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Development of a Human 3D Co-Culture Platform to Study Microenvironmental Modulation and Drug Response in Breast Cancer Liver Models

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Background and rationale

- Metastasis is the leading cause of death in breast cancer patients
- The liver is one of the major sites of metastatic dissemination
- The microenvironment actively shapes tumor cell response to treatment

Problem

- Current in vitro models – lack of combining stromal and vascular complexity
- Limited predictive power for drug screening

Aim **To develop a minimal yet functional 3D liver niche model to study Triple Negative Breast Cancer (TNBC) metastasis and improve drug testing in a physiologically relevant context *ex vivo*.**

Model Design

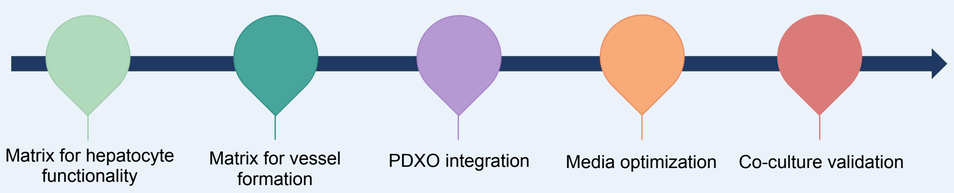
Reconstructing key liver components

Hepatocytes
Metabolic function

Stellate cells
ECM remodeling
Structural support

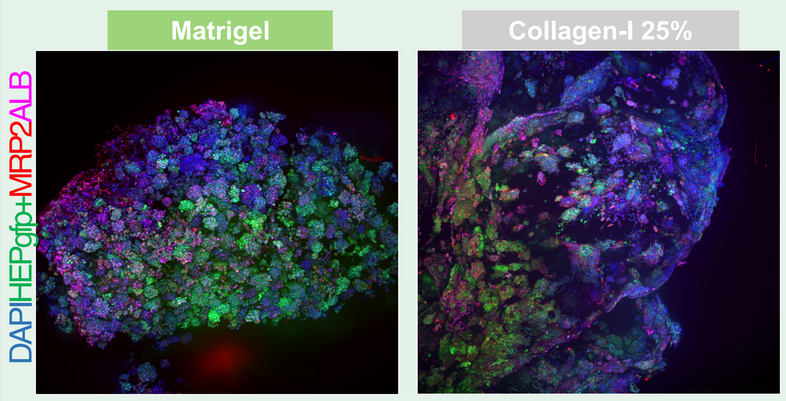
Endothelial cells
Vessels

Development timeline



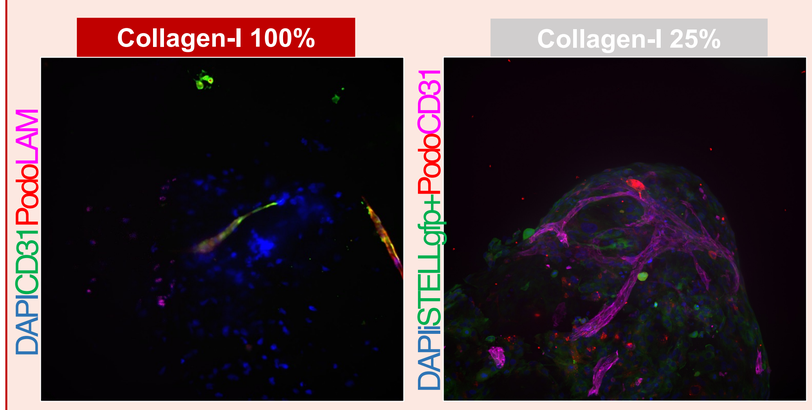
Matrix selection

Hepatocyte compartment
Albumin secretion and morphology



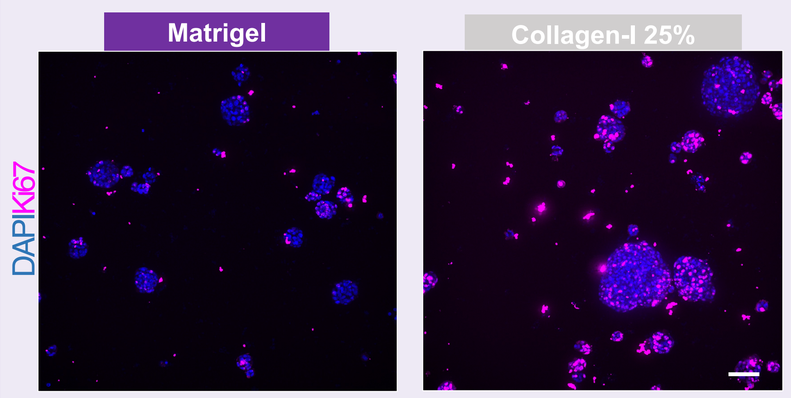
- Higher albumin production in Matrigel
- Statistically similar secretion of albumin in low-concentrated Collagen-I

Vascular compartment
Vessel formation with a lumen



- Requires a matrix low in laminin content
- Needs stromal support (Stellate cells)

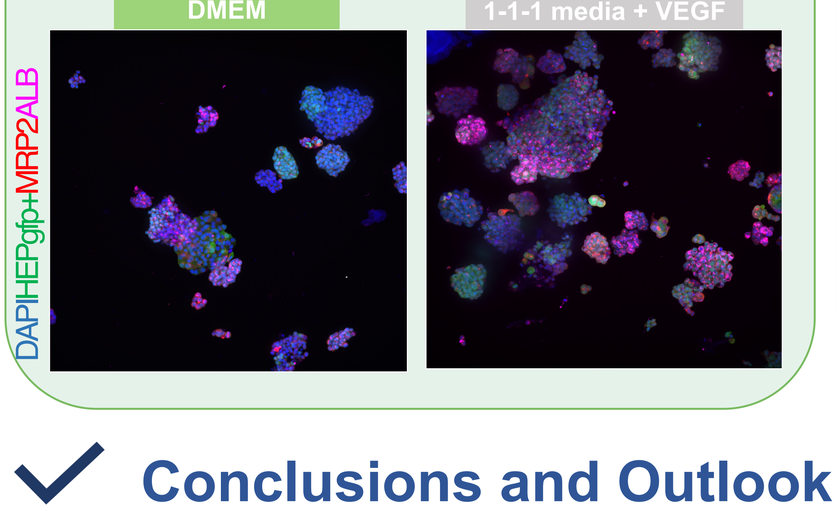
Tumor compartment (PDXO)
Structure and proliferation



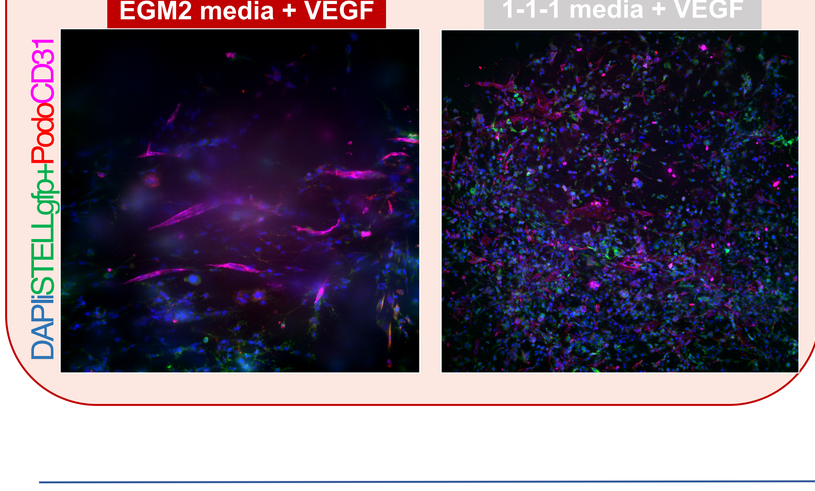
- Standard 3D culture condition in Matrigel
- Morphology and proliferation capacity maintained in low-concentrated Collagen-I

Media optimization

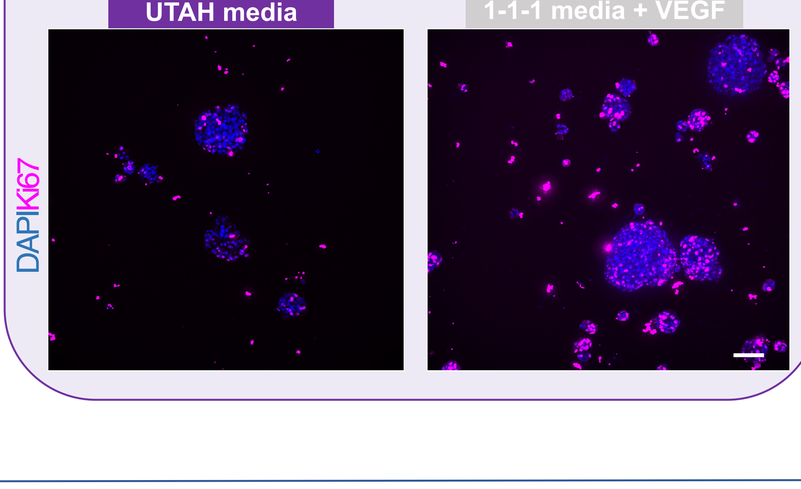
Hepatocyte compartment
Albumin secretion and morphology



Vascular compartment
Vessel formation with a lumen



Tumor compartment (PDXO)
Structure and proliferation



Conclusions and Outlook

A minimal functional liver niche has been established, allowing coexistence of tumor, stromal, and vascular components

- Define optimal culture conditions, validate the functionality of cell components and rheological measurement of matrices
- Tune the co-culture for drug screening - Compare drug response in co-culture vs. PDXO mono-culture

TERMIS EU-Chapter 2026 PALMA DE MALLORCA 21-24 APRIL / SPAIN

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