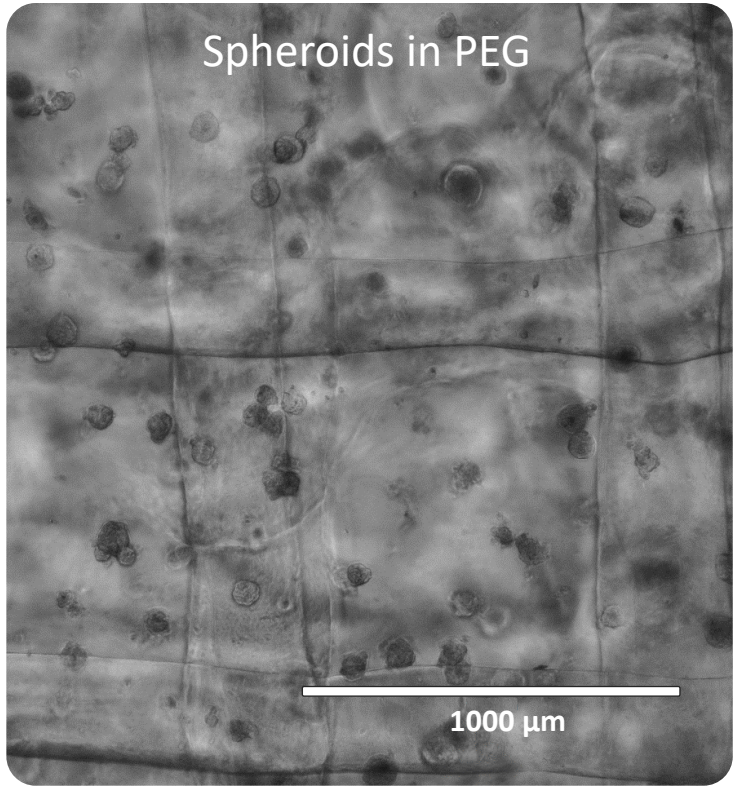
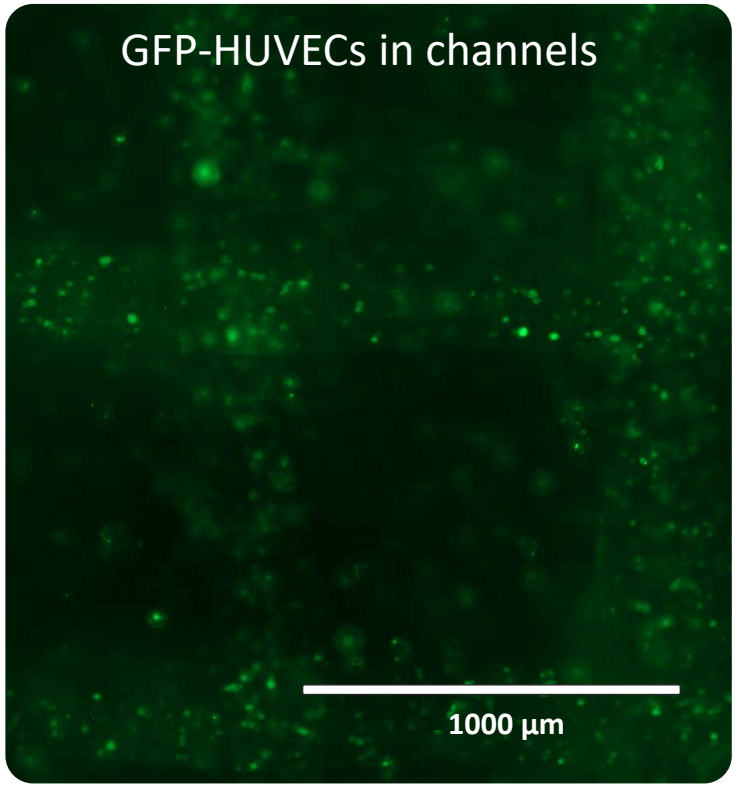
Liver tissue engineering

Viable liver construct





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Dr. Gilles Weder
Project Coordinator
CSEM
gilles.weder@csem.ch
+41 79 176 54 70

Dr. Mariana Pacheco Blanco
Project manager
AMIRES s.r.o.
pacheco@amires.eu
+420 226 217 422

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Process for organoids transplantation

Thank you for your attention

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