RESEARCH TOPIC PRIME1

Patient-Specific cholangiocarcinoma-on-Chip to Investigate Chemo-Immunotherapy Response

Thematic field of the project

Organ-on-chip

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Main facility

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Other facility

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Main field of interest

Cholangiocarcinoma

Abstract

Background: Cholangiocarcinoma (CCA) is an aggressive biliary tract cancer with a poor prognosis and limited therapeutic options. While combining immune checkpoint inhibitors (ICI) with gemcitabine/cisplatin chemotherapy has shown potential in enhancing anti-tumor T cell responses, patient outcomes remain highly variable. Understanding the mechanisms underlying immuno-chemotherapy effects within the tumor microenvironment (TME) is therefore critical.

Aims: This project aims to investigate how T cell behavior is influenced by patient-specific immune checkpoint (IC) expression, and to elucidate tumor cell and cancer-associated fibroblast (CAF) susceptibility to immuno-chemotherapy. We further aim to identify cellular and stromal phenotypes associated with favorable treatment responses.

Methods: Using a CCA-on-chip platform co-culturing patient-derived CCA cells, CAFs, and endothelial cells, we will model the 3D TME in 20 patient-specific devices. After establishing a mature CCA niche (Day 3), autologous T cells will be introduced and treated with clinically relevant immuno-chemotherapy doses. Three tasks will be pursued: (1) comparative TME characterization in high- versus low-IC-expressing patients using flow cytometry and Luminex cytokine profiling; (2) assessment of T cell trafficking, functional dynamics, and cytotoxic activity via live-cell imaging and high-dimensional mass cytometry; and (3) evaluation of extracellular matrix (ECM) remodeling and stromal changes post-treatment using scanning

electron microscopy, immunofluorescence, and qRT-PCR. Clinical follow-up data will be correlated with on-chip findings.
Expected Outcomes: This project is expected to uncover how IC expression shapes the TME, define T cell recruitment and activation kinetics during immuno-chemotherapy, and reveal how treatment restructures the TME's mechanical and signaling environment. These findings may refine CCA treatment strategies and support the development of personalized therapeutic approaches through organ-on-chip technology.

Main technical approaches
Design and improvement of organs-on-chip

Scientific references

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