PROJECT

Supervisor:	Cristina Scielzo
Title:	**Reconstructing the tumor microenvironment in vitro: 3D Bioprinting for precision immunotherapy in B-cell malignancies**
Curriculum:	Basic and Applied Immunology and Oncology

Link to the personal page of the University or relevant hospital site website:	https://research.hsr.it/en/divisions/experimental-oncology/malignant-b-cells-biology-and-3d-modelling.html

Description of the Project (max 3,000 characters including spaces)

Background/gap of knowledge

Mature B-cell malignancies such as chronic lymphocytic leukemia (CLL) remain largely incurable despite major advances in targeted therapies and immunotherapy. Disease heterogeneity and the critical role of the tumor microenvironment (TME) limit the predictive value of current preclinical models. Conventional 2D cultures fail to reproduce tissue architecture and cell-cell interactions, while animal models lack reproducibility and human specificity. There is therefore a critical unmet need for reliable, patient-specific platforms to predict therapeutic responses, particularly to immunotherapies such as CAR T-cells.

Rationale and hypothesis

We hypothesize that advanced 3D bioprinted models recapitulating lymphoid tissue microenvironments (bone marrow, lymph node, spleen) can faithfully reproduce tumor–microenvironment interactions and enable accurate prediction of patient-specific responses to targeted therapies and CAR T-cells. These models are expected to overcome current limitations and establish a functional platform for precision medicine, particularly in CLL, where immunotherapies have thus far yielded limited efficacy.

Objectives and specific aims

The objective of this project is to develop advanced 3D bioprinted models that faithfully recapitulate lymphoid microenvironments using patient-derived cells, thereby enabling a more physiologically relevant platform to study CLL biology. Within these engineered tissue-like systems, we will functionally characterize tumor cell behavior, survival dynamics, and signaling pathways across distinct microenvironmental conditions. Furthermore, we will investigate how these contexts influence therapeutic responses by comparing the efficacy of targeted agents, including BTK, BCL2 inhibitors, in 3D models versus conventional 2D cultures. Finally, we will assess

the antitumor activity of patient-derived CAR T cells (in collaboration with Prof Marta Coscia ASST dei Sette Laghi), both as monotherapy and in combination with targeted treatments, to better understand how microenvironmental complexity shapes therapeutic outcomes and to identify strategies for improving efficacy.

Expected outcomes

This project will establish robust and reproducible 3D preclinical platforms capable of predicting therapeutic responses at the individual patient level. It will identify microenvironment-driven resistance mechanisms and optimize immunotherapy strategies, ultimately contributing to personalized treatment approaches in B-cell malignancies.

Skills that the student should acquire (max. 600 characters including spaces):

Advanced skills in 3D bioprinting, primary cell culture, flow cytometry, and immunophenotyping; experience in translational hematology research; data analysis including multi-omics; understanding of tumor microenvironment biology and precision medicine approaches.

References (max. 15)

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